

# INTERNATIONAL MULTIDISCIPLINARY SCHOOL - CONFERENCE IN MEDICAL AND HEALTHCARE SCIENCES

December 09-11, 2022 / Tbilisi, Georgia

## PROCEEDINGS BOOK

EDITOR:  
Assist. Prof. Dr. Sümeyye ALTIPARMAK

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# PROCEEDINGS BOOK

Science  
Georgia



## INTERNATIONAL MULTIDISCIPLINARY SCHOOL - CONFERENCE IN MEDICAL AND HEALTHCARE SCIENCES

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### Editor

Assist. Prof. Dr. Sümeyye ALTIPARMAK

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TR: +90 342 606 06 75

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# CONFERENCE ID

## TITLE OF CONFERENCE

INTERNATIONAL MULTIDISCIPLINARY SCHOOL - CONFERENCE IN  
MEDICAL AND HEALTHCARE SCIENCES

## PARTICIPATION

Keynote & Invited

## DATE - PLACE

Tbilisi State Medical University  
December 09-11, 2022 / Tbilisi, Georgia

## ORGANIZATION

Science Georgia  
&  
IKSAD-Institute of Economic Development and Social Researches

## CHAIRMAN OF THE ORGANIZING COMMITTEE

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*Director of Scientific Research-Skills Center of Tbilisi State Medical University,*

## CHAIRMAN OF THE SCIENTIFIC COMMITTEE

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*Associate Professor, Senior Specialist of Scientific Work Coordination, Master's  
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Visiting Fellow at Bournemouth University (UK)

**Bukhatem Mohamed Nadjib**

Phd. Université Saad Dahlab Blida (Algeria)

## PARTICIPATING COUNTRIES (11)

Georgia, Türkiye, Azerbaijan, Romania, Pakistan, Serbia, Morocco, Armenia, Iraq,  
India, Nigeria

## TOTAL PAPERS: 131

The number of papers from foreign countries: **111**

The number of papers from Türkiye: **20**

**PHOTO GALLERY**



















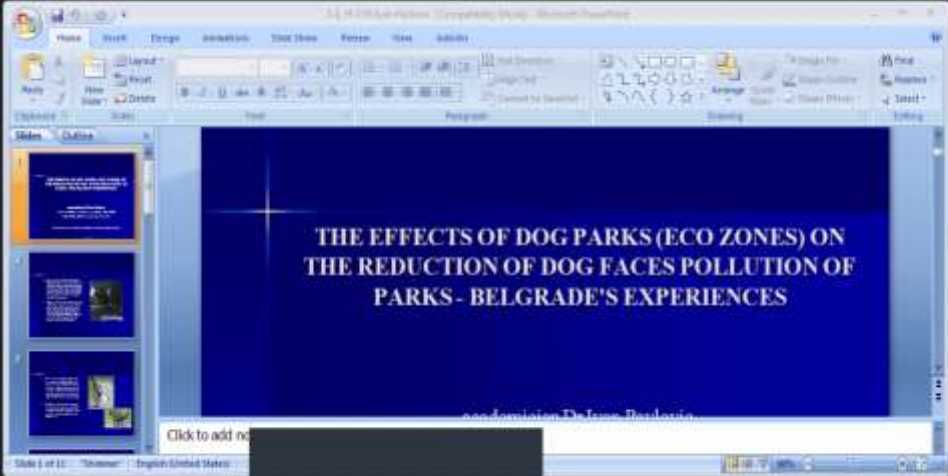








Kayıtlıdır... S-1, N-3 Dr. Ivan Pavlovic ekran görüntüsünü Seçenekler Görüntüle - Zaman: 09:40:34 Görünüm



THE EFFECTS OF DOG PARKS (ECO ZONES) ON THE REDUCTION OF DOG FACES POLLUTION OF PARKS - BELGRADE'S EXPERIENCES

Click to add notes

2 atanmış katılımcı

Ses Aç Videoyu Başlat Katılımcılar Sohbet Ekran Paylaşımı Kayıt Duraklat/Durdur Ara Ödeller Reaksiyonlar Uygulamalar Oturum Çık


Dr. Ivan Pavlovic

Hall-3 Observer

Hall-3 Observer

George Gurgu

Kayıtlıdır... Zaman: 09:49:39 Görünüm



Hall 6 - Observer

RASHIDHO PATTADHY

Hall 6 - Observer

Ses Aç Videoyu Başlat Katılımcılar Sohbet Ekran Paylaşımı Kayıt Duraklat/Durdur Ara Ödeller Reaksiyonlar Uygulamalar Oturum Çık

# **International School-Conference in Medical and Health Sciences**

**9-11/XII/2022**

## **Program**

**Tbilisi, Georgia**

# Section 1 – Advances in Basic Biomedical Sciences and Best Clinical Practice: "From Bench to Bedside"

Day 1 - 16:00-19:00

Moderators: Tamar Kandashvili, Nino Gogokhia, Devi Tabidze

## Reports:

- **Ashot Avagimyan, L. Kakturskiy**  
Trimetazidine as modifier of AC-mode of chemotherapy-driven hyperdyslipidemia
- **Maia Gotsadze, T. Khandashvili, N. Narsia, N. Momtselidze, M. Mantskava**  
Rheological properties during the atrial fibrillation
- **Ivane Kurtiashvili**  
Hyperuricemia as a new risk factor for cardiovascular diseases.
- **Natia Chkhaidze, M. Kherkheulidze**  
Hospital-acquired and ventilator-associated pneumonia in children
- **Robert Avalishvili, M. Gurgenidze, G. Asatiani**  
Role of Corticosteroid therapy in acute pancreatitis treatment and prevention of  
disease complications
- **Nino Nemsitsveridze, T. Chumburidze, N. Gorgaslidze, N. Nikuradze, M. Ghonghadze**  
Pharmaceutical care during the hepatoprotective drug selection
- **Tamar Korinteli, A. Bakuridze, N. Gorgaslidze**  
Formulation and characterization of ethosomal gel from papain
- **Ketevan Ghambashidze, M. Namoradze, N. Pkhaladze, M. Katsadze, M. Topuridze**  
Effects of Plaferon-LB and  $\alpha$ -tocopherol on paraneoplastic disorders of  
erythrocytes and microhemocirculation
- **Neli Nikuradze, N. Gorgaslidze, N. Nemsitsveridze, T. Zarqua, M. Baduashvili**  
Innovative pharmaceutical products in the Georgian pharmaceutical market
- **Tamar Sharashenidze, T. Sanikidze, M. Buleishvili**  
Impact of  $\beta$ -blockers on the immune status of patients with essential hypertension
- **Tamaz Chumburidze, I. Tomadze, N. Nemsitsveridze, T. Zarqua, E. Tsitsilashvili**  
Management of drug development life cycle of original anti-allergic "Dualler-G"
- **Ekaterine Labadze, M. Mantskava, N. Narsia, T. Kandashvili**  
Complex Analysis of Rheological, the Electro-physical Properties of Blood, and  
some Factors of Iron Metabolism in the Blood in Gastric Cancer

## Section 1 – Advances in Basic Biomedical Sciences and Best Clinical Practice: "From Bench to Bedside"

Moderators: Tamar Kandashvili, Lela Maskhulia, Nona Janikashvili, Eka Ekaladze

Day 2 - 11:00-13:30

- **Kakhaber Kviloria, G. Kochiashvili, D. Kochiashvili**  
Spontaneous perinephric subcapsular hematoma in a case of AIDS
- **Avtandil Bakradze**  
Factors causing occlusal anomalies: Contemporary approach
- **Vasil Potskhveria, V. Akhalkatsi, M. Matiashvili, L. Maskhulia**  
The significance of post-operative bracing in preventing  
Knee arthrofibrosis after ACL reconstruction
- **Davit Subeliani, L. Chikvatia**  
A comparative analysis of the surgical treatment of  
fractures of the proximal end of the humerus.
- **Irine Katsarava, N. Gamkrelidze, N. Pavliashvili, L. Kvatchadze**  
Restoration of voice through electrophonopathic laryngeal stimulation  
in patients with laryngeal paresis and paralysis
- **Nodar Sulashvili, N. Gorgaslidze, M. Giorgobiani**  
Assessment of safety features in pharmaceutical institutions in Georgia
- **Sopio Tsertsvadze, I. Chkhaidze**  
Prevalent multidrug resistant bacterial isolates from a paediatric clinic  
Are highly susceptible to bacteriophages
- **Nino Kuridze, L. Gabunia, K. Ghambashide, N. Chelidze, D. Delibashvili**  
The effect of steroid, silicone, siloxane and heparin-containing drugs  
on the development of postoperative scars
- **Magda Rurua, L. Ratiani, T. Sanikidze, K. Machavariani, E. Pachkoria**  
Peculiarities of severe respiratory distress syndrome caused by novel coronavirus  
(COVID 19) and other respiratory pathogens in patients with hyperferritinemia taking  
ACE inhibitors

## Section 2 – Contemporary Approaches and Challenges of Biomedical and Clinical Sciences

16:00-19:00

Moderators:, Nana Gorgaslidze, Irine Zarnadze, Marina Giorgobiani

### Reports:

- **Irine Zarnadze, Sh. Zarnadze , D. Kitovani, L. Lomtadze**  
Digital Health, Contemporary Challenges and Perspectives
- **Shafiga Topchiyeva, N. Gorgaslidze, N. Sulashvili**  
The features of exploring of management of pharmaceutical market from individual to society wellbeing in Georgia
- **Irakli Khabeishvili, T. Nozadze, L. Chikvatia, N. Avazashvili**  
Knee joint medial compartment osteoarthritis treatment with high tibial opening wedge osteotomy and arthroscopic chondroplasty
- **Ekaterine Zarkua, M.Mamaladze, L.Sanodze**  
The Composite Masses Adhesion Peculiarities on the Tooth Enamel-cement Connection (CEJ) Strip 1
- **Devi Tabidze, E. Mirvelasvhili, N. Khachapuridze, M. Kajrishvili**  
Medical tourism as a branded product in the European medical market
- **Miranda Jankhoteli, N. Tchanturia, M. Buleishvili, M. Todadze**  
Role of nurses in implementing innovative projects in primary healthcare sector
- **Valeri Akhalkatsi, L. Maskhulia, M. Matiashvili, N. Pavliashvili**  
Treatment of traumatic soft tissue injuries of the shoulder with the combination of interferential current and laser therapy
- **Devi Tabidze, M. Shakarashvili, M. Abuladze, L. Baramidze**  
The need to maintain a healthy way of life to ensure the physical and mental health of the population”
- **Edisher Kvesitadze, K. Museliani, T. Khobelia**  
Medical pre-clinical laboratory sciences
- **Ana Tughushi, N. Dugashvili, K.Kakabadze, N. Ghvedashvili, N. Kvizhinadze**  
Marketing Plan of Diflucan
- **Lily Petriashvili, T. Lominadze**  
Digital transformation and challenges in the supply chain

**Section 3**  
**Students' Case Reports Section**  
**16:00-19:00**

**Moderators: Maia Beridze, David Tskhomelidze , Davit Kelenjeridze**

- **Nino Kikvadze, Gigi Gorgadze**  
Case Report: Low-grade Endometrial Stromal Sarcoma
- **Syed Amaan Ali, Peter Samuel, Yusuf Hassoun**  
A Case of Cerulean Cataract
- **Rohit Parab, Laya Chadalawada, Shaina Machado**  
Acantholytic squamous cell carcinoma mimicking angiosarcoma in the oral cavity – A case report and a literature review
- **Sheeda Jabeen, Shifa Mohamed Rafi**  
A challenging case of PTEN hamartoma tumor syndrome in a juvenile male with congenital macrocephaly: case report
- **Rabea Salah Al-Tamary, Mohammed Fathi Farhan Alrawashdeh, Peter Samuel**  
Tacrolimus induced subconjunctival hemorrhage : case report
- **Nithesh Hariharan**  
Thrombotic microangiopathy due to solitary lymphoma of spleen
- **Roman Babaevi, Natia Shakaridze, Elene Gaprindashvili**  
A Case Report: central part cystadenoma of pancreas
- **Mariam Gigiadze, Mariam Beriashvili**  
A case report: median arcuate ligament syndrome
- **Mariam Kipshidze**  
A Case Report: COVID-19 vaccination on asthmatic individual
- **Mariam Beriashvili, Mariam Gigiadze**  
A case report: Graves' disease (diffuse toxic goiter)
- **Ana Bitskinashvili**  
Human Heart transplantation – New Challenges and Outcomes
- **Boris Bendeliani, Nino Kikvadze, Gigi Gorgadze**  
Multiple located independent malignant tumors – Malignant mixed mullerian tumor, Invasive ductal carcinoma with MTS in axillary lymph nodes and right lung - A Case Report
- **Vakhtang Mazanashvili, Mariam Kipshidze**  
A Case Report: Clarithromycin-nifedipine interaction as possible cause of vasodilatory shock
- **Temur Kopadze**  
Acute myocardial infarction and death in asystole after primary coronary angioplasty
- **Peter Samuel, Naser Izziddin Abdel Hadi Rawashdeh**  
Food protein-induced allergic proctocolitis in three month old infant: Case report
- **Giorgi Zhorzholiani, Gigi Gorgadze**  
Cushing's syndrome or common acute cardiologic patient? – a Case Report

## Section 4 – Students' Oral Presentations Section

Session 1- 11:00-13:30

Moderators: Marina Giorgobiani, Maia Okujava, Boris Bendeliani

- **Sopo Goglidze, M. Jincharadze**  
Correlation of periodontitis to cardiovascular diseases
- **Bhushan Jayade Shreyas**  
Diagnostic challenges encountered in differentiating high-grade prostatic adenocarcinoma and high-grade urothelial carcinoma – A literature review
- **Ani Gorgadze, M. Bokhua, G. Gorgadze**  
Depression rate in first-year medical students due to Zung Questionnaire
- **Ria Pillai, Syed Mukarram**  
Biomedical research opportunities and ethical challenges
- **Mariam Alavidze, E. Dolidze, M. Melikishvili**  
Impostor Syndrome and its correlation with depression and burnout among medical students in Georgia with regards to their future choice of specialty
- **Gigi Gorgadze**  
History of Ophthalmology in Georgia – Literature Research
- **Maduri Balasubramanian, Adithya Lal, Naga Harika Korrapati**  
Analyzing Neurological and Psychiatric disorders using Connectome
- **Veriko Gergauli**  
Recurrent aphthous stomatitis in children
- **Tinatin Bukhrashvili, N. Vardosanidze**  
Irrational use of antibiotics and antibiotic resistance in Georgia

**Lunch Break: 13:30-14:30**

## Section 4 – Students' Oral Presentations Section

Session 2 – 15:00-17:30

Moderators: Marina Giorgobiani, Maia Okujava, Mariam Gigiadze

- **Eldar Gasimov, Taryel Omerov, Rashad Abizade, Fuad Rzayev**  
Ultrastructural characteristics of structural elements of gastric mucosa in obesity
- **Aleksandre Asanidze**  
The impact of the Coronavirus (COVID-19) on the menstrual cycle and mental health of Georgian young women
- **Asraf nasim Muhammed, Latheef Shifna, Sherin Ziya**  
Clinical cases of borreliosis in Georgia
- **Anastasia Maskharashvili, T. Nebieridze, A. Akhvlediani**  
A Stem-cell therapy in a treatment of stroke – Literature Review
- **Elene Didbaridze**  
CRISPR –The Simplest Way of Gene Editing
- **Nutsa Karselishvili, L.Lavrelashvili**  
Oral contraceptive associated risks and prevention
- **Chodnekar Swarali**  
An experimental clinical therapy with a novel bacteriophage
- **Davit Mamatsashvili, David Kelenjeridze, Nikoloz Lobjanidze**  
FLUORESCENCE MICROSCOPY - A METHOD OF STUDYING CELLULAR PROCESSES AND ITS ROLE IN DIAGNOSING DISEASES
- **Ashok Sukhmani; G. Dugashvili**  
CRISPR-Cas9 and its application as a gene-editing strategy for  $\beta$ -hemoglobinopathies: A Literature Review
- **Sophiko Dvalishvili**  
Kidney injury in COVID-19 patients in First University Clinic of Tbilisi State Medical University
- **Nino Kochuashvili, N.Zhuzhniashvili**  
The Most Common Urological Diseases in females – a Brief Review
- **Alexis Tressa Babu, Asiya Fatima, Sreelakshmi Kathru**  
Clinical Manifestations and Etiology of Enteroviral Infections in Georgia: A Case Series and Review



## Section 5 – COVID-19, Post-Covid, Infectious Diseases, their Prevention and Management Issues

14:30-17:30

Moderators: Levan Ratiani, Malvina Javakhadze, Elza Vashakidze, Elene Pachkoria

- **Malvina Javakhadze, N.Iakobashvili**  
Respiratory viral infections in children in Georgia in the post-COVID period
- **Ana Shamanadze, T.kandashvili**  
Study of Gut microbiota in Hemodialysis Patients
- **Ana Maghradze, I. Chkhaidze, N. Kavlashvili**  
Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with  
COVID-19: A Case Series Experience in M.Iashvili children's central  
hospital, Georgia
- **Maia Beridze**  
Covid-19 and probable mechanisms of post SARS-CoV-2 neurological  
consequences
- **Paata Kervalishvili, N.Gordeladze**  
Investigations of Vibrational Properties of Pathogenic organisms by Computing  
Methods
- **Nino Gogokhia**  
Correlation of the results of the immunophenotypic and morphological  
analysis in diagnosing acute leukemias
- **Giorgi Mgeladze, Sh.Khetsuriani**  
Isolation of Inducible Clindamycin and Methicillin Resistant Staphylococcus  
aureus Strain in Patient with Community-Acquired Pneumonia: Case Report
- **Tamar Gudashvili**  
"Innovation and safety in one device! Wear Bioplasm and be protected from  
viruses and bacteria!"
- **Luiza Gabunia**  
Polypharmacy and associated risks/complications  
in the management of covid-19
- **Lela Tsakadze, I.Chkhaidze**  
Influenza seasonality in the different parts of the world
- **Natia Uzarashvili, T.Korakhashvili, M.Javakhadze**  
Clinical Cases of Intestinal Infections with Bloody Diarrhea
- **Irma Bubashvili, T. Levidze**  
A new era in tuberculosis treatment

# Students' Poster Reports Section

14:00-15:00

Moderator: Nodar Sulashvili

- **Divya Sunil Kumar, Ranasinghe Arachchige Dona Kashmiri Nawodi eerasekara, Naga Harika Korrapati** - Association between SARS-COV-2 and psoriasis
- **Debleena Chand** - CRISPR gene editing to uncover potential HIV therapy
- **Rushikesh Rajesh Patil** - Role of water-soluble vitamins in reducing the risk of cardiovascular heart disease in premature ovarian insufficiency patients.
- **Proma Ajoy Shil, Varsha Wadhe, Naga Harika Korrapati** - Advancement of skin grafting into 21<sup>st</sup> century
- **Anzor Kvirikashvili** - Importance of deep brain stimulation in treating Gilles de la Tourette syndrome and criteria used in selection of patients for the procedure
- **Tsisana Ugulava** - How oral contraceptives use can lead to liver cancer
- **Akaki Robakidze, E. Mirvelashvili** - The main trends in the organization of leukemia treatment measures in the children's contingent
- **Aleksandre machaidze, S. Malakmadze, L. Begadze** - Breastfeeding practice in Georgia, Nigeria, Brazil and the UK – meta analysis
- **Nia gogokhia** - Fluorescence spectrophotometry and its use in Modern Medicine
- **Elmir Aivazov** - Sacubitril/valsartan to treat heart failure
- **Elene Makaridze, M. Pruidze** – Mitochondrial diseases and modern approaches to their diagnostics and management.
- **Nini mikadze, N. kikvadze** - Transposition of the great arteries
- **Liana Jalagania, N. Kikvadze, G. Gorgadze** – Schizophrenia and modern approaches to its treatment
- **Keso Khachidze** - Approaches and challenges in the management of Addison's disease
- **Mariam Mikuchadze** - Maturation and circuit integration of transplanted human cortical organoids influencing animals' behavior
- **Nino Akhuashvili, E. Kurdgelashvili** - Covid 19 and Parkinson's disease: olfactory system impairments.
- **Lika Bedinashvili** - Impact of Diabetes on Chronic Renal Failure

International Multidisciplinary School -  
Conference in Medical and  
Healthcare Sciences

December 09-11, 2022 / Tbilisi, Georgia  
Tbilisi State Medical University

# CONFERENCE PROGRAM

## ONLINE PRESENTATIONS

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Meeting ID: 845 6570  
2704

Passcode: 091011

ZOOM LINK:

<https://us02web.zoom.us/j/84565702704?pwd=OU5HRHpaVjJsQ3dlcXhaNndhbXV1UT09>

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- To be able to make a meeting online, login via <https://zoom.us/join> site, enter ID instead of “Meeting ID or Personal Link Name” and solidify the session.
- The presentation will have 15 minutes (including questions and answers).
- The Zoom application is free and no need to create an account.
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- All congress participants can connect live and listen to all sessions.
- During the session, your camera should be turned on at least %70 of session period
- Moderator is responsible for the presentation and scientific discussion (question-answer) section of the session.

## **TECHNICAL INFORMATION**

- Make sure your computer has a microphone and is working.
- You should be able to use screen sharing feature in Zoom.
- Attendance certificates will be sent to you as pdf at the end of the congress.
- Moderator is responsible for the presentation and scientific discussion (question-answer) section of the session.

**Before you login to Zoom please indicate your name surname and hall number,  
exp. Hall-1, Shahla Tahirgizi**

## **PARTICIPANT COUNTRIES: (12)**

**Croatia, Türkiye, Azerbaijan, Romania, Pakistan, Serbia,  
Morocco, Russia, Armenia, Iraq, India, Nigeria**

**10.12.2022****Session-1 / Hall-1**Tblisi Time: 16<sup>00</sup>-18<sup>00</sup>Ankara Time: 15<sup>00</sup>-17<sup>00</sup>**HEAD OF SESSION: Assist. Prof. Prof. Dr. Sümeyye ALTIPARMAK**

TOPIC TITLE	AUTHORS	AFFILIATION
<b>IN-HOSPITAL TRANSPORT OF PEDIATRIC PATIENTS: SYSTEMATIC REVIEW</b>	Res. Asst. Dr. Selin DEMİRBAĞ	Manisa Celal Bayar University, Türkiye
<b>THE ROLE OF INFLAMMATORY INTERLEUKINS IN DIAGNOSIS OF NECROTIZING ENTEROCOLITIS</b>	Sevinj Nasirova	Scientific Research Institute of Pediatrics named after K.Y. Farajova, Baku, Azerbaijan
<b>VAGINAL ERBIUM-DOPED YTTRIUM ALUMINUM GARNET(Er-yag) LASER APPLICATIONS (VELA); A NEW APPROACH FOR LONG- TERM TREATMENT OF SEXUAL DYSFUNCTION IN BREAST CANCER DURING AND AFTER TREATMENT</b>	Asst. Prof. Dr. Seçil GÜNAY AVCI	Haliç University, Türkiye
<b>ADOLESCENT PREGNANCY AND MIDWIFERY APPROACHES</b>	Sümeyye ALTIPARMAK Ayşe Nur YILMAZ	Inonu University, Malatya, , Türkiye Firat University, Elazig, , Türkiye
<b>IDENTIFICATION OF INTEGRON GENE CASSETTES IN ANTIBIOTIC-RESISTANT ESCHERICHIA COLI STRAINS ISOLATED FROM DRINKING WATER</b>	Lect. Dr. Erva RAKICI Lect. Elif AYDIN Prof. Dr. Osman Birol ÖZGÜMÜŞ	Recep Tayyip Erdoğan University Kütahya University of Health Sciences

**10.12.2022****Session-1 / Hall-2****Tblisi Time: 16<sup>00</sup>-18<sup>00</sup>****Ankara Time: 15<sup>00</sup>-17<sup>00</sup>****HEAD OF SESSION: Assoc. Prof. Dr. Nilgün ULUTAŞDEMİR**

<b>TOPIC TITLE</b>	<b>AUTHORS</b>	<b>AFFILIATION</b>
<b>THE PERSPECTIVE OF NURSING STUDENTS ON SCHIZOPHRENIA: A QUALITATIVE STUDY</b>	Sevda UZUN Assoc. Prof. Dr. Nilgün ULUTAŞDEMİR	Gümüşhane University, Türkiye
<b>PSYCHIATRIC NURSING AND THERAPEUTIC RELATIONSHIP</b>	Sevda UZUN Assoc. Prof. Dr. Nilgün ULUTAŞDEMİR	Gümüşhane University, Türkiye
<b>CRYPTOCURRENCIES AS ONE DIMENSION OF ADDICTION AMONG YOUNG PEOPLE</b>	Selma KAHRAMAN Suzan HAVLIOĞLU	Harran University, Türkiye
<b>THE EFFECT OF HELPER SKIN TAP TECHNIQUE ON PAIN ASSOCIATED WITH INTRAMUSCULAR INJECTION IN ADULTS: LITERATURE REVIEW</b>	Res. Asst. Dr. Sevgi PAKIŞ ÇETİN Asst. Prof. Dr. Ebru BAYSAL	Manisa Celal Bayar University, Türkiye
<b>CHALLENGES FACED BY NURSES WORKING IN ISTANBUL PALLIATIVE CARE CENTERS</b>	Sibel ÖZDEMİR ÖZMEN Asst. Prof. Dr. Alev YILDIRIM KESKİN	Tev Ezel Gülen Kiray Vocational and Technical Anatolian High School, Healthcare Area, Türkiye Selcuk University, Türkiye
<b>CLINICAL SYMPTOMS AND CARE BEHAVIORS USED BY NURSES TO IDENTIFY CHANGES IN THE CONDITIONS OF THEIR PATIENTS</b>	Lect. Dr. Halil İbrahim TUNA Res. Asst. Dr. Pınar TUNÇ TUNA	Selcuk University, Türkiye
<b>DETERMINATION OF NURSES' PERCEPTIONS OF PATIENT SAFETY CULTURE AND ATTITUDES TO MEDICAL ERRORS</b>	Sümeyye YOZGAT Asst. Prof. Dr. Alev YILDIRIM KESKİN	Sultanbeyli State Hospital, Istanbul, Turkey Selcuk University, Türkiye
<b>NURSING CARE AND HUMOR</b>	Süreyya BULUT	Aydın Adnan Menderes University
<b>REASONS TO PREFER THE ALTERNATIVE MEDICINE: THE CASE OF SANLIURFA</b>	Asst. Prof. Dr. Suzan HAVLIOĞLU Asst. Prof. Dr. Hüseyin ERİŞ Prof. Dr. Şevket ÖKTEN	Harran University, Türkiye
<b>TURKISH VALIDITY AND RELIABILITY STUDY OF FAMILY MANAGEMENT SCALE FOR CHILDREN WITH ASTHMA</b>	Tubanur ÖZMEN Türkan KADİROĞLU	Ağrı İbrahim Çeçen University, Türkiye Atatürk University, Türkiye

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<b>TOPIC TITLE</b>	<b>AUTHORS</b>	<b>AFFILIATION</b>
<b>THE IMPACT OF GUT MICROBIOTA ON PSORIASIS AND PATHOGENESIS</b>	Major Gheorghe GIURGIU Prof. Dr. Manole COJOCARU	Deniplant-Aide Sante Medical Center, Biomedicine, Bucharest, Romania Titu Maiorescu University, Romania
<b>EXPOSURE OF HEALTHCARE PROFESSIONALS TO VIOLENCE DURING THE COVID-19 PANDEMIC PROCESS: THE CASE OF SANLIURFA</b>	Assist. Prof. Dr. Hüseyin ERİŞ Assoc. Prof. Dr. Hasan BÜYÜKASLAN Lect. Feray BUCAK Dr. Aslı KAYA	Harran Üniversitesi Sağlık Hizmetleri MYO
<b>THE EFFECTS OF DOG PARKS (ECO ZONES) ON THE REDUCTION OF DOG FACES POLLUTION OF PARKS - BELGRADE'S EXPERIENCES</b>	Ivan Pavlovic	Scientific Institute of Veterinary of Serbia, Serbia
<b>ANTIBIOTIC UTILIZATION STUDY IN TERTIARY CARE HOSPITALS IN KARACHI PAKISTAN: AN ESTIMATE OF RATIONAL PRESCRIBING AND OUTCOME</b>	Prof. Dr.Huma Ali, Dr. Anum Tariq, Yousra Shafiq	Jinnah Sindh Medical University Karachi Pakistan
<b>ACUTE AND SUBACUTE TOXICITY ASSESSMENT MODEL OF FERULA GROWING IN NORTHERN MOROCCO</b>	NOUIOURA Ghizlane, TOURABI Maryem, LYOUSSI Badiaa, DERWICH El houssine	Laboratoire des Substances Naturelles, Pharmacologie, Environnement, Modélisation, Santé & Qualité de Vie (SNAMOPEQ). Faculté des Sciences Dhar Mahraz, Université sidi Mohammed ben Abdellah, Fès, Maroc.

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<b>TOPIC TITLE</b>	<b>AUTHORS</b>	<b>AFFILIATION</b>
<b>EFFECT OF PRIME SOLUTIONS USED DURING CARDIOPULMONARY BYPASS ON OXIDATIVE STRESS</b>	<b>Bişar AMAÇ</b>	<b>University of Health Sciences, Sanliurfa, Türkiye</b>
<b>EFFICACY OF USING POSTOPERATIVE PHOTOGRAPH AND LEG LENGTH RADIOGRAPHY ON SATISFACTION AND QUALITY OF LIFE SCORES IN PATIENTS UNDERGOING OPEN WEDGE HIGH TIBIAL OSTEOTOMY</b>	<b>Dr. Cem YILDIRIM</b>	<b>SBÜ Başakşehir Çam and Sakura City Hospital, Türkiye</b>
<b>PROTECTIVE EFFECT OF THE NARINGENIN ON OXIDATIVE DAMAGE IN THE KIDNEY IN RATS WHICH APPLIED TO CHRONIC MERCURY CHLORIDE</b>	<b>Merve KAHRAMANOĞULLARI Prof. Dr. Mine ERIŞİR Prof. Dr. Mine YAMAN</b>	<b>Firat University, Türkiye</b>
<b>STEREOLOGICAL VOLUME ANALYSIS IN EXPERIMENTAL STUDIES: CAVALIERI METHOD</b>	<b>Asst. Prof. Dr. Ömür Gülsüm DENİZ</b>	<b>Bolu Abant İzzet Baysal University, Türkiye</b>
<b>THE ROLE OF PRE-THERAPY THYROGLOBULIN LEVEL IN PREDICTING COMPLETE RESPONSE TO TREATMENT IN PATIENTS WITH DIFFERENTIAL THYROID CANCER REQUESTING RADIOACTIVE IODINE THERAPY</b>	<b>Dr. Ferat KEPENEK</b>	<b>University of health sciences, Diyarbakır, Türkiye</b>
<b>DETERMINATION OF BARRIERS TO HEALTHY NUTRITION AND LEVELS OF SELF-MANAGEMENT IN TYPE 2 DIABETES PATIENTS</b>	<b>Assoc. Prof. Serap GÖKÇE ESKİN Assoc. Prof. Nükhet BALLIEL Uzm. Hem. Fatma KURT</b>	<b>Aydın Adnan Menderes University, Faculty of Health Science, Nutrition and Dietetic Department, Aydın, Türkiye</b>
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<b>SAFE MOTHERHOOD AND MIDWIFERY PRACTICES</b>	<b>Ayşe Nur YILMAZ Sümeyye ALTIPARMAK</b>	<b>Firat University, Elazig, Türkiye Inonu University, Malatya, Türkiye</b>



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HEAD OF SESSION: Asst. Prof. Dr. Taha YILMAZ

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PREVALENCE OF MICROSPORUM CANIS FROM STRAY KITTENS AND PET CATS IN GANJA, AZERBAIJAN	Narmin Alasgarova Asaf M. Omarov	Azerbaijan State Agrarian University, Azerbaijan
COMPETITIVE STUDY OF THE DIFFERENT VACCINE EFFECTIVENESS OF COVID-19 INFECTION	Hasanzade Dinara Suada Najafova Elvin Allahverdiyev Asaf M. Omarov	Azerbaijan State Agricultural University, Ganja, Azerbaijan
THE USE OF ENDONASAL DEXAMETHASONE ELECTROPHORESIS IN THE COMPLEX TREATMENT OF POSTERIOR UVEITIS	Rakhshanda Mirzazade	National Center of Ophthalmology named after acad. Z.Aliyeva, Baku, Azerbaijan
AN EVALUATION OF THE STUDIES DONE IN TURKEY ON THE RELATIONSHIP BETWEEN RELIGIOSITY AND MENTAL AND PHYSICAL HEALTH	Asst. Prof. Dr. Mehmet Emin KALGI	Ardahan University, Türkiye

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<b>DIABEFIT FITOCOLLECTION AS A MODIFIER OF FRUCTOSE-INDUCED ENDOTHELIAL DYSFUNCTION</b>	Lilit M. Sukiasyan	YSMU after M. Heratsi, Yerevan, Armenia. L.A. Orbeli Institute of Physiology NAS RA, Yerevan, Armenia
<b>COMPARATIVE STUDY OF MICROBIAL ETIOLOGY AND ANTIBIOGRAMS OF URINARY TRACT INFECTION AND GENITAL TRACT AMONG WOMEN IN SHEKHAN DISTRICT, IRAQ</b>	Asst. Prof. Dr. Najim A. Yassin	Duhok University, Iraq
<b>HEALTHY LOCAL GOVERNANCE: PRACTICE ON SUSTAINABLE DEVELOPMENT IN KERALA'S HEALTH SECTOR</b>	Ramshad KHAN R	University College, Thiruvananthapuram, India
<b>THE PREVALENCE OF TUBERCULOSIS IN GENERAL HOSPITAL MINNA, NIGER STATE, NIGERIA</b>	Fatima Mohammed Chado Kamaludeen Hussaini Stephen Olamide Ajibi	Department of Public Health, Newgate University Minna, Nigeria

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**EFFECTS OF PLAFERON-LB AND A-TOCOPHEROL ON PARANEOPLASTIC DISORDERS OF ERYTHROCYTES AND MICROHEMOCIRCULATION.**

***Ketevan Ghambashidze***

*Associate Professor of Pathophysiology Department, Tbilisi State Medical University (TSMU), Georgia*

*ORCID ID: 0000-0002-3845-9306*

***Manana Namoradze***

*Associate Professor of Pathophysiology Department, TSMU*

***Neli Pkhaladze<sup>3</sup>***

*Assistant Professor of Pathophysiology Department, TSMU*

***Maia Katsadze<sup>4</sup>,***

*Assistant Professor of Pathophysiology Department, TSMU*

***Maka Topuridze<sup>5</sup>***

*Associate Professor of Pathophysiology Department, TSMU*

**ABSTRACT**

Cancer growth is accompanied by various paraneoplastic processes that support disease progression and very often are the major cause of death in cancer patients. Detection of paraneoplastic disorders of erythrocytes and microcirculation is of great diagnostic value, since they are very vulnerable, immediately reflecting any pathological deviations occurring in the organism.

**Aim:** study deformability of erythrocytes (ED) and intensity of local hemocirculation (LH) in mice with Ehrlich carcinoma after treatment with antioxidants and membrane stabilizing drugs.

**Results:** Malignant growth decrease ED and LH significantly, especially at late stages of cancer growth.  $\alpha$ -tocopherol (1,2 ml/100g a day, IM injections during 3 weeks) on the 7<sup>th</sup> day of cancer growth improved LH by 37.1% ( $p<0,05$ ), on the 14<sup>th</sup> day - by 47,9% ( $p<0,001$ ) and on the 21<sup>st</sup> day - by 31% ( $p<0,01$ ) compared to control. On the 7<sup>th</sup> day of cancer growth ED was improved by 25,0% ( $p<0,001$ ). On the 14<sup>th</sup> and 21<sup>st</sup> days, increase in ED by 14,3% ( $p>0,02$ ) and by 8,1% ( $P>0,02$ ) compared to control was not statistically significant. Plaferon-LB (2 ml/100g a day, IP injections during 3 weeks) on the 7<sup>th</sup> day of cancer growth improved LH by 27,9% ( $p<0,01$ ), on the 14<sup>th</sup> day by 23,0% ( $p<0,001$ ) and on the 21<sup>st</sup> day have shown only increase tendency by 12,9%, ( $p>0,05$ ). ED was improved on the 7<sup>th</sup> day of cancer growth by 16,5% ( $p<0,01$ ). Later, on the 14<sup>th</sup> and 21<sup>st</sup> days ED improvement by 12,7% and 10,9% ( $p>0,05$ ) were not statistically reliable.

**Conclusion:** Cancer growth decrease ED and LH significantly.  $\alpha$ -tocopherol and Plaferon-LB improve ED and LH indicating the leading role of lipid peroxidation in pathogenesis of paraneoplastic disorders of erythrocytes and LH. Treatment effects are better expressed at early stages of cancer growth using optimal doses of preparations.

**Key words:** cancer, erythrocytes, local hemocirculation,  $\alpha$ -tocopherol, plaferon-LB

**Introduction**

It is generally recognized that cancer growth is accompanied by paraneoplastic processes. Investigation of disorders of "intact" organs (organs that are not directly affected or involved in the malignant process) is of great diagnostic value because, in most cases, they are the first messengers of the disease and are manifested long before the malignant process reveals itself. They aggravate course of the disease and

often play the leading role in lethal outcomes of cancer patients (Ferri, 2022; Dalmau, 2022; Santacroce, 2021).

Among paraneoplastic disorders of nervous system, endocrine system, blood, kidneys, etc., paraneoplastic disorders of erythrocytes and local hemocirculation could be distinguished, since the mentioned structures are one of the major determinants of tissue perfusion, they are very vulnerable, fragile, immediately reflecting any deviations developed in organism. Early diagnostics and correction of paraneoplastic disorders along with surgical interventions, radio- and chemotherapy supposedly will increase the treatment efficiency of cancer patients.

We were aimed to study deformability of erythrocytes (ED) and intensity of local hemocirculation (LH) at malignant tumor growth in experimental animals and effects of antioxidants and membrane stabilizing drugs on paraneoplastic disorders of ED and LH.

### **Material and methods**

Experiments have been carried out on 40 albino male lab. mice with body mass 25-30 g. All animals were fed standard laboratory chow and given free access to water. The care and use of the animals complied with the Georgian regulations on protection of animals, with Guidelines prepared by the Ethics Committee of the Institutional Animal Care and with the National Institutes of Health Guide for the Care and Use of Laboratory animals.

For creation of cancer model experimental animals were subjected to subcutaneous inoculations with Ehrlich carcinoma cells ( $2 \times 10^6$  tumor cells).

Lab mice randomly were divided into 4 major groups: the group I (10 healthy mice), the group II (control, 10 untreated mice), the group III (10 mice, treated with  $\alpha$ -tocopherol, 1,2 ml/100g a day, intramuscular injections (IM), beginning from the next day after cancer implantation, during 3 weeks) and the group IV (10 mice, treated with plaferon-LB, 2 ml/100g a day, intra-peritoneal injections (IP), during 3 weeks after cancer implantation).

The LH was studied using the method of polarography ( $H^+$  clearance). The blood flow was defined by the formula  $f = 100 \times K \cdot 0,693/T_{1/2}$  ml/min/100g; where  $T_{1/2}$  - is the biological half live of  $H^+$  in tissue (defined by semi-algorithmic scale); K - is the partial coefficient of gas distribution in tissue. For reliable electrical contact, indifferent chlorine-silver electrode with 10 cm<sup>2</sup> was placed in high density KCl solution. In the same solution was placed the experimental mouse-tail. Recording of LH in skeletal muscle was performed by insertion of platinum electrode with active surface 0,15 - 0,3 mm<sup>2</sup> in biceps femoris at 1-2 mm depth. Active and indifferent electrodes were connected to polarographic scheme and polarogram owing to millivoltmeter (pH-450). Data were registered on the paper of potentiometer KCP-4.

The ED was defined with filtration-computed photometry method (Khuluzaury, 1990), which completely excludes subjectivity in measuring of the time of erythrocytes spread and passage through the filter paper (Filtrac-388). 1 ml blood was centrifuged during 5 minute (3000 rpm). 0,02 ml from the received suspension was instilled on the filter. The ED is inversely proportional to the time needed for passage of cells through the filter. The time of erythrocytes passage was registered and processed by computer.

Obtained data were analyzed statistically with the use of SPSS 16.0 for Windows. Differences between tumor control and treated animals were determined by using the Student's t-test. The criterion for significance was set to  $p < 0.05$ .

### **Results**

The results of investigation have shown that during malignant tumor growth the LH in experimental animals was decreased significantly and progressively compared to norm. On the 7<sup>th</sup> day of malignant growth the LH was decreased by 36,7%, on the 14<sup>th</sup> day - by 42,7% and on the 21<sup>st</sup> day - by 57,1% ( $p < 0,001$ ).

In treated with  $\alpha$ -tocopherol animals on the 7<sup>th</sup> day of cancer growth the LH was improved by 37,1% ( $p < 0,05$ ) and on the 14<sup>th</sup> day - by 47,9% compared to control ( $p < 0,001$ ). On the 21<sup>st</sup> day of malignant

growth the LH was decreased compared to data of 14<sup>th</sup> days of treated lab mice by 13% ( $p < 0,02$ ), but the LH was still increased by 31,0% ( $p < 0,01$ ) compared to control. This progressive decrease in LH could be explained by the negative effect of  $\alpha$ -tocopherol long-term use.

After treatment with plaferon-LB on the 7<sup>th</sup> day of the cancer growth the LH was improved by 27,9% ( $p < 0,05$ ). On the 14<sup>th</sup> day LH was increased by 23,0% and on the 21<sup>st</sup> day - by 12,9%, but it was not statistically significant ( $p > 0,05$ ). Thus, it could be said that plaferon-LB has the better treatment effect when it is started at the early stage of cancer growth.

Investigation of ED revealed that during cancer growth the time of erythrocytes' passage through the filter is increased, directly indicating decreased deformability of erythrocytes. On the 7<sup>th</sup> day of Ehrlich carcinoma growth the ED was decreased significantly by 36,9% ( $p < 0,001$ ), on the 14<sup>th</sup> day by 39,7% ( $p < 0,05$ ) and on the 21<sup>st</sup> day - by 47,7% ( $p < 0,001$ ).

In treated with  $\alpha$ -tocopherol lab. mice on the 7<sup>th</sup> day of cancer growth ED was improved by 25,0% ( $p < 0,001$ ). On the 14<sup>th</sup> day of cancer growth the increase in ED by 14,3% ( $p > 0,02$ ) and on the 21<sup>st</sup> day – by 8,1% ( $p > 0,02$ ), compared to control, was not statistically significant.

After treatment with plaferon-LB ED was improved also only on the 7<sup>th</sup> day of the cancer growth by 16,5% ( $p < 0,01$ ). Later, on the 14<sup>th</sup> and 21<sup>st</sup> days the ED improvement by 12,7% and by 10,9% were not statistically reliable.

### **Discussion**

As the results of investigation have shown in the process of experimental malignant tumor growth ED decreases significantly that could be explained by decreased antioxidant protection of organism which in turn supports activation of lipid peroxidation leading to the disorders of membrane structures (Mattioli, 2021; Kasapovi, Peji, Stojiljković, 2010). Activation of peroxidative processes and its effect on biomembranes in case of malignant growth was detected in our previous experimental studies (Gambashidze, Kipiani 2000).

Disorders of LH expressed during experimental malignant growth could be explained by the reduced ED. Decrease in linear speed of blood flow and reduced ED supports aggregation of RBCs which in turn leads to progression of disorders of microhemocirculation.

The results of investigations have shown that administration of  $\alpha$ -tocopherol positively effects on ED, however long-term use of  $\alpha$ -tocopherol reveals opposite reaction and ED worsens. There are suggestions that  $\alpha$ -tocopherol injections are positively tolerated in experimental mice during 10 to 12 days, and long-term use has negative effect, because  $\alpha$ -tocopherol serves as a substance for oxidation and exaggerates the process of lipid peroxidation (Chiabrando, Rivalta, 2002; Spirievich, Matusis, Bronshtein, 1979). In lab mice treated with  $\alpha$ -tocopherol the LH was improved in all cases that is probably the result of improved ED however, plaferon-LB revealed the less treatment effect.

### **Conclusion**

Could be concluded that in case of experimental malignant tumor growth ED and LH decrease significantly. Treatment with antioxidants and membrane-stabilizing drugs ( $\alpha$ -tocopherol and plaferon-LB) improve ED and LH that indicates the leading role of lipid peroxidation in pathogenesis of paraneoplastic disorders of erythrocytes and LH. Treatment effects are better expressed at early stages of cancer growth and with the use of optimal doses of preparations

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**STEM-CELL THERAPY IN THE TREATMENT OF STROKE – LITERATURE REVIEW**

*Maskharashvili Anastasia, Nebieridze Tamazi, Akhvlediani Ana*

*Tbilisi State Medical University, Tbilisi, Georgia*

**ABSTRACT**

Stroke is still the largest cause of long-term disability worldwide, despite the fact that early therapies to repair damage caused by reperfusion, such as intravenous thrombolysis and endovascular revascularization, have shown significant benefits in patients [8].

As the brain stores little or no energy on its own, disruption of the energy supply, even for a short duration, may lead to irreversible damage. An injured brain might theoretically be separated into two different damaged regions: the ischemic core and the penumbra. Because blood flow in the ischemic core is lower than the threshold required for cell survival, its cells are irreversibly damaged and die due to necrosis, for which there is no rescue. Blood flow in the penumbra, which is the region around the ischemic core, is too low to maintain neurological functions, but provides the minimal energy required for preventing cells from immediate death and has the potential to be recovered if perfusion is increased quickly. Therefore, current treatment strategies for stem cell transplantation involve rescuing the penumbra before it dies, or regaining a new neuronal network via cell transplantation. Recent studies have demonstrated that stem cell therapy is a promising method for improving the functional outcomes of ischemic stroke. Stem-cell therapy is attracting much attention as a new potential treatment for certain neurological disorders, including stroke due to its unique properties that include easy isolation, multipotent differentiation potential and strong paracrine capacity [5] [6].

**Potential Mechanisms of Stem-Cell Therapy**

During the various phases of an ischemic stroke, transplanted stem cells are known to have a variety of neuro- and vascular-protective effects. In addition to reorganizing the neural network, the transplanted cells also decrease local and systemic inflammatory levels; increase synaptic sprouting and axonal regeneration, and reduce glial scars. These mechanisms can be divided into 3 categories: 1) cell differentiation (cell replacement); 2) secretion of paracrine factors (Bystander effect); 3) mitochondrial transfer.

**Cell differentiation-** Mesenchymal stem cells (MSCs) are pluripotent adult mesenchymal cells that have the ability of self-renewal and differentiation into the same cell type as the tissue or organ, including neuronal cells, and effect repair. In order to restore lost functions, transplanted stem cells can be differentiated into neuronal or vascular cells, or they can be directly settled and grown into neural progenitor cells. Stem cells can migrate to the damaged area. Intracerebrally injected stem cells express the CXCR4 receptor, which can bind to the chemoattractant: stromal cell-derived factor-1 (SDF-1). SDF-1 is expressed from the damaged brain and the stem cell uses this CXCR4/SDF-1 connection to migrate to the damaged regions of the brain [5] [6].

**Secretion of paracrine factors-** An important aspect of stem cells' functional multipotency is their ability to release paracrine factors, including cytokines, chemokines, basic fibroblast growth factor, vascular endothelial growth factor and exosomes. Immune regulation is one of the paracrine functions. Stem cells produce soluble molecules that are involved in immune regulation and can modulate the damaging inflammatory response. These factors, which are released into the environment by direct permeation or extracellular vesicles (EV), directly reduce ischemic damage and local and systemic inflammation. EVs are membrane structures of the lipid bilayer, which are attracting attention due to their low immunogenicity and high blood-brain barrier (BBB) permeability, which reduces damage and facilitates recovery. According to recent studies, EVs can reduce ischemic damage by upregulating angiogenesis, neurogenesis, and autophagy. In addition to promoting anti-inflammatory and immunomodulatory effects, these factors induce anti-apoptotic effects and mobilize inactive endogenous stem cells (NSC)/neural progenitor cells for neuroregeneration, especially those located around the subventricular zone (SVZ). Another manifestation of paracrine effect is the promotion of



angiogenesis. Endothelial cell proliferation and migration are induced by basic fibroblast growth factor and vascular endothelial growth factor in order to create new vascular branches from existing vascular branches. For example, it has been demonstrated in stroke lesions, that human bone marrow mesenchymal stem cells (BM-MSCs) enhance cerebral vascular formation by secreting endogenous angiogenic factors that improve the stability of new blood vessels [5] [6].

**Mitochondrial Transfer**-Mitochondrial transfer is an innovative mechanism for stem cell therapy that has attracted wide attention. In affected cells, mitochondrial dysfunction is caused by oxidative stress during ischemia/reperfusion. Mesenchymal stem cells (MSC) can transfer mitochondria to injured cells to restore cell aerobic respiration and mitochondrial function, in order to rescue damaged cells. There is increasing evidence that tunneled nanotubes and microvesicles play a major role in mediating mitochondrial transfer between MSCs and injured cells. The researchers marked MSCs and observed the transfer of mitochondria and a protective impact on the impaired cerebral microvascular system. As a result, mitochondrial transfer from MSCs to injured cells may offer a new therapy option for stroke [6].

Various types of cells, including bone marrow mononuclear cells, bone marrow mesenchymal stem cells, umbilical cord blood cells, and neural stem cells have been investigated. The kind of stem cell and method of administration have a significant impact on the mechanism by which stem cell therapies mediate their therapeutic effect [2].

#### **Bone marrow mononuclear cells (MNCs)**

MNCs can be collected autologously right before injection, which may be advantageous in acute clinical care settings compared to alternative cell sources for stem cells like bone marrow mesenchymal stem cells (BMSCs) and pluripotent stem cells (iPSCs), which require a period of cell culture before transplantation. Several mechanisms of action are involved in the use of MNCs in stroke treatment, such as the modulation of local and systemic inflammation, stimulation of angiogenesis and endogenous neurogenesis and differentiation into cell types that facilitate cellular repair processes. MNCs increase vascular density and blood flow. Initial studies suggested that the main mechanism contributing to recovery was the differentiation into endothelial cells (ECs). MNC subpopulations that differentiate into smooth muscle cells (SMCs) and endothelial cells (ECs), such CD34+/M-cadherin+ cells, can encourage angiogenesis and arteriogenesis in ischemic hindlimbs of rodents. MNC treatment increased cerebral blood flow (CBF) in a mouse model of bilateral common carotid artery stenosis by upregulating Ser1177 phosphorylation and elevating endothelial nitric oxide synthase levels beginning in the early phase after stroke and restoring endogenous responses, such as angiogenesis, in the later phase. In stroke patients with severe ischemia, intravenous infusion of autologous MNCs is a safe and effective treatment that improved functional recovery and increased CBF and metabolism. On the other hand, a multicenter, randomized clinical investigation showed that an intravenous infusion of autologous MNCs was safe at a median of 18.5 days after the beginning of a stroke but did not show any positive therapeutic effects. These clinical findings show that early MNC transplantation right after the onset of a stroke may be more effective in encouraging recovery [8].

#### **Bone Marrow Mesenchymal Stem Cells (BMSC)**

BMSCs have self-renewal potential. They are easily cultured in vitro and have been considered to be ideal seed cells in the treatment of ischemic stroke. They are the most extensively investigated cells because of their potent immunosuppressive effects by producing a various paracrine factors, safety or lack of ethical issues, easy to obtain, lack of immunogenicity, and ability to differentiate into tissue-specific cell line [7].

In vivo studies showed that after intracerebral transplantation in rat stroke models, BMSCs could migrate to the site of ischemic brain damage and convert into neural cells, which was associated with neurological recovery. Additional in vivo studies explored the migratory capabilities of BMSCs and showed that BMSC injected intravenously (IV) and intraarterially (IA) could also migrate to the brain. Even though BMSC were firstly investigated for their ability to generate new neurons, later research has mostly demonstrated that they do not provide therapeutic advantages through neuronal replacement. Instead, it has been discovered that BMSC produce substances that support neurogenesis and reduce inflammation through the secretion of anti-inflammatory factors or by decreasing interleukin 1 beta (IL-

1 $\beta$ ), interleukin 6 (IL-6), and tumor necrosis factor alpha (TNF- $\alpha$ ) levels. In mouse models of stroke, BMSC travel to ischemic areas where they increase the synthesis of neurotrophins and growth factors linked to neurorestoration [2] [8].

Clinical studies for BMSC therapies that are administered through IV or IA are more common than those for intracerebral transplantation, which is likely a reflection of their safety and less rigorous technical requirements. Three published phase I clinical trials have investigated the safety of BMSC therapy using IA. According to one study, two out of every ten patients experienced isolated partial seizures at the three-month follow-up and were treated with antiepileptic drugs. The other two studies did not report any major adverse events. A phase II study found similar results, demonstrating the safety of IA administration of BMSC. Although IA or IV injection of BMSC improved animal stroke models, similar effects in human patients have not yet been shown. The differences between animal models and patient outcomes may be due to variability in timing of BMSC administration. Pre-clinical studies which demonstrated improved neurological outcomes with BMSC treatment often administered IA or IV within three days of stroke. Neurological improvement did not happen when therapy was initiated more than seven days after the onset of the ischemic stroke in rats, according to a time-course investigation of BMSC administration [2].

Additional routes for BMSC transplantation have been examined. They have been transplanted directly into the brain. Despite having a limited sample size (n = 5), patients tolerated dosages of BMSC up to 55 million cells without experiencing any serious side effects, and they showed improved neurological results. Another route studied for administering BMSC is intrathecal transplantation. In a phase I trial, BMSC was injected intrathecally into the L4-L5 lumbar space in 24 chronic stroke patients (diagnosed between 4 and 144 months before). Without any adverse effects being noted, there were ambulation, hand control, and balance improved in several patients. While the outcomes of studies using IA and IV injection of BMSC show that there could be a limited time window for therapeutic advantages, intracerebral and intrathecal transplantations seem to have a wider window for clinically useful effects [2].

### **Umbilical Cord Blood Stem Cells (UCBSC)**

Human umbilical cord blood (hUCB) contain mesenchymal stem cells (MSC) and has been shown to exhibit strong immunomodulatory factors. After the induction of ischemic stroke in rats, intravenously given hUCB moved preferentially to the site of ischemic injury and therapy with hUCB was linked to a reduced lesion volume. In ischemic rat models treated with hUCB, neuronal-like human cells were present, but they were few in number, that shows that hUCB likely mediated therapeutic benefits are caused by trophic factors and cytokines rather than by cell replacement. After a stroke, inflammatory macrophage migration to the brain is increased. Elevated levels of T cells, NK cells, and neutrophils are also observed in the brain following ischemic injury. Although the initial immune reaction is considered to have a good impact on the healing process, the prolonged inflammatory state induced by a stroke is associated with worse results. In rats with ischemic stroke, treatment with UCBSC led to a reduction in the number of inflammatory macrophages, microglia, T-cells, NK cells, and neutrophils in the brain. That was associated with improved neurological function in rats. By reducing post-stroke inflammation, UCBSC may decrease the intensity of the initial damage and promote recovery [2].

### **Neural Stem Cells(NSC)**

Neurons and glial cells are derived from common immature NSCs, which are defined as self-renewing and multipotent cells that can differentiate into neurons, astrocytes, and oligodendrocytes. NSCs have been found to exist not only in the developing but in adult mammalian brains, mainly in the subventricular zone (SVZ) of the lateral ventricle and the subgranular zone (SGZ) of the hippocampus. Several research have investigated the use of NSC transplantation to treat ischemic brain damage in animal models. Analysis of graft-derived neuronal cells using immuno-electron microscopy and electrophysiological recording demonstrated increased connectivity in the neural network. Transplanted NSCs could develop into functioning neurons to improve recovery from stroke and brain injury in rats. Also, they prevent neuronal apoptosis, exert immunomodulatory effects, increase endogenous neuronal regeneration and angiogenesis, and inhibit glial scar formation mainly via the paracrine and autocrine secretion of various neurotrophic factors. These cells continue to function in the host brain and show

neuroprotective properties by growing, producing neurotransmitters, and creating functional synapses. The intracerebral transplantation of up to 20 million neural stem cells was acceptable and had no negative consequences and patients showed improvements in NIH Stroke Score, the summed arm and leg Ashworth scale, and Barthel Index scores. That proves, that neurological recovery was increased. While embryonic tissue has been the main source of hNPC, attempts are also being performed to produce hNPC using induced pluripotent stem cells. It has been demonstrated that induced human neural progenitor cells (ihNPC) generate functioning neurons and increase recovery after stroke in rat models, because they directly generate new neurons. They can derive from embryonic, fetal, or adult tissue and can be easily amplified in culture. Additionally, they show migratory and pluripotency abilities, but their use remains controversial because of ethical considerations (embryonic and fetal origin) and their tumorigenic risk [2] [4] [5] [8].

### **Challenges of MSC Therapy for Strokes**

Despite the positive outcomes of many animal studies and clinical trials of MSC-based treatment for stroke, there are still many challenges to be overcome, before MSCs can be commonly used in clinical practice.

First, the proper time for MSC administration remains controversial. The most of preclinical studies advise transplanting MSCs when a stroke is still acute (within 48 hours). In the acute phase, it has been reported that stroke can increase reactive oxygen species, activate immune cells, and produce pro-inflammatory cytokines, causing secondary brain damage. Cell therapy is best during the acute to subacute period (up to 6 months) in order to prevent cell loss through neuroprotective and anti-inflammatory effects, or to replace lost cells. Cell therapy during the chronic phase (>6 months) aims at functional recovery, when MSCs can produce a number of growth factors to encourage neurogenesis, activate the body's natural repairing mechanisms, reduce glial scars and promote cell proliferation in the subventricular region [4] [6].

Second, it's hard to select the best treatment. Despite the fact that MSCs have shown universal immune tolerance in clinical trials of stroke, an increasing number of preclinical studies have proved the therapeutic efficacy of extracellular vesicles (EVs) derived from MSCs that reduce the dependence on cells. It is possible to cryopreserve these cell-free substitutes without worrying about cell viability. More clinical studies are required to define their therapeutic role in stroke [6].

Third, the route of MSC administration is another major challenge. Minimally invasive routes (e.g., IV and IA approaches) may cause less damage at the injection site than more invasive routes (e.g., intrathecal and IC approaches), but each route has its own advantages and disadvantages [6].

Fourth, the best source of MSCs for stroke treatment has not been identified yet. Even though that in the majority of preclinical trials (>90%) fresh MSCs from young, healthy donors are used, half of the clinical studies involved autologous MSCs, which have been proven to be more effective than those obtained from donors, but it takes a long time to produce enough stem cells for transplantation, so it is hard to use autologous MSC cells in the acute phase of stroke. Unfortunately, an amplification of MSCs by genetic engineering or reprogramming may run the risk of uncontrolled proliferation and genetic abnormalities. Furthermore, it is still unclear if modified MSCs can properly develop into fully functioning brain cells [6].

Fifth, another challenge is that MSCs have a limited lifespan. Age-related changes could affect certain biological features of MSCs. After a certain amount of divisions, MSCs start senescence, which is morphologically characterized by enlarged and abnormal cell shapes. Eventually, proliferation and paracrine functions will be decreased and apoptosis increased, which may reduce the neurogenic potential of MSCs [1] [6].

Sixth, a serious issue with stem cell treatment is cell-mediated adverse effects, e.g., tumor formation of transplanted cells (e.g., iPSC or ESC) that may delay the recovery after stroke [1].

Finally, another difficulty for MSC treatment is the patients' comorbidities. Many stroke patients have coexisting conditions including hypertension, diabetes, and heart disease, which might have an impact on therapy efficacy. The medications like antiplatelet and antidiabetic drugs frequently have an impact on MSC activity, which limits the therapeutic benefits [6].

### **Strategies to Overcome Challenges**

**Differential sources of stem cells-**Although bone marrow-derived MSCs are the most often used, clinical practice is increasingly utilizing MSCs from other sources, such as adipose tissue or the umbilical cord. These other MSC sources outside of the bone marrow may help aged persons with decreased number and function of bone marrow MSCs. Large number of adipose tissue stem cells (ADSCs) can be separated from subcutaneous fat tissue with minimally invasive techniques. According to studies, ADSCs have more paracrine capabilities and angiogenic potential than bone marrow MSCs. Also, umbilical cord MSCs released neuroprotective secreted factors and showed effective neurogenesis, and angiogenesis, and favorable differentiation capabilities [1].

In the body, nerve cells are not only present in the brain. They are also presented in the periphery. A highly structured neural network known as the enteric nervous system (ENS) is presented in the gastrointestinal tract and is a valuable source of nerve tissue. They are self-renewing and detectable in the gut even in adulthood. Evidence shows that the adult gut has active neurogenesis and a remarkable rate of neuronal turnover, which retains a constant amount of enteric neurons. Recent research have demonstrated that intestinal glia has a neurogenic potential. Human EGCs (enteric glial cells), which can be derived from a patient's own intestinal biopsy, are proliferative, neurogenic, and non-immunogenic and don't require genetic modification. They could be the body's most easily available neuronal precursor cells, so they are worth investigating. In mouse models with brain damage, the efficacy of enteric neural stem cell (ENSC) transplantation into the brain parenchyma was confirmed. The realization of cell therapy by local or systemic route has shown that transplanted ENSCs survived and successfully proliferated and differentiated into neuronal and glial cells. Also, transplanted cells had the ability to promote local endogenous neurogenesis. This has a significant advantage over the brain's restricted neurogenesis and might have important therapeutic consequences. As a result, they have improved neurological outcomes in animal models of stroke, and clinical studies examining their effectiveness in patients with stroke, are still being conducted [6].

**Mode of Application-** The mode of application of stem cells can have a significant influence on the number of cells delivered to target regions as well as on the frequency of adverse effects. Stem cells may become trapped in organs that filter blood, which is a serious issue when injecting them systemically (first-pass effect). To avoid this, strategies to reduce lung adhesion and improve the homing of systemically delivered cells are used, including different routes of administration. The advantage of intravenous (IV) transplantation is that it is the least invasive, allowing for numerous injections. Also, this method does not require specialized transplanting equipment. The main therapeutic mechanisms of IV transplantation are considered to be neurotrophic factors' impact, which reduces inflammation and apoptosis. This is effective during the acute phases of an ischemic stroke, but it might not be beneficial during the chronic phase when cell damage and inflammation are mostly settled. However, despite its efficacy, most IV transplanted stem cells are not found in the brain. They are often trapped in the other organs, such as the lungs, spleen, and bladder in 2-24 h after transplantation. For instance, in contrast to intravenous infusions, pulmonary circulation can be bypassed in an intra-arterial (IA) route, resulting in better delivery and maintained presence of stem cells in the ischemic brain longer. However, an arterial approach might cause arterial occlusion, which would induce a stroke. Studies show that cells that are transplanted intravenously or intra-arterially are unable to stay in the brain for a long time. According to several researches intranasal delivery of MSCs improved neurovascular regeneration and functional recovery after stroke [1] [5] [6].

One of the most important and noteworthy route of implanting stem cells into the brain is intracerebral administration, because this way the cells are directly delivered to the focus of the injury. Its advantage is a direct effect on the microenvironment, and this should improve the regeneration process, for example, by promoting migration and differentiation, producing trophic factors and regulating neuroinflammation. As for the safety of the way of introducing the stem cells into the body, the invasiveness of the intracerebral injection route should be taken into account. To determine this, an experiment was conducted on rats, some of which were injected with human adipose-derived mesenchymal stem cells (hASC) intracerebrally. The experiment was successful and the procedure did not cause any complications, which was verified by neurofunctional testing. Recent phase 0/1 clinical trials show that in patients with chronic ischemic stroke, intracerebral delivery is safe. Also, recently

revealed that intracerebrally injected iron labeled BMSCs can migrate, settle in the ischemic area, and survive for more than 2 years [3].

**Ex vivo manipulation of stem cells and culture medium-** Decreased functional activity of stem cells may be caused by reduced telomerase activity, changes of the cell secretome and altered interactions with the microenvironment. There are several methods of culture expansion, that improves the proliferation, survival of cells and trophic support, and reduce senescence of MSCs. According to some studies, hypoxic conditions (i.e., 0.1-2% O<sub>2</sub>, conditions similar to bone marrow) were beneficial to MSCs and might stimulate MSCs to reveal adaptive responses. Preclinical studies of various ischemic models showed that treatment with trophic factors or chemical agents (valproate and lithium) during MSC cultivation, can change the characteristics of MSCs, including migration of MSCs and trophic support in the ischemic brain. Last but not least, genetic modification of MSCs had improved trophic support (e.g., brain-derived neurotrophic factor gene-modified MSCs) and increased migration to infarcted brain regions [1].

**Application of 3D bioprocessing techniques-** Today, the focus is on the development of new 3D bioprocesses that can facilitate the therapeutic potential of stem cell research. With 3D bioprocessing techniques, the biological properties of stem cells can be manipulated, their natural microenvironment can be studied and changed. Current research has shown that by simple 3D bioprocessing techniques MSCs can be easily prepared as spheroid-shaped cellular aggregates. The formation of MSC aggregates can reproduce natural 3D interactions between cells and the extracellular matrix or other neighboring cells, creating an “in-vivo-like” microenvironment where the characteristics of the MSCs can be better maintained. These 3D MSC aggregates may have advantages over MSCs from monolayer cultures for many therapeutic applications. With 3D technique stem cell quality increases for adipogenic, osteogenic, and potentially epithelial-like or neuronal-like phenotypes. 3D modeling can also increase the degree of differentiation for each of them. Recently, an electrically conductive polymer scaffold was developed as a unique NSC (neural stem cell) delivery system. In this study, human NSCs were planted onto the scaffold and electrically preconditioned in 3D, which led to a faster recovery of neurological functions after stroke. In today's static, monolayer cultures of MSCs, the transport of nutrients, oxygen and metabolic waste is restricted, which causes a necrotic center in the cell mass. However, some cells of the outer layer of the necrotic center are viable. Therefore, dynamic culture conditions are needed to improve the cellular and biomolecular composition of 3D stem cell-based structures. In dynamic culture, the transport of metabolic products is much more accessible and the loss of cells is decreased [1].

**Cell-Free Paradigm-** Cell therapy using the secretome (trophic factors, cytokines, or chemokines produced through paracrine secretion) or extracellular vesicles (EVs) (e.g., microvesicles and exosomes) derived from stem cells could provide a novel, clinically effective, and cell-free paradigm that prevents cell-related issues like tumor development. Stem cells secrete EVs, which play a critical role in the exchange of information between stem cells and damaged cells and alter the behavior of the target cells. Bioactive molecules are more stable and bioavailable when they are encapsulated in EVs, which also improves their capacity to traverse the blood-brain barrier (BBB). In recent studies, microvesicles secreted from MSCs stimulated sciatic nerve regeneration in rats. Following a stroke in rats, intravenous administration of EVs derived from MSC culture encourages functional recovery and neuro-vascular plasticity.

The effectiveness of stem cells may be improved by regulating miR expression in stem cells or EVs. MiRs are small non-coding RNAs that have the ability to suppress a wide range of target genes. MiR-based therapies, including miR inhibitors, amplifiers and artificial miRs, are currently being developed. Transplantation of MSCs over-expressing miR-126 increases functional angiogenesis in the ischemic areas. Extracellular miRs can be protected from degradation by RNase by encapsulating them inside EVs. Stem cell-derived EVs, that carry miR to their target cells, help in the recovery of brain damage after a stroke. For example, MSC administration increased miR-133b expression levels in rat brain after stroke and this exosomal miR-133b, which was transferred from MSCs to neurons and astrocytes, regulated neurite outgrowth and neurovascular remodeling to increase stroke recovery.

Stem cell activity can also be regulated by small molecules that modulate specific targets involved in stem cell signaling and functions.

Small molecules, biomaterials, and biologics that modulate specific targets involved in the signaling and mechanisms of stem cells may be used to modulate stem cell function. Compared to cell therapy, small molecules are relatively cheaper, more convenient to use, and suggest better temporal/spatial control. However, there aren't performed many studies for treatment of stroke with small molecules, so convincing results do not exist yet [1] [7].

### **Conclusion**

It's still hard to select the best treatment for stroke, but regenerative medicine in brain injury appears promising. Recent studies show the potential of stem cell therapy to treat stroke but also demonstrate the challenges that must be solved to provide patients with a reliable, effective method of treatment. Several preclinical studies and clinical trials try to find the best source and cell type. The type of stem cells defines the mechanism of action and predicts the outcomes of therapy. Therefore, the stem cell type must be chosen based on the targeted therapeutic objectives, including anti-inflammatory or regenerative. There are many sources of stem cells, but the enteric nervous system (ENS) might find its place as a source of cells for providing transplantation. Evidence shows that the adult gut has active neurogenesis and a remarkable rate of neuronal turnover, which retains a constant amount of enteric neurons. This has a significant benefit compared to the restricted neurogenesis in the CNS. More clinical trials are required to find out the suitable population and determine the best option of stem cell-based therapy in the treatment of stroke. The effectiveness of stem cell treatment may increase with the advances in techniques to regulate stem cell characteristics, such as biotechnology and bioengineering.

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**A CASE REPORT: CENTRAL PART CYSTADENOMA OF PANCREAS**

***Roman Babaevi***

*Tbilisi state medical university, faculty of medicine, Tbilisi, Georgia*

***Natia Shakaridze***

*Tbilisi state medical university, faculty of medicine, Tbilisi, Georgia*

***Elene Gaprindashvili***

*Tbilisi state medical university, faculty of medicine, Tbilisi, Georgia*

**ABSTRACT**

**Case:** A 35-year-old male complained of discomfort and painful attacks in the epigastric area. Three years earlier, an MRI revealed a 10 × 11 mm cystadenoma in the pancreatic body. A year later, the cyst was enlarged up to 12 × 17 mm. Two months before surgery, pain episodes became daily and much worse; therefore, was planned laparoscopic central pancreatectomy. The only significant comorbidity was first-class obesity (BMI: 32.3 kg/m<sup>2</sup>).

**Results:** The organ was transected proximally with a linear stapler but distally with ultrasonic shares, and a caudal stump was used for the creation of the pancreaticogastrostomy. By pathological examination was found mixed mucinous cystadenoma with serous cystadenoma of the pancreas. The postoperative period was uneventful. The four-month follow-up did not reveal any exocrine or endocrine insufficiency.

**Discussion:** Depending on the localization there are head, body and tail pancreatic tumors. Pancreaticoduodenectomy and distal pancreatectomy are radical procedures for pancreatic lesions with high postoperative morbidity and mortality even in experienced hands. Central pancreatectomy is an alternative less radical procedure for centrally located pancreatic lesions that are benign or have a low malignant potential. It involves removing the central portion of the pancreas and has the advantage of preserving the pancreatic parenchyma. |Other advantages of laparoscopic central pancreatectomy includes low incidence of exocrine insufficiency, possibility to perform a second-look laparoscopy after surgery and there is no risk of de novo diabetes development.

**Keywords:** Cystadenoma of pancreas.

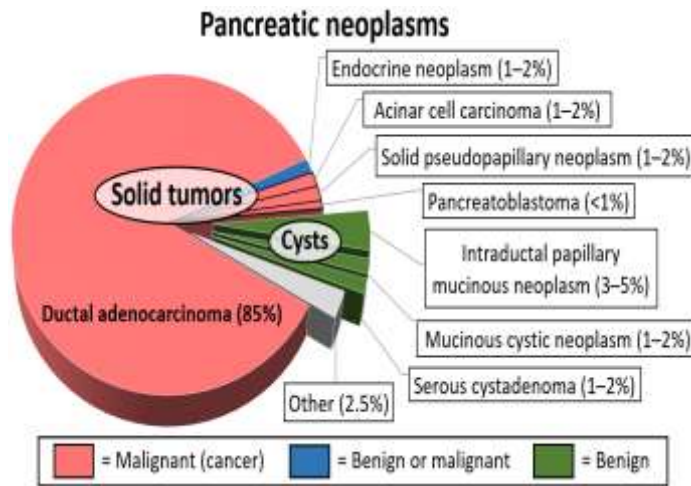
**Introduction**

The pancreas is a small, hockey stick-shaped gland located behind the stomach. The main jobs of the pancreas are to aid in food digestion and regulate blood sugar levels in the body. The pancreas is involved in maintaining blood sugar levels because it makes insulin and glucagon, two hormones that control blood sugar levels.

Pancreatic cancer occurs when mutations in the pancreas cells lead them to multiply out of control. There are two types of tumors that grow in the pancreas: exocrine or neuroendocrine tumors. About 93% of all pancreatic tumors are exocrine tumors. The rest of the pancreatic tumors — about 7% of the total — are neuroendocrine tumors (NETs), also called pancreatic NETs (PNETs), an islet cell tumor or islet cell carcinoma. According to the American Cancer Society, pancreatic cancer represents approximately 3% of all cancers and 7% of all cancer deaths in the United States. It occurs slightly more often in men than in women.

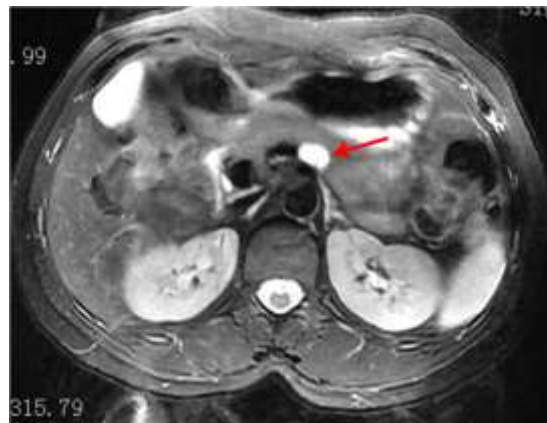
one of the types of pancreatic tumors is cystic tumor. Cystadenomas represented 76% of all primary pancreatic cystic tumors. Pancreatic cystic neoplasms have a wide range of diagnostic possibilities, including serous cystic neoplasm, mucinous cystic neoplasm, intraductal papillary mucinous neoplasm and solid-pseudopapillary neoplasm. An asymptomatic tumor was discovered in 32% of patients with

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SCA, 26% of those with MCA. A mixed mucinous cystadenoma (MCA) with serous cystadenoma (SCA) of the pancreas is rare. We present here a case of mixed MCA with SCA in the middle of pancreas. The cystic neoplasm was resected by laparoscopic central pancreatectomy (LCP).

Central pancreatectomy (CP) is a surgical approach which have the advantage of preserving pancreatic parenchyma and can be used as a good alternative to major pancreatic resections, such as distal pancreatectomy (DP). central pancreatectomy preserves pancreatic tissue, preventing parenchyma insufficiency. Also, this method prevents leakage because it does not leave pancreatic ducts exposed. It also decreases the risk of post-splenectomy infection.



**Figure 2**  
**Magnetic resonance imaging.** There is a 10 × 11-mm cystic neoplasm (arrow) in the

### Case report

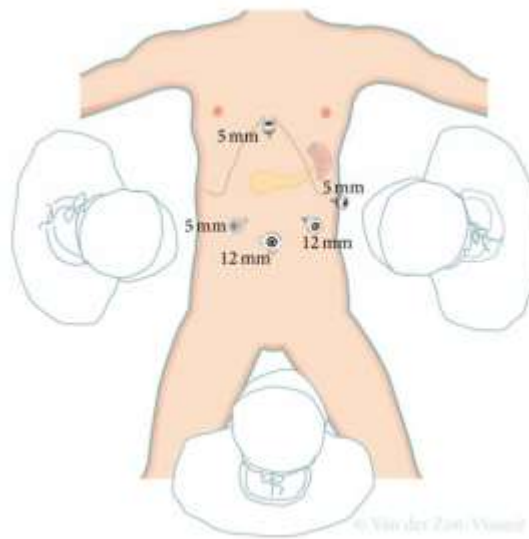
here we represent a case report of a central part cystadenoma of pancreas in 35 years old male.

A 35-year-old male complained of discomfort and painful attacks in the epigastric area. Three years earlier, Computed tomography and magnetic resonance imaging disclosed a 10 × 11-mm cystic neoplasm (Figure 2) in the dorsal/proximal body of the pancreas with a clear-margin multilocular cavity and enhanced internal septum. A year later, the cyst was enlarged up to 12 × 17 mm. Two months before surgery, pain episodes became daily and much worse; therefore, was planned laparoscopic central pancreatectomy. The only significant comorbidity was first-class obesity (BMI: 32.3 kg/m<sup>2</sup>). The patient had a history of SARS-CoV-2 infection of moderate severity four months prior to the operation. Laparoscopic central pancreatectomy was performed.



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The patient was placed supine in a lithotomy position under balanced narcosis combined with thoracic epidural anesthesia. The surgeon was standing between the legs of the patient, and the first assistant and the scrub nurse worked from the right and the left side of the patient.



**Figure 3**

**The location of the trocars.**

One initial 10-mm trocar was placed supraumbilically. then 30° telescope was inserted to examine the peritoneal cavity to rule out metastasis disease. after general examination, two 5-mm trocars in the right subcostal, and 5- and 12-mm trocars in the left hypochondrium were placed. After accessing the lesser sac, a lesion was found in the body of the pancreas. The stomach was displaced upward. The inferior border of the pancreas was dissected using a LigaSure® device and the superior mesenteric vein was identified under the pancreatic neck. The tunnel was created behind the body, and a splenic vein was exposed. The upper border of the pancreas was dissected, isolating common hepatic and gastroduodenal arteries and identifying the portal Intraoperative ultrasound was utilized to determine the lateral borders of the lesion. The pancreas was transected close to the head by an linear stapler using a golden cartridge. Distally to the tumor, the pancreas was transected by ultrasonic shares, preserving splenic vessels. The specimen was placed in the bag and retrieved through the enlarged 12-mm trocar incision in the left hypochondrium. The lesion was sent for express histology, and the abdomen was deflated. After confirming the diagnosis, invaginated pancreaticogastrostomy was created on the back wall of the stomach. After the checkup of hemostasis, the drain was placed under the anastomosis. The operating time was 315 minutes. Blood loss was 55 mL.

After the surgery, the patient was placed in the ICU. Noninvasive monitoring of vitals and laboratory control of homeostasis parameters were continued. An epidural catheter was used for pain control and stimulation of bowel peristalsis. On postoperative day (POD) 2, the patient was transferred to the ward, and walking was allowed. On POD 4, urinary and epidural catheters were removed, and bowel movements occurred. A nasogastric tube was removed on POD 5, and a liquid diet was started. The patient was discharged on POD 7. No hypoglycemia was noted in the postsurgical period.

After one and four months following the surgery there were no signs of recurrence, or pancreatic exocrine or endocrine insufficiency.

The final pathological diagnosis confirmed mixed MCA with SCA of the pancreas. The gross finding was a 15 mm × 18 mm round cystic mass. The cystic mass was multilocular with a fibrous capsule. (Figure 5)

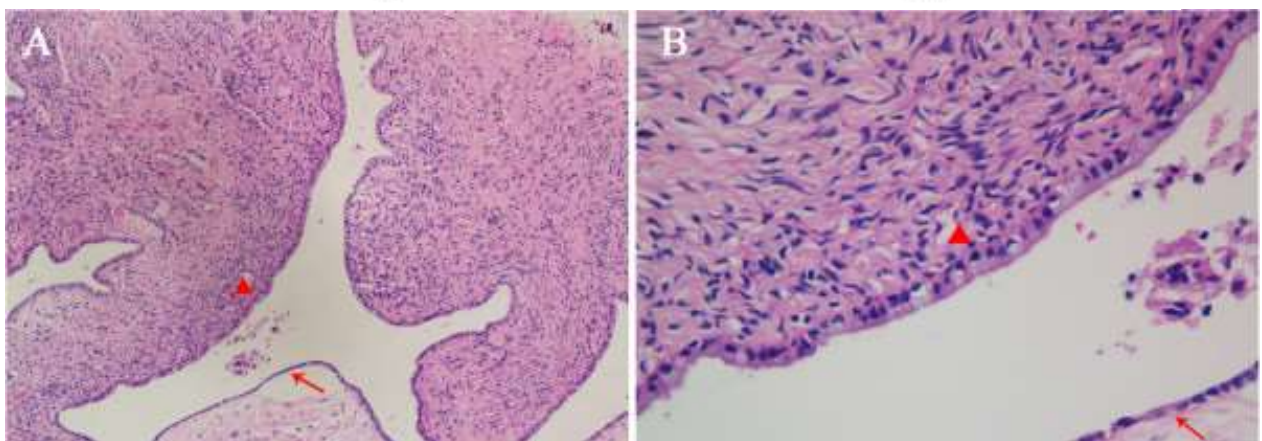
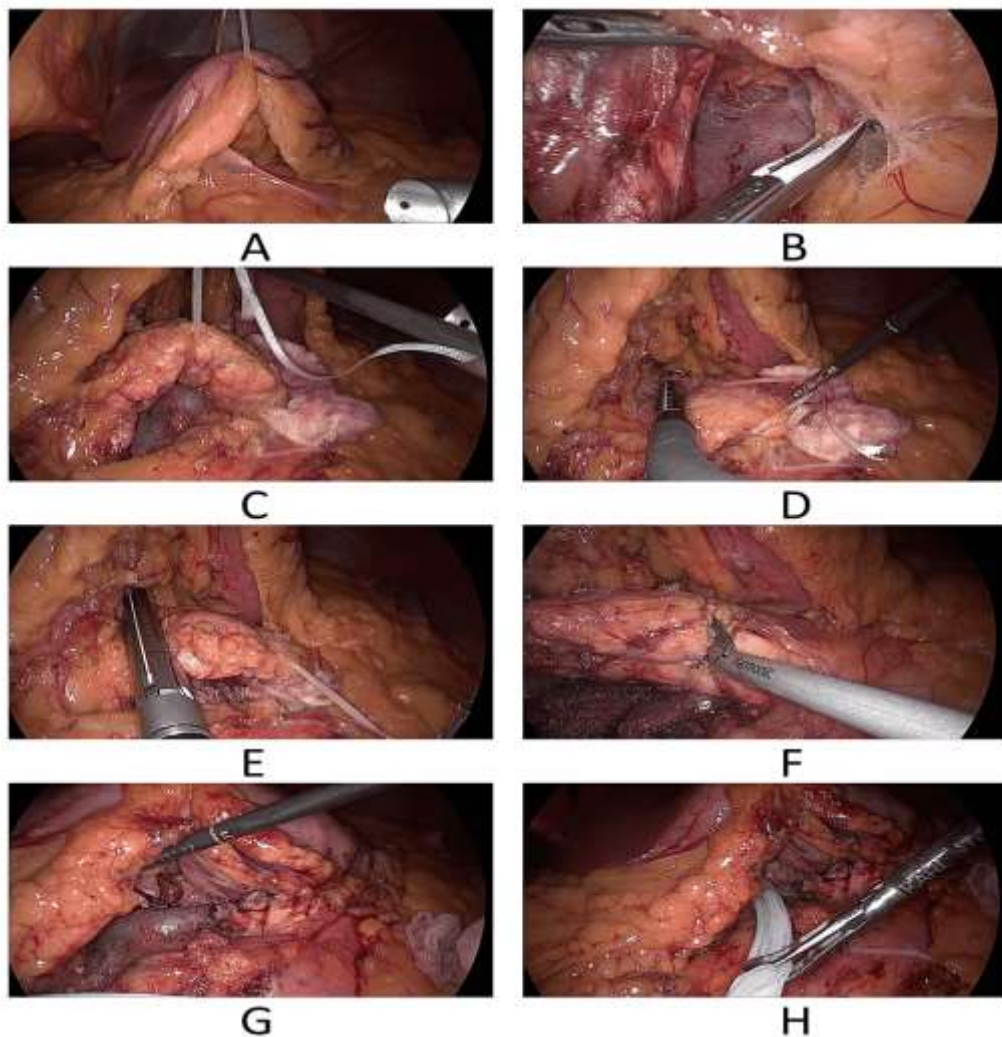


Figure 5

Microscopically, the cystic wall consisted of fibrous tissues with ovarian-like stroma. The cysts were lined by mucous columnar epithelium or cuboidal epithelium. The arrowhead indicates the mucous columnar epithelium or cuboidal epithelium.

**Discussion**

laparoscopic central pancreatectomy is the parenchyma-sparing technique mostly used for benign and low-grade malignant lesions of the proximal body as a better alternative to the distal (left) pancreatectomy. In medical literature, it is also called middle segment pancreatectomy, segmental pancreatectomy, and medial or median pancreatectomy. Central pancreatectomy is an alternative procedure, if the tumor is close to the main pancreatic duct. The advantage of this method is less postoperative exocrine and endocrine insufficiency and low postoperative morbidity compared to distal pancreatectomy. Compared with open surgery, LCP is associated with lower blood loss and shorter hospital stay, which show its advantages as a minimally invasive operation.

<b>Advantage</b>	<b>Disadvantage</b>
Low incidence of exocrine insufficiency	Having two pancreatic stumps increases the risk of fistula
Virtually no risk of de novo diabetes development	Pancreaticogastrostomy or pancreaticojejunostomy carries the risk of leakage
Possibility to perform a second-look laparoscopy after surgery	Roux limb creation needs additional anastomosis - jejunojejunostomy*

Laparoscopic pancreatic surgery is superior to the open approach for less postoperative pain, improved cosmesis, quicker recovery, and better results. The morbidity of the open central pancreatectomy is 43.2%, and the mean mortality is 0.24%, while the laparoscopic or robotic technique is associated with a morbidity of 37.3% and a mean of 0%. The possibility of performing a second look into the abdominal cavity is considered to be an advantage of laparoscopic pancreatectomy.

Despite the rapid development of laparoscopic pancreas surgery, tumor enucleation, distal pancreatectomy, and pancreatoduodenectomy are the techniques used commonly. Distal pancreatectomy is associated with significant exocrine (5%) and endocrine (4%) insufficiency compared with central pancreatectomy (15.6% and 38%, respectively).

Laparoscopic central pancreatectomy is performed relatively rarely. The reason is the necessity of pancreatic anastomosis creation, which increases the technical complexity of the procedure and carries the risk of leakage from the proximal or distal stump or both, potentially increasing postsurgical morbidity and mortality. The transection of the affected part of the pancreas is not difficult, but creating the anastomosis requires good dexterity. Leakage after central pancreatectomy was reported in as high as 22%-33% of patients, but the source of the fistula was a cephalic stump in all cases. A multi-institutional retrospective study confirmed that central pancreatectomy preserves long-term endocrine function.

Pancreaticojejunostomy is the most common technique of reconstruction employed, and typically, it is performed with a Roux-en-Y jejunal loop. Leakage and pancreatic fistula incidence after central pancreatectomy followed by pancreaticojejunostomy is 10.6%. Mason analyzed 733 cases of pancreaticogastrostomy after pancreatoduodenectomy. The incidence of leakage for both reconstruction types is similar, and the aggregate leakage rate was as low as 4%. The better results of pancreaticogastrostomy could be caused by several factors: the proximity of the stomach to the pancreas allows to minimize tension; the stomach has an excellent blood supply; gastric acid may prevent the activation of pancreatic juice; gastric wall thickness provides better suture-holding capacity than the jejunum; pancreatoduodenectomy needs the creation of extra anastomosis - jejunojejunostomy; pancreaticogastrostomy excludes the development of the Petersen's hernia. Fixation of the gastric wall

on the pancreatic stump can affect gastric motility and delay gastric emptying. However, this suggestion is not confirmed in practice.

Two types of pancreaticogastrostomy are being done: duct-to-mucosa and invagination of the pancreatic stump into the stomach.

### **Conclusion**

Mixed MCA with SCA of the pancreas is very rare, and an accurate preoperative diagnosis is difficult. Performing this operation by laparoscopic technique requires mastery and skills, but quick recovery from surgery and less postoperative pain compensate for this practical drawback. Central pancreatectomy is a feasible and safe surgical technique for benign or low malignancies (pancreatic cystic lesions or neuroendocrine tumors) and its aim is to reduce the risk of developing endocrine or exocrine pancreatic insufficiency by preserving as much pancreatic tissue. Creating pancreaticogastrostomy instead of pancreaticojejunostomy allows to make a single anastomosis and potentially decreases the likelihood of leakage. The laparoscopic approach has the advantages of lower perioperative pain, lower hospitalization time, lower blood loss. Main complications after laparoscopic central pancreatectomy are pancreatic fistula and acute pancreatitis. In this case, the advantage of the minimally invasive technique used for pancreatic resection was the possibility to perform a second look (also by laparoscopic approach) into the abdominal cavity at 2 days after the main surgery. The laparoscopic approach established the diagnosis of a necrotic pancreatitis at the level of proximal pancreatic stump, indicated a conservative treatment and relieved the patient of an exploratory laparotomy.

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**DIAGNOSTIC CHALLENGES ENCOUNTERED IN DIFFERENTIATING HIGH-GRADE PROSTATIC ADENOCARCINOMA AND HIGH-GRADE UROTHELIAL CARCINOMA – A LITERATURE REVIEW**

*Shreyas Bhushan Jayade<sup>1</sup>*

*<sup>1</sup>American MD program, Tbilisi State Medical University, 33 Vazha Pshavela Ave. 0186, Tbilisi, Georgia;*

*ORCID ID: 0000-0002-5875-2497*

*Manana Jikurashvili<sup>2</sup>*

*<sup>2</sup>The Department of Pathology, Tbilisi State Medical University, 33 Vazha Pshavela Ave. 0186, Tbilisi, Georgia*

*ORCID ID: 0000-0002-1472-7417*

**ABSTRACT**

Two of the most prevalent types of cancer in men are prostate adenocarcinoma and urothelial carcinoma. Both can appear separately in the prostate and bladder, simultaneously as separate tumors affecting either organ or sporadically as a collision tumor. Distinguishing these tumors by the pathologist can be challenging, especially when the high-grade, poorly differentiated forms infiltrate the surrounding organs. The correct approach by the pathologists is important due to the different treatment modalities for these two entities. This review of the literature gives a comprehensive overview, our succinct understanding of the significance of correctly differentiating between these two tumors, the challenges involved in doing so, and the best collection of crucial and useful immunohistochemical markers for better diagnostic performance.

The scientific papers used in this review were retrieved from the PubMed and Google Scholar databases. All the studies in this review have recently been peer-reviewed and published in academic journals. The literature was sifted through to find the most relevant and up-to-date information for medical professionals, specifically pathologists. The review concluded that: 1) Prostatic and urothelial markers such as NKX3.1, p63, thrombomodulin, and GATA3 are very useful for distinguishing prostatic adenocarcinoma from urothelial carcinoma. 2) Prostate Specific Antigen (PSA) is a good (clinical) screening tool, but because of its inverse relationship with tumor grade (the higher the grade, the lower the sensitivity of PSA staining), it is not recommended for high-grade tumor differentiation. 3) High molecular weight cytokeratin (34βe12) and p63 are said to be more effective than thrombomodulin and S100p in detecting urothelial cancer. 4) Thrombomodulin is only moderately sensitive to urothelial carcinoma. 5) Cytokeratins 7 and 20 can be positive in both urothelial carcinoma and prostatic adenocarcinoma, therefore their use is restricted. The optimal combination of these markers may improve the ability to distinguish these tumors.

**Keywords:** prostate adenocarcinoma, urothelial carcinoma, immunohistochemistry, pathologic diagnosis, collision tumor

**Introduction**

Prostate adenocarcinoma (PAC) and urothelial carcinoma (UC) are two of the most common cancers affecting men worldwide. Both can manifest independently in each organ (prostate and urinary bladder), concurrently as separate tumors involving either organ or occasionally as a collision tumor. Pathologic differentiation between these tumors can be difficult, particularly in poorly differentiated, high-grade forms that infiltrate neighboring organs. Because of the different treatment modalities for these two entities, the distinction between histologic and immunohistochemical patterns is important. This review of the literature provides an overall summary and our concise understanding of the importance of proper

differential diagnosis between these two tumors, the difficulties encountered in this process, and the best set of critical immunohistochemical markers for improved diagnostic performance.

## **Methods**

The scientific papers used in this review were retrieved from the PubMed and GoogleScholar databases using various combinations of the following search keywords: prostate adenocarcinoma, urothelial carcinoma, immunohistochemistry, pathologic diagnosis, differential diagnosis, and collision tumor. Papers were restricted to human subjects and the English language. All the studies in this review have recently been peer-reviewed and published in academic journals. Small-scale studies that produced no statistically significant results were excluded. The inclusion criteria for UC were muscle-invasive, a high-grade disease with no variant morphology. The inclusion criteria for PAC were high-grade tumors with Gleason score of 9 or 10, according to WHO/ISUP 2014. Studies that assessed patients who had received neoadjuvant chemotherapy, hormone therapy, or radiation therapy were not included in this study. A total of 27 publications were selected. The literature was critically evaluated, to find the most relevant and up-to-date information for medical professionals, specifically pathologists, to help distinguish between high-grade urothelial carcinoma and high-grade prostatic adenocarcinoma.

**Discussion:** Prostate and urothelial carcinoma are two of the most common cancers in men worldwide. One in every eight men will be diagnosed with prostate cancer during his lifetime. Prostate cancer is more common in older men and non-Hispanic Black men. About 6 out of 10 cases are diagnosed in men 65 and older, and it is uncommon in men under 40.

Men are diagnosed at an average age of 66. Bladder cancer is more common in older people. Approximately 9 out of 10 people diagnosed with this cancer are over the age of 55. People are diagnosed at an average age of 73. Overall, men have a one in 27 chance of developing this cancer during their lifetime. Women have a chance of about 1 in 89 [1]. In the Western world, prostate cancer is the most common cancer in men aged 60 and up, while urothelial carcinoma is more common in men aged 65 to 84, and is more common in men than women.

These cancers can appear as separate carcinomas, collision tumors, or tumors infiltrating the bladder or the prostate. A collision tumor is a rare but well-studied type of neoplastic lesion composed of two benign tumors, one benign and one malignant tumor, or two malignant tumors. Because of the close anatomic proximity of these organs, UC invasion into the prostate and vice versa is a common occurrence [3]. UC can affect the prostate by directly invading cancer cells into the prostatic stroma or intraductal extensions without invasion. Prostatic adenocarcinoma can involve the bladder either through metastasis or through direct extension, accounting for 12% of all UCs [2].

Diagnostic difficulties do not arise in well-differentiated PAC or even well-differentiated UC because the hematoxylin and eosin stain easily distinguish these tumors based on their common histologic features. The urothelial origin is suggested by the presence of surface neoplasia, nested growth, prominent nuclear pleomorphism, glassy eosinophilic cytoplasm, and high mitotic activity. Furthermore, squamous differentiation foci strongly suggest UC. Conversely, PAC is distinguished by predominantly acinar or cribriform architecture, minimal nuclear pleomorphism, nucleolar prominence, foamy and pale cytoplasm, and low mitotic activity [1].

Distinguishing poorly differentiated urothelial carcinoma from high-grade prostatic adenocarcinoma is a common challenge in genitourinary pathology, especially when the tumor involves the bladder neck, or prostatic urethra. Because of the morphologic overlap, hematoxylin and eosin staining are ineffective.

PSA is a serine protease found in the prostatic epithelium and seminal fluid that has remained the mainstay biomarker for prostate cancer diagnosis and management since its widespread use as a screening tool nearly 25 years ago. Although it has resulted in a significant increase in prostate cancer detection, PSA has significant drawbacks in sensitivity and specificity, especially in high-grade adenocarcinomas. As the Gleason score rises, so does the drop in PSA sensitivity. According to immunohistochemistry, up to 13% of high-grade cancers are completely negative for PSA [4].

The distinction between poorly differentiated prostate cancer of the urinary bladder neck and high-grade urothelial carcinoma with prostatic extension has important therapeutic and staging implications. For example, cystoprostatectomy, the standard surgical procedure for the treatment of bladder cancer, is

ineffective for prostatic cancer, and determining the tumor stage for prognosis would necessitate correct diagnosis because the extension of bladder cancer into the prostate, as well as prostate cancer into the bladder, would indicate pT4 disease. As a result, distinguishing them is critical to providing appropriate treatment

[5].

Many studies have used immunohistochemistry to assess the use of various lineage markers in distinguishing urothelial carcinomas from prostate adenocarcinomas. In most cases, a panel of markers is useful in distinguishing between the two entities. Prostatic differentiation is supported by markers such as prostate-specific antigen (PSA), prostate-specific acid phosphatase (PSAP), prostate-specific membrane antigen (PSMA), P501s, NKX3.1, and erythroblast transformation specific-related gene (ERG); whereas urothelial differentiation and origin are supported by markers such as high molecular weight cytokeratin (34 $\beta$ e12), CK7, p63, thrombomodulin, uroplakin III, GATA 3 [6, 7, 8, 9, 10, 11, 12]. Not all of these indicators are required in every case. It is best, to begin with, a few markers with high sensitivity and specificity and then add markers as needed. In the majority of cases, PSA, CK34 $\beta$ e12, and p63 are excellent starting points.

Prostate-specific membrane antigens include prostate marker protein (P501s) (prostein), prostate-specific membrane antigen (PSMA), and NKX3.1 [27].

P501s, a 553-amino acid protein found in the Golgi complex, is a newer prostate-specific protein discovered using high-throughput microarray screening and cDNA subtraction. Both benign and malignant prostatic epithelial cells contain P501s [2].

PSMA, a type II membrane glycoprotein containing 750 amino acids, is expressed by both benign and malignant prostatic epithelial cells, with malignant prostatic epithelial cells staining more strongly. PSMA is a highly specific marker of prostatic lineage, but it is also found in non-prostatic tissues such as the duodenum, neuroendocrine cells, endothelial cells in some neoplasms, and proximal renal tubules [2].

NKX3-1 is an androgen-regulated, prostate-specific homeobox gene with predominant expression in the prostate epithelium. It functions as a transcription factor and is essential for prostate development and tumor suppression. It inhibits the growth of epithelial cells in prostate tissue. The NKX3-1 gene encodes the NKX3-1 homeobox protein, which is also found in urothelial cells, normal testis, lobular breast carcinoma, and bronchial mucous glands [2].

In prostate cancer, AMACR (alpha-Methylacyl-CoA Racemase) is consistently overexpressed compared to benign prostatic tissue. It codes for a cytoplasmic protein that participates in the  $\beta$ -oxidation of branched-chain fatty acids. AMACR is not specific to prostate cancer; it is also expressed by other cancers, most notably colorectal carcinomas and papillary renal cell carcinomas. The expression of AMACR is cytoplasmic, with a granular staining pattern. Apical predominance and heterogeneity are evident in the staining. Currently, AMACR is used to supplement basal cell markers in antibody cocktail formats. The average sensitivity for detecting limited prostate carcinoma in needle biopsies is 70-80%, with lower sensitivity reported in certain morphologic variants such as foamy, pseudohyperplastic, and atrophic variants of typical acinar prostate adenocarcinoma [13, 14, 15].

Urothelial markers include high molecular weight cytokeratin (HMWCK), p63, thrombomodulin, S100P (placental S100), and GATA3.

HMWCK (34 $\beta$ e12) and p63 are more sensitive to high-grade urothelial cancer than novel markers like thrombomodulin and S100P [27]. HMWCK (34 $\beta$ e12) is a highly sensitive urothelial lineage marker (CK), which also includes CK1, CK5, CK14, and CK20. It is only reactive against high-molecular-weight cytokeratins (CKs). It has the same sensitivity as p63 and is said to outperform uroplakin III and thrombomodulin [2].

p63, a tumor suppressor gene homolog, encodes at least six different proteins with various biologic functions, one of which is urothelial differentiation. With consistent diffuse nuclear positivity, p63 is a fairly sensitive and highly specific marker of urothelial carcinoma [2,16].

HMWCK (34 $\beta$ e12) and p63 are basal cell markers in prostatic tissue and are typically absent in invasive prostatic adenocarcinoma.

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Thrombomodulin, also known as CD141, is a surface glycoprotein that regulates intravascular coagulation and is expressed in a variety of tumors including mesothelioma, endothelial vascular tumors, squamous carcinomas, urothelial carcinomas, and various adenocarcinomas in both primary and metastatic settings. This marker's lack of specificity to urothelial differentiation limits its utility in this context. However, as demonstrated in several studies mentioned in this section, this marker can be useful in the workup of a potential urothelial tumor when used in conjunction with other markers [2, 17].

S100P is a protein from the S100 family discovered in the placenta and was thus named S100P (it is different from the S100 widely used in melanocytic and nerve sheath tumors). S100P expression by IHC has been described in benign and malignant urothelial cells, pancreatic carcinoma, esophageal squamous mucosa, and breast carcinoma, in addition to the placenta [2, 11].

GATA3 is a transcription factor of the GATA family that regulates genes involved in the luminal differentiation of breast epithelium, genes involved in T-cell development, and genes involved in the development or maintenance of skin, trophoblasts, and some endothelial cells. GATA3 has been identified as an IHC marker for both primary and metastatic mammary and urothelial carcinomas. Despite the promising specificity and sensitivity, recent studies have shown that not all cases of prostatic adenocarcinoma can be positive for GATA3, posing a potential diagnostic challenge. McDonald, Timothy M recently represented nine cases of prostatic adenocarcinoma with aberrant positive GATA3 staining. All nine cases were PAC, with a Gleason grade of 5. GATA3 positivity was strong and diffuse in four cases, strong and patchy in two cases, and strong and focal in three cases. All of the patients tested positive for NKX3.1, six tested positive for p501s, and six tested positive for PSA, with seven of the nine cases expressing at least two prostate-specific markers. To avoid the diagnostic blunder, poorly differentiated carcinomas of the prostate, bladder neck, or trigone should be assessed not only with GATA3 but also with prostate-specific markers, according to the current research. GATA3 can still be useful in the workup of a neoplasm with a possible urothelial origin if used in the right context and in the right conjunction with other antibodies [2, 18, 19, 20, 21, 22].

Uroplakins are widely considered to be urothelium-specific proteins of terminal urothelial cell differentiation, and they are positive in both primary and metastatic urothelial carcinoma. Despite being specific to urothelial differentiation, they are not very sensitive because some urothelial carcinomas do not express these markers, limiting their practical use and necessitating the inclusion of other markers in the workup for a potential urothelial tumor [23, 24, 25, 26].

## **Conclusion**

High-grade prostatic adenocarcinoma and urothelial carcinoma of the urinary bladder can have ambiguous morphologic features that make a definitive diagnosis impossible. The distinction between these two tumors has important implications for staging and treatment. As a result, accurate diagnosis is critical for optimal patient care and may necessitate the use of highly sensitive immunohistochemical markers.

The review concluded that: 1) Prostatic and urothelial markers such as NKX3.1, p63, thrombomodulin, and GATA3 are very useful for distinguishing prostatic adenocarcinoma from urothelial carcinoma. 2) PSA is a good (clinical) screening tool, but because of its inverse relationship with tumor grade (the higher the grade, the lower the sensitivity of PSA staining), it is not recommended for high-grade tumor differentiation. 3) HMWCK (34 $\beta$ e12) and p63 are said to be more effective than thrombomodulin and S100p in detecting urothelial cancer. 4) Thrombomodulin is only moderately sensitive to UC. 5) Cytokeratins 7 and 20 can be positive in both UC and Prostatic adenocarcinoma, therefore their use is restricted.

The optimal combination of these immunohistochemical markers may improve the ability to distinguish PCA from UC.

## **Limitations**

The immunohistochemical markers for urothelial carcinoma and prostatic adenocarcinoma are based on the research and clinical expertise of pathologists who have worked on cases and conducted studies to support their hypotheses. However, in a clinical scenario, the immunohistochemical panel is not absolute



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but depends on the individual case presented. This panel mentioned is solely based on research and functions to provide an overall understanding of the topic.

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**Abbreviations:**

PAC - Prostatic AdenoCarcinomaUC - Urothelial Carcinoma

WHO/ISUP – World Health Organization/the International Society of Urologic Pathologists  
PSA - Prostate-Specific Antigen

PSAP - Prostate-Specific Acid Phosphatase PSMA - Prostate-Specific Membrane Antigen

ERG - Erythroblast transformation specific-Related Gene AMACR - Alpha-Methyl-Acyl-CoA Racemase

HMWCK - High Molecular Weight Cytokeratin

**December 09-11, 2022 / Tbilisi, Georgia**

**PHARMACEUTICAL CARE DURING THE HEPATOPROTECTIVE DRUG SELECTION**

*Nino Nemsitsveridze<sup>1</sup>*

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

**ORCID ID: 0000-0002-5659-1714**

*Tamaz Chumburidze<sup>2</sup>*

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

**ORCID ID: 0000-0003-1053-6901**

*Nana Gorgaslidze<sup>3</sup>*

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

**ORCID ID: 0000-0002-4563-5224**

*Nestan Nikuradze<sup>4</sup>*

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

**ORCID ID: 0000-0002-4614-5075**

*Manana Ghonghadze<sup>5</sup>*

*TSMU, International Faculty of Medicine and Stomatology, Department of Medical Pharmacology, Tbilisi, Georgia.*

**ORCID ID: 0000-0002-6224-6458**

**ABSTRACT**

In Georgia liver pathologies, the cases of which mostly relate to the use of different drugs, are one of the most pressing and yet unresolved medical problems.

The goal of this study was to investigate the nuances of the relationship between the patients with liver pathology and the pharmacist, their questions, complaints and wishes. For this purpose, we interviewed 40 people with liver pathologies and 40 doctors with a pre-prepared questionnaire. The study found that liver related illnesses caused by medicines in most cases happen due to self-medication. The main risk factors when it comes to liver damage is an unhealthy lifestyle, 57% of the cases are caused by this, the remaining 43% are related to the irrational usage of the medicine. The study also revealed that doctors rarely prescribe hepatoprotective drugs to prevent or avoid the negative impact that could be caused by medicine. They do so after the damage is clinically detected. As previously mentioned, to avoid the fetal results of self-treatment, the role of clinical pharmacist is vital.

Even though the doctors take the hepatotoxicity of the prescribed medicine into account, during pharmaceutical care, clinical pharmacists have to explain the risks involved while taking such medicine and its peculiarity. In case if any dangerous symptoms are detected they should refer the patients to the doctor.

Based on received data an algorithm is developed, which will ease for the pharmacist to correctly provide the care needed for the patients with liver pathology, as well as allow them to minimize the negative effects of incorrect medicine utilization.

**Keywords:** Pharmaceutical care, hepatoprotective drugs

## **INTRODUCTION**

In Georgia, liver pathologies caused by the use of various medicines remain one of the most urgent and still unresolved medical problems.

Main risk factors of a chronic liver disease are unhealthy lifestyle, stress, overeating, low physical activity, tobacco and alcohol consumption as well as ecological environment.

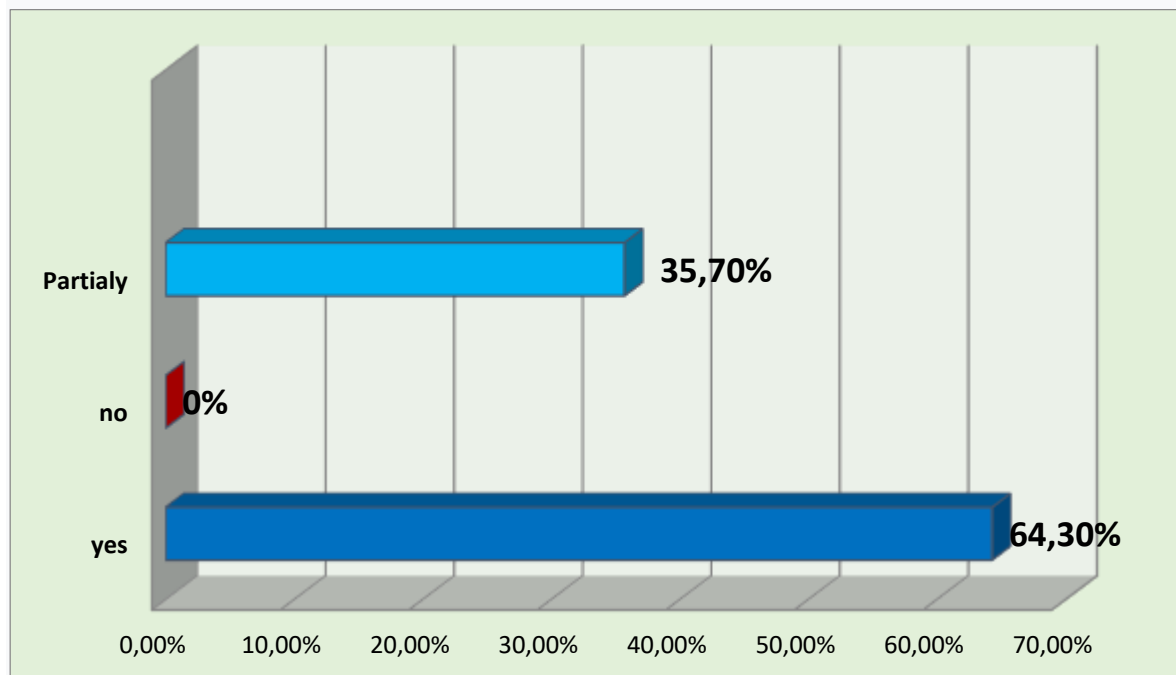
One of the causes of liver pathologies is drug-induced liver damage, which largely relates to self-medication. In the recent period, the increase in the number of medicines led to the patient taking them without the doctor's recommendation, which is a frequent cause of morbidity and mortality of the population.

Incorrect dosage of non-steroidal anti-inflammatory drugs, antifungals and some other drugs can cause serious damage to the liver and gastrointestinal tract. One of the main figures in the fight against uncontrolled self-medication and polypharmacy is the clinical pharmacist, because he is well versed in the medical aspects of pharmaceutical care and strives to improve the wellbeing of the population and prevent misuse and of drugs. Drug-induced liver damage is very relevant among the safety problems associated with the use of medicinal products, evidenced by the statistics of registration of side effects of medicines: 1-10 patients per 1000 cases.

The aim of this work was to determine the importance of the role of the clinical pharmacist in the implementation of care for patients with liver disease and in the selection of hepatotoxic drugs.

For this purpose, we interviewed 40 people with liver pathology and 40 doctors through a pre-prepared questionnaire.

Question of whether the hepatotoxicity of the medicine is taken into account when prescribing (diagram 1)

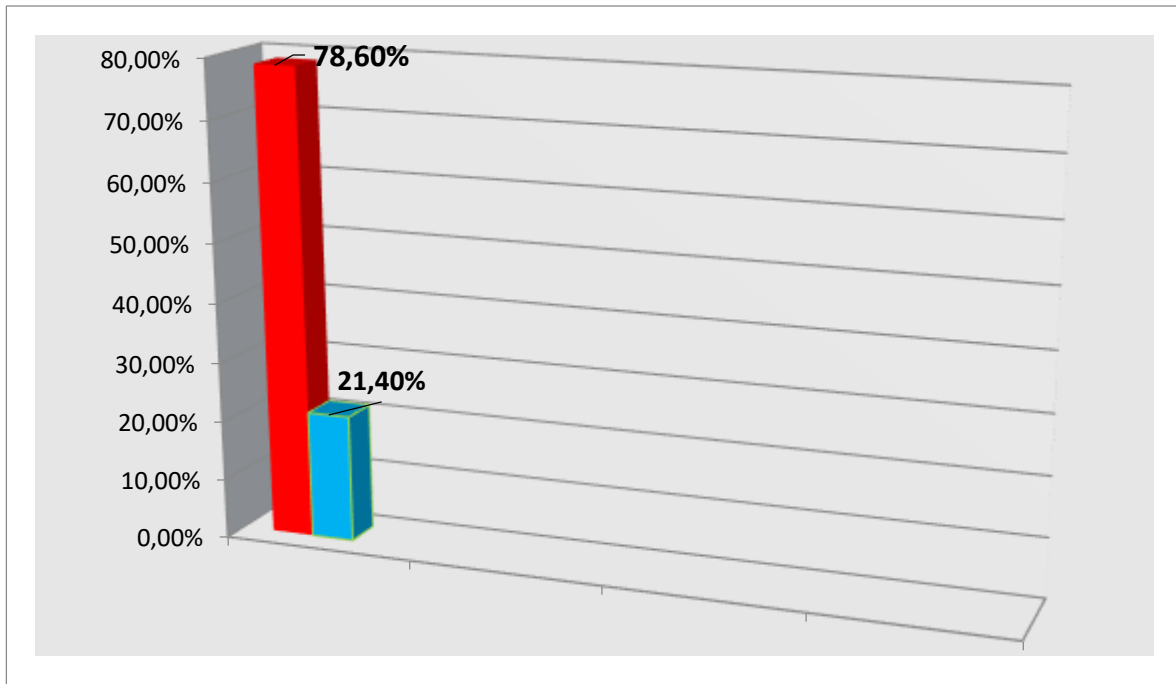


The given diagram shows the results of a survey of doctors, the 64.3% of doctors consider the hepatotoxicity of drugs in their prescriptions, and 35.70% partially, which is quite a high percentage, since liver function disorders caused by drugs can, in many cases, be life threatening. When dispensing hepatotoxic medication, the clinical pharmacist must warn the patient about the side effects of the drug and, if necessary, check the prescription with the doctor;

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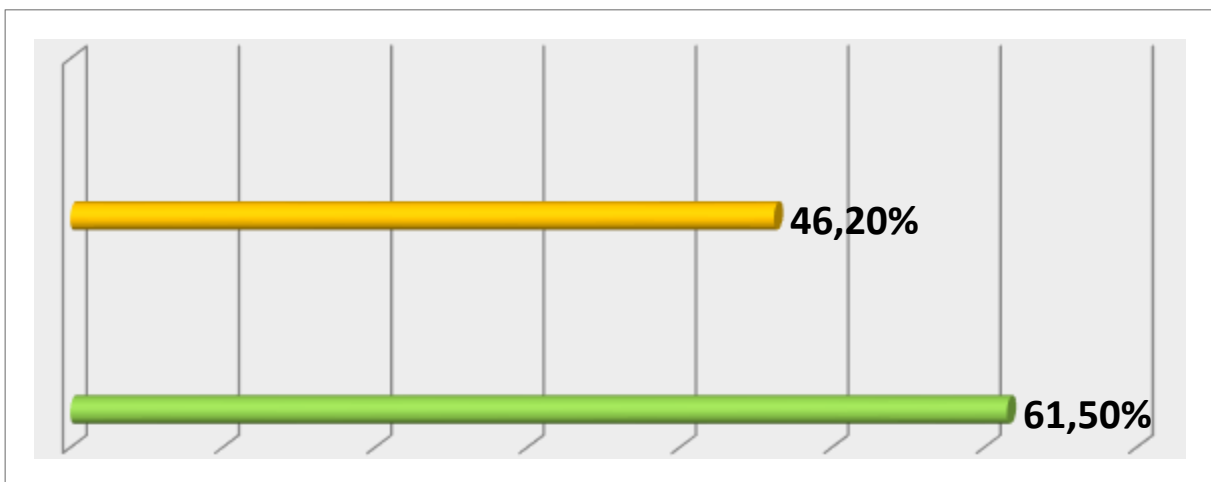
do you use hepatoprotective drugs in combination with the prescribed toxic medicine? (Diagram 2)

Doctors who use hepatoprotective drugs



■ Doctors who do not use hepatoprotective drugs

As can be seen in the diagram, the majority of doctors 78.6% use hepatoprotective drugs, and 21.40% do not. Despite the fact that some doctors prescribe hepatoprotective drugs, 21% of patients still find themselves in danger of developing liver pathologies; the pharmacist should explain the risks and recommend the use of hepatoprotective drug. Question: is the use of hepatoprotective drug more frequent for the purpose of prevention or for treatment? (Diagram 3)



The 61.50% of doctors use hepatoprotective drugs for treatment, and only 46.20% for prevention. Unfortunately, the percentage of hepatoprotective drugs prescribed for prevention is significantly lower than for treatment. However, treatment with such drug has more benefits at the initial stage, while prescribing hepatoprotective drugs after the case becomes more complicated is less effective. Therefore,

the clinical pharmacist, based on the conversation with the patient, should advise the patient to take prophylactic hepatoprotective drugs if he complains of liver irritation. Based on the results obtained through the research the main symptoms of liver pathology are: the majority of patients, 50%, complain of pain in the upper part of the abdomen, 30% with changes in the condition of the skin, chronic fatigue, jaundice and loss of appetite, constipation and weight loss in 20% of the patients. All these probably indicate that the toxic processes taking place in the liver. If a patient with such symptoms goes to the pharmacy, the pharmacist will identify dangerous symptoms based on the survey. He may advise the patient to contact to the doctor so that he can change the prescription or prescribe a hepatoprotective drug; the pharmacist should explain to the patient what might be the cause of his complaint, check the dosage and compatibility with other drugs. When asked which hepatoprotective drugs they prefer in their medical practice, most doctors name Hepa-Mertz, as well as Hepato-Ritz, Karsil, Liv, Heptral, Asretaa, Silarsil and Montmars. If the patient does not have a doctor's prescription for selected hepatoprotective drug, the clinical pharmacist, within the scope of his competence, will determine, based on the survey, which drug is more effective for the patient. He will also select a more affordable drug at the patient's request. A clinical pharmacist can save the doctor's time and provide patients with the necessary information about hepatoprotective drugs, as well as data on the effectiveness, dosage, side effects and compatibility with all the other hepatoprotective drugs available in the clinic or pharmacy.

In conclusion, it can be said that in order to prevent the unfortunate consequences of self-medication, the role of the clinical pharmacist becomes even more relevant. In the process of pharmaceutical care, the clinical pharmacist has to explain to the patient the peculiarities of taking the drug and the risks associated with taking it, help the patient and, in case of detecting dangerous symptoms, refer him to the doctor.

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**December 09-11, 2022 / Tbilisi, Georgia**

***ACANTHOLYTIC SQUAMOUS CELL CARCINOMA MIMICKING ANGIOSARCOMA IN THE ORAL CAVITY – A CASE REPORT AND LITERATURE REVIEW***

***Rohit Parab<sup>1</sup>***

*<sup>1</sup>American MD program, Tbilisi State Medical University, 33 Vazha Pshavela Ave. 0186, Tbilisi, Georgia;*

*<sup>1</sup>ORCID ID: 0000-0001-5362-6128*

***Laya Chadalawada<sup>2</sup>***

*<sup>2</sup>American MD program, Tbilisi State Medical University, 33 Vazha Pshavela Ave. 0186, Tbilisi, Georgia;*

*<sup>2</sup>ORCID ID: 0000-0002-0894-2356*

***Shaina Machado<sup>3</sup>***

*<sup>3</sup>American MD program, Tbilisi State Medical University, 33 Vazha Pshavela Ave. 0186, Tbilisi, Georgia;*

*<sup>3</sup>ORCID ID: 0000-0003-1251-2794*

***Manana Jikurashvili<sup>4</sup>***

*<sup>4</sup>The Department of Pathology, Tbilisi State Medical University, 33 Vazha Pshavela Ave. 0186, Tbilisi, Georgia;*

*<sup>4</sup>ORCID ID: 0000-0002-1472-7417*

**ABSTRACT**

Although angiosarcoma and squamous cell carcinoma represent completely different tumor entities their histologic features in some cases might be similar, especially in the head and neck region. Interestingly the clinical features might be also identical.

We report a case of an acantholytic squamous cell carcinoma, observed in a male individual in his 7<sup>th</sup> decade of life. It presented as a polyp-like, ulcerated mass in the oral cavity. The histologic findings revealed diffusely infiltrative malignant tumor composed of the clusters of ovoid to spindle neoplastic cells with hyperchromatic nuclei and densely eosinophilic cytoplasm and with anastomosing vessel-like channels lined by a single layer of atypical epithelioid and hobnail-like cells on slightly myxoid background. Some atypical cells also had the tendency of forming pseudoglandular structures. Few keratin globules were also observed in subepithelial connective tissue. The surface mucosal epithelium showed dysplastic changes. No mucin was identified. Because of these morphologic features seen on H&E stained slides the diagnosis of squamous cell carcinoma and angiosarcoma was considered. Immunohistochemical analysis led to a conclusive diagnosis of acantholytic variant of squamous cell carcinoma – the tumor cells expressed an epithelial marker cytokeratin 5/6 and a nuclear stain - p63, confirming the squamous differentiation.

Acantholytic squamous cell carcinoma is an uncommon variant of squamous cell carcinoma which is characterized by a combination of typical squamous cell carcinoma and pseudovascular structures, dyskeratotic cells and prominent acantholysis – loss of coherence between epithelial cells due to breakdown of intercellular bridges. This cancer is known to have an aggressive nature, especially when it occurs intraorally.

In conclusion, careful attention should be paid to the histological features of this rare variant of squamous cell carcinoma because tissue biopsy samples can easily be mistaken for angiosarcoma due to the presence of pseudoangiomatoid patterns. Immunohistochemical analysis is generally helpful in establishing an accurate diagnosis.

**Keywords:** acantholytic, squamous cell carcinoma, oral cavity



## **INTRODUCTION**

Acantholytic Squamous Cell Carcinoma (ASCC) is a very rare variant of the most common form of cancer found in the oral cavity which is Squamous Cell Carcinoma (SCC). It occurs mostly after the age of 60. UV radiation significantly increases the risk of ASCC. A great deal of evidence points to the significance that acantholytic squamous cell carcinoma of the oral cavity has an uncanny resemblance to that of an angiosarcoma under the pathological microscopic view. The similarity is due to the separation of layers between cells known as acantholysis. It can present as a fast locally growing mass that has a poorer prognosis compared to conventional SCC of the oral cavity. The acantholytic squamous cell carcinoma and angiosarcoma both have pseudovascular spaces, however on immunohistochemistry they can be distinguished. Hence it is important to know the differences between these two as treatment options are separate.

## **CASE REPORT**

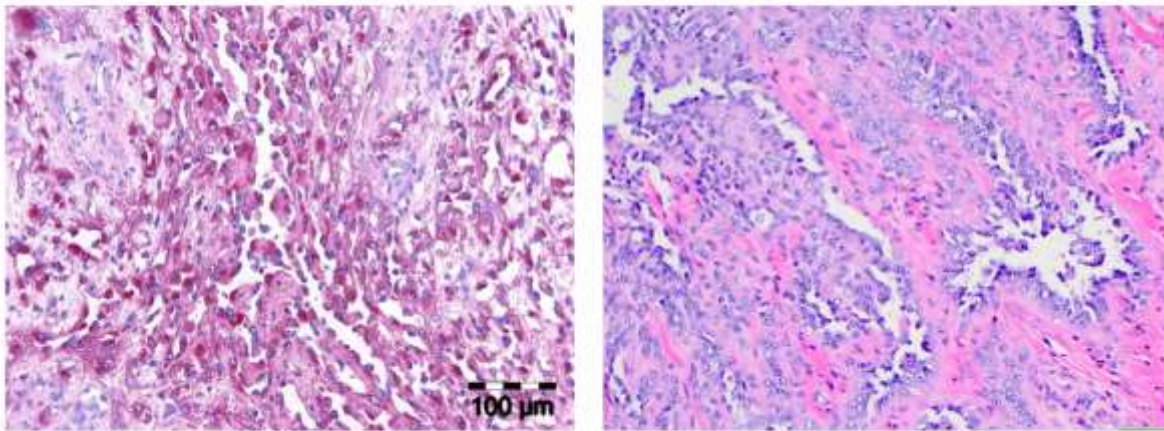
The formalin-fixed paraffin-embedded (FFPE) tissue samples with the material from the oral cavity of a 72 year old male individual has been provided to the pathology laboratory of High Technology Medical Centre – University clinic for the consultation. On routine microscopic examination, the biopsy showed diffusely infiltrative malignant tumor composed of the clusters of ovoid to spindle neoplastic cells with hyperchromatic nuclei and densely eosinophilic cytoplasm and with anastomosing vessel-like channels lined by a single layer of atypical epithelioid and hobnail-like cells on slightly myxoid background. Some atypical cells also had the tendency of forming pseudoglandular structures. Few keratin globules were also observed in subepithelial connective tissue. The surface mucosal epithelium showed dysplastic changes. No mucin was identified. Because of these morphologic features seen on H&E stained slides the diagnosis of squamous cell carcinoma and angiosarcoma was considered. Immunohistochemical analysis led to a conclusive diagnosis of a moderately differentiated acantholytic variant of squamous cell carcinoma as the atypical cells showed positivity on cytokeratin 5/6 and p63. Vascular markers like CD34 and smooth muscle actin showed to be negative and only remained positive in internal control – true vessel channels.

## **DISCUSSION**

In this article, we are trying to emphasize how similar the acantholytic variant of squamous cell carcinoma and angiosarcoma are in histopathology. Currently, there is a lot of literature about ASCC in the head and neck region available that describes the similarities between the two pathologies and why it is important to distinguish them. But, there are not many intraoral cases of ASCC.

Squamous cell carcinoma (SCC) is the most common cancer in the oral cavity. Acantholytic squamous cell carcinoma (ASCC) is a rare variant of SCC.[4] Acantholysis is the loss of adhesion molecules like E-cadherin, catenin, syndecan-1 and others that bind the cells tightly to each other resulting in separation of layers of cells.[7,12,13] Loss of these adhesion molecules also aids in the invasion of malignant cells in the tissue architecture.[7] In ASCC, these spaces are large enough to mimic pseudovascular or pseudoglandular spaces.[4] Angiosarcoma on histology has similar findings - irregularly anastomosing vascular channels with endothelial and stromal infiltration. Sometimes, reactive fibrosis within the tissue along with artifactual clefts lined by malignant cells create angiomatous pattern.[11] Hence, it is difficult to distinguish the two based on histology only and requires the need for immunohistochemistry for confirming the diagnosis. In Fig. 1 we can see and compare how closely both mimic each other in histology. Other characteristics on H&E staining that can be seen are neoplastic cells, hyperchromatic nuclei, eosinophilic cytoplasm, atypical epithelioid cells and keratin pearls; what the biopsy fragments in this case report revealed.

## ASCC vs. ANGIOSARCOMA



Delencel, O., Müller-Richter, U.D., Harkin, S.G., et al. Oral acantholytic squamous cell carcinoma shares clinical and histological features with angiosarcoma. *Head Face Med* 4, 77 (2008). <https://doi.org/10.1186/1745-2912-4-77>

Lin SS, Beherakonda V, Pinnig TL. Angiosarcoma. *PathologyOutlines.com website*. <https://www.pathologyoutlines.com/topic/solidtumorsangiosarcoma.html>. Accessed December 28, 2022 [2]

Figure 1: Comparison of ASCC and Angiosarcoma on H&E biopsy samples

The clinical presentation of both are usually the same in the oral cavity. They are locally aggressive and rapidly growing lesions with a poor prognosis. They can present as a polyp, mass or ulcer with irregular borders.[1,5] Both ASCC and angiosarcoma can have hemorrhagic regions.[1] Regional lymph nodes may be enlarged. Both present in the late stages of life with average incidence of ASCC and Angiosarcoma in age 60 and 70, respectively.[5] UV radiation is thought to have a role in the etiology of cutaneous ASCC because most tumors grow on sun-exposed regions with signs of actinic keratosis.[1,7,14] In contrast to oral angiosarcoma, ASCC has a tendency to present 1 to 3.5 times more common in males.[1] According to some articles, ASCC is more aggressive than classic SCC but some studies deny this claim as current literature does not have enough number of cases reported to make conclusions.[6,10]

Not to be confused, ASCC term is interchangeably used with a lot of other terms - adenoid SCC, pseudoglandular SCC, angiosarcoma-like SCC, and pseudoangiosarcomatous carcinoma.[1,5]

In our case, after H&E staining two differentials were considered - Acantholytic SCC and Angiosarcoma. Immunohistochemistry was planned to confirm diagnosis. This test is specific and can distinguish between tumors by checking for cell markers. Carcinoma has epithelial origin and will stain positive for epithelial markers whereas sarcoma has mesenchymal origin and will stain positive for mesenchymal markers.

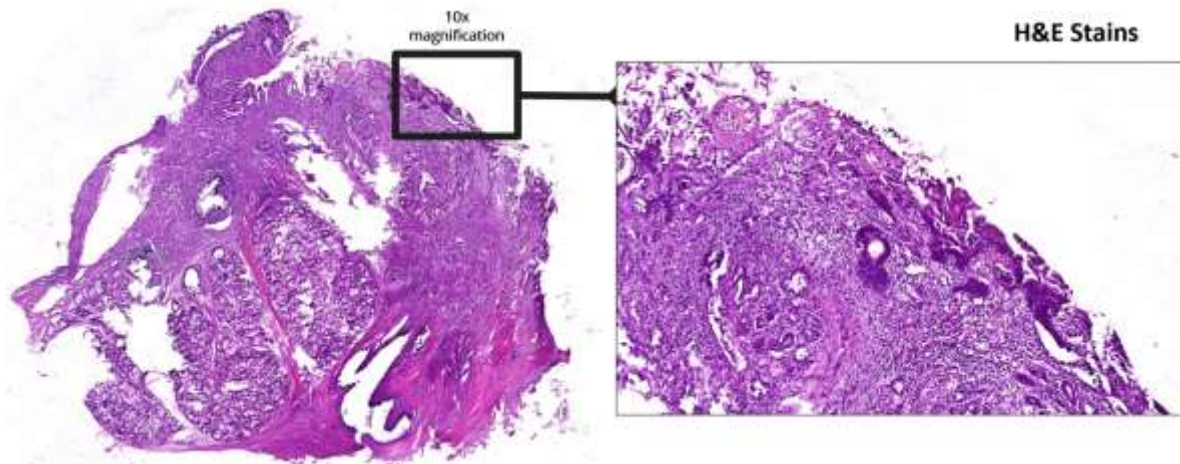


Figure 2: Low power magnification H&E stains

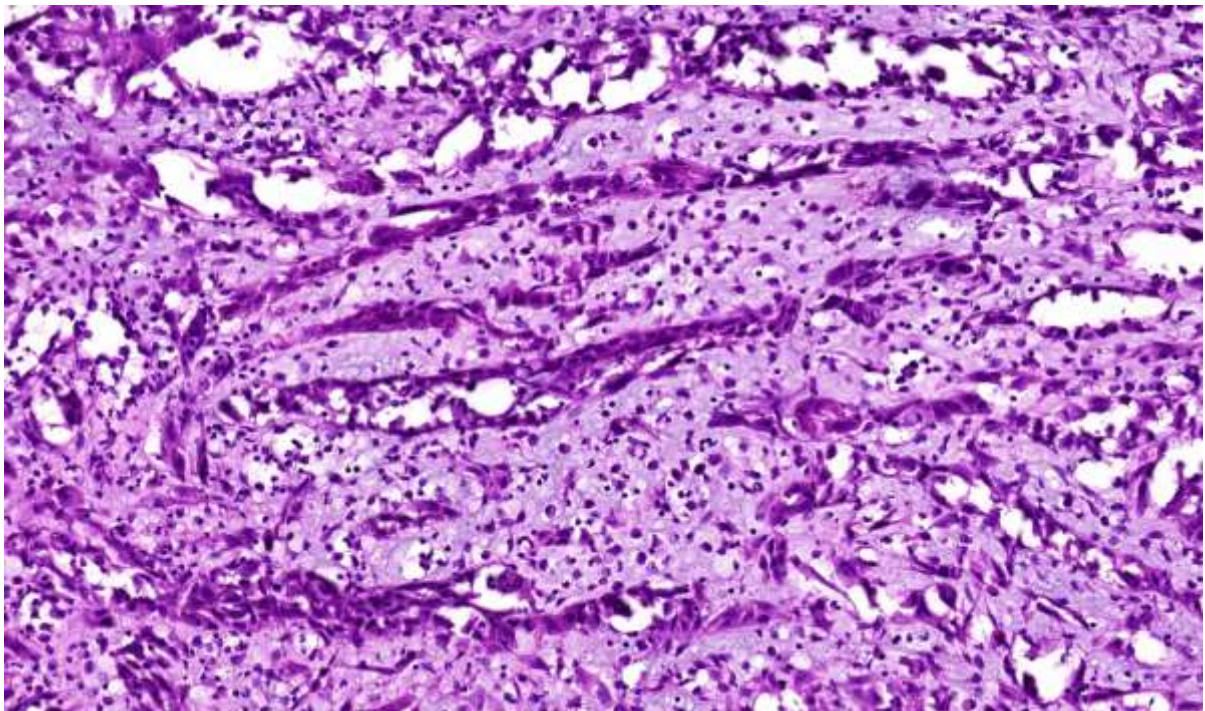


Figure 3: H&E stain 20x power magnification

In immunohistochemistry, angiosarcoma will stain positive for vascular antigens like CD 31, CD 34, von willebrand factor (vWF) and smooth muscle actin.[4,9] A novel vascular differentiation marker, Fli-1 protein, a DNA binding transcription factor from the ETS family is positive in angiosarcoma.[4,9] ASCC will stain positive for cytokeratin, p63 and epithelial membrane antigens. Laminin-5 is a new marker that stains positive in the cytoplasm of ASCC. It is also known as a biological indicator for the poor prognosis of ASCC.[4] In a study, it was discovered that both ASCCs and angiosarcoma were cytokeratin-positive but angiosarcoma had less cytokeratin-positive tumor cells than ASCC did.[1] Pictures of H&E staining and immunostains cytokeratin 5/6 (Fig. 4), p63 (Fig. 5), CD 34 (Fig. 6) and SMA (Fig. 7) from our patient are added here. The pictures were received from Dr. Manana Jikurashvili, High Technology Medical Centre-University Clinic, CSD-Georgia. In these images, diffuse acantholysis (white spaces) and malignant infiltrative cells staining brown in color are noted.

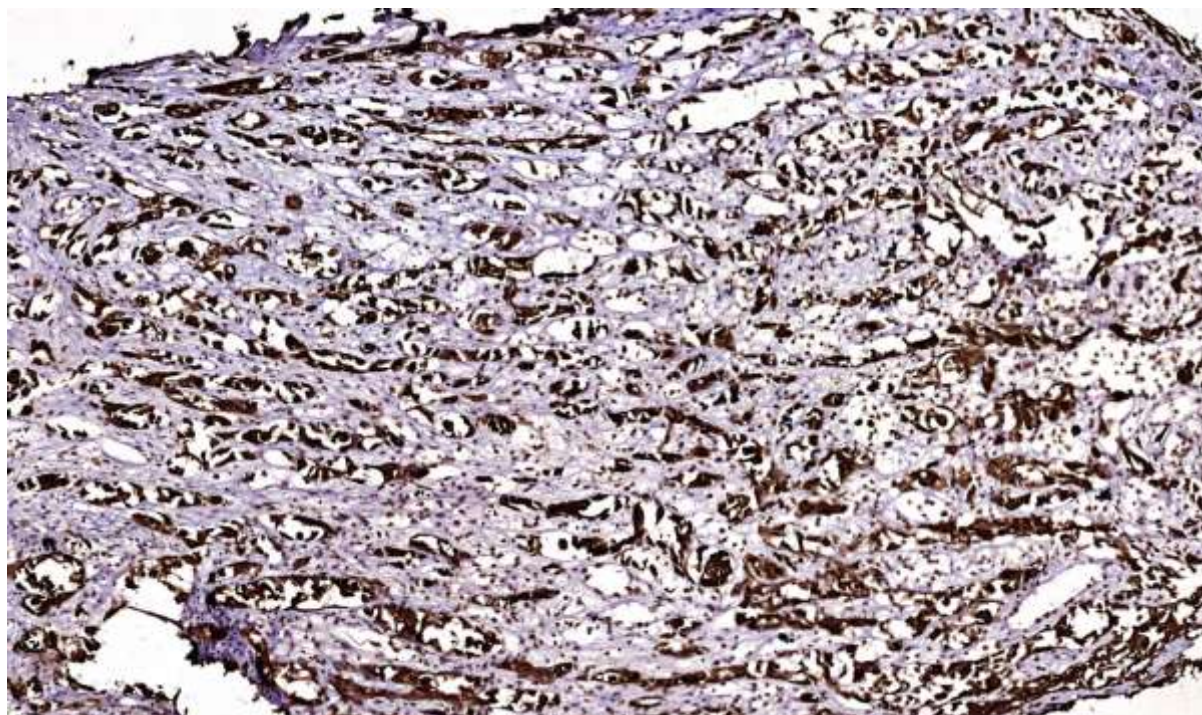


Figure 4: Cytokeratin 5/6 stain, 10x power magnification

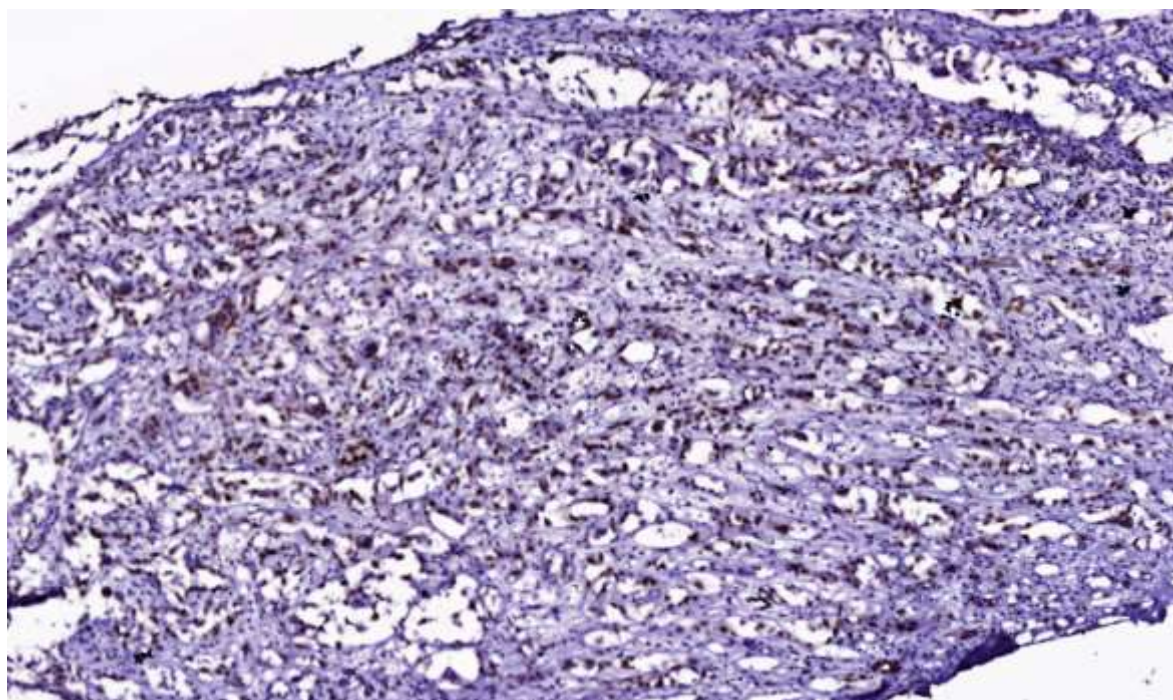


Figure 5: p63 immunostain, 10x magnification stain

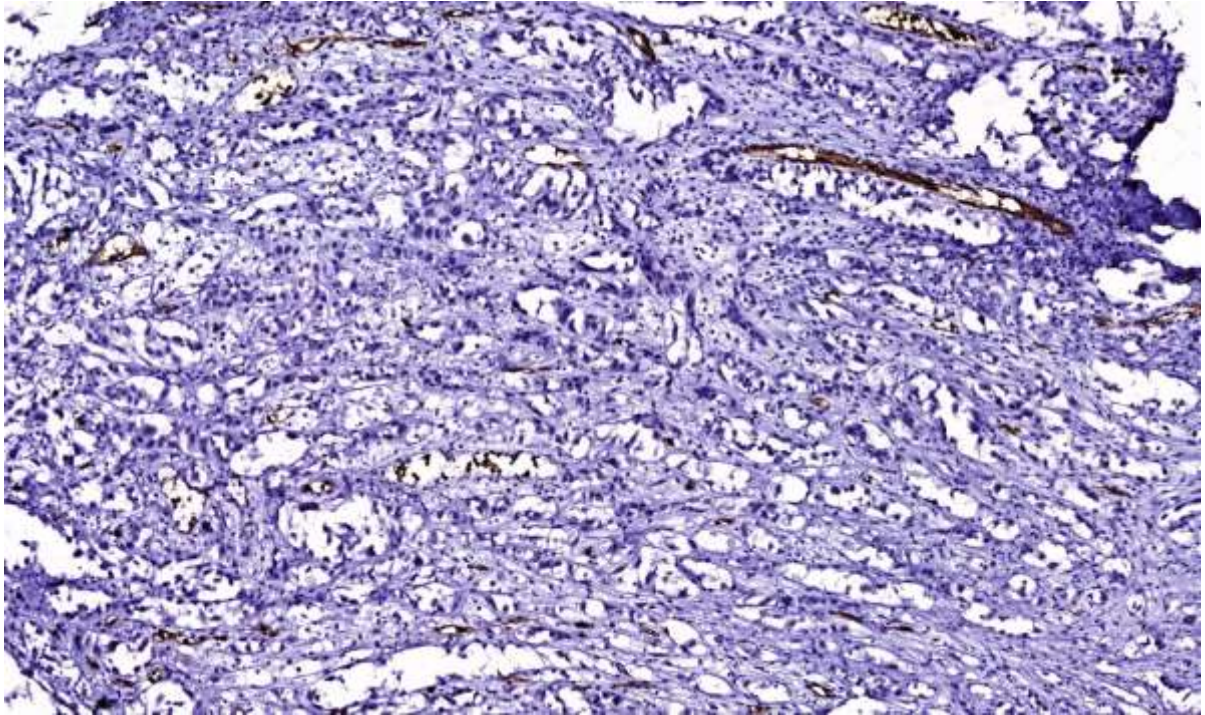


Figure 6: CD 34 stain, 10x power magnification

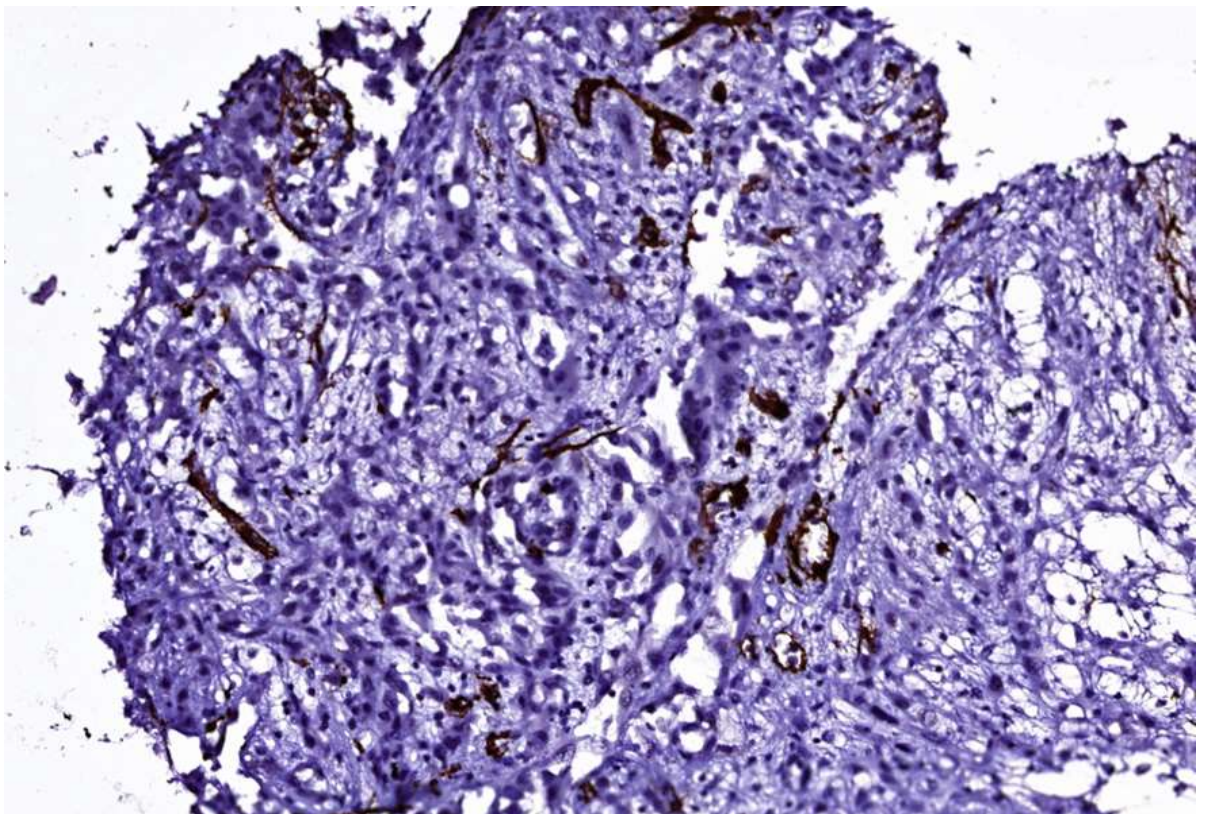


Figure 7: Smooth muscle actin stain (SMA), 20x power magnification

## **CONCLUSION**

After immunohistochemistry, Acantholytic Squamous Cell Carcinoma was confirmed as the diagnosis. From the figures attached we can also confirm it by identifying the brown colored areas in immunostains. There is brown discoloration in cytokeratin 5/6 and p63 stain which verifies cell origin

is epithelial and confirms carcinoma. There is no brown discoloration in CD 34 and SMA stain which verifies cell origin is not mesenchymal and rules out sarcoma. There is a small brown discoloration in figure 6 (CD 34) and figure 7 (SMA)- this is the internal control smooth muscle in the blood vessel wall, the area which is normal and healthy. Internal control also tells us that the staining method was performed correctly.

The patient was consulted at the oncology department and is currently on radiation therapy.

To conclude our study, the tissue biopsy H&E samples of ASCC can be confused for angiosarcoma due to the presence of pseudovascular or pseudoglandular patterns arising from acantholytic areas. Hence, extra caution should be made towards the histological characteristics of this uncommon type of squamous cell carcinoma and confirmed with immunohistochemistry to avoid misdiagnosis.

#### **ACKNOWLEDGEMENTS**

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#### **CONFLICT OF INTEREST**

The authors declare that they have no conflict of interest.

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**CLINICAL CASES OF INTESTINAL INFECTIONS WITH BLOODY DIARRHEA**

*Natia Uzarshvili*

*Tbilisi State Medical University, Faculty of Medicine, Infectious Diseases, Tbilisi, Georgia*

*Tamar Korakhashvili*

*Tbilisi State Medical University, Faculty of Medicine, Infectious Diseases, Tbilisi, Georgia*

*Malvina Javakhadze*

*Tbilisi State Medical University, Faculty of Medicine, Infectious Diseases, Tbilisi, Georgia*

*ORCID ID: 0000-0002-1090-8106*

**Introduction**

Diarrheal illnesses are the second leading cause of pediatric deaths worldwide which result in annual 500 000 pediatric deaths around the globe. In developing countries infants have at least 6 diarrheal illnesses each year and toddlers around 3 episodes. Variations between mortality and morbidity depend on the region as in Georgia so Worldwide. Some regions may need much more interventions to improve results.

Diarrhea is defined as passing a mucinous or watery stool at least 3 times in 24 hours. Diarrhea might be acute: watery, invasive (bloody) and chronic >14 days . In developing countries most common causes of diarrhea are infectious gastroenteritis. Sometimes diarrhea may be a symptom of systemic infection or intra abdominal surgical pathology. Etiologies of infectious gastroenteritis differ between age groups, geographical regions and types of diarrhea.

In recent years as worldwide so in Georgia incidence of bacterial gastroenteritis has declined due to increasing viral GI tract infections. Shigella is the most common pathogen between bacterial causes of gastroenteritis and this infection in turn is associated with life-threatening complications. There are four different species of Shigella: Shigella dysenteriae, Shigella flexneri, Shigella sonnei, Shigella boydii. In developing countries most common Shigella isolate is Shigella flexneri along with some other common pathogens like Salmonella Enterica, Campylobacter Spp., Enterohemorrhagic E.Coli, Enteroinvasive E.Coli and Entamoeba Histolytica. E. Coli is a normal inhabitant of human gut flora and most frequently isolated microorganism from stool samples. To pathogenic E.Coli pathotypes belong: Enterotoxigenic E.Coli (ETEC), Enteroinvasive E.Coli (EIEC), Enteropathogenic E.Coli (EPEC), Enteroaggregative E.Coli (EAEC) and Enterohemorrhagic E.Coli (EHEC). The most commonly isolated serotype of enterohemorrhagic E.Coli is E.Coli O157:H7 serotype and the most virulent of those are Shiga Toxin 2 producing E.Colis. Most severe cases of STEC infections and HUS are usually seen in children under the age of 5 years.

The research objective was to identify the most common agents causing bacterial gastroenteritis including bloody diarrhea in Georgia in hospitalized patients, disease course, severity and specificities according to patients' ages.

Research material and method: The research is retrospective. 100 patients' cards had been studied who were hospitalized in the pediatric department of Acad. V. Bochorishvili clinic due to gastroenteritis with bloody diarrhea. The indication of hospitalization in every case was gastroenteritis and colitis. We performed stool culture on each patient and also performed toxin detection testing for the presence of E.Coli Verotoxins in the stool. In every case the disease would start with subfebrile fever which afterwards would be accompanied with nausea, vomiting and increased frequency in bowel movement. Disease severity was determined by the duration of illness and the patient's age. In children under 2 years, there were episodes of hypoglycemia and dehydration due to poor oral intake of food and ORS. Most of those patients were given antibiotics along with symptomatic treatment. In standard cases the disease would resolve within 6-7 days without complications. From those cases only one patient developed HUS and required dialysis sessions and that case later also resolved with complete recovery.



Analysis of the obtained results: In 60 % of hospitalized patients gastroenteritis etiology had not been specified (identified), 10% accounted for viral pathogens and 30% for bacterial pathogens. From bacterial pathogens 60% accounted for Shigellosis and 40% to Salmonellosis.

Bacterial gastroenteritis with bloody diarrhea usually has moderate severity and main etiologies according to our results are Shigella, Salmonella and E.coli and in those cases only severe HUS complication has been documented.

**Case:**

10 y.o. patient who was hospitalized on the first day of the disease onset. The disease started acutely with abdominal cramping, subfebrile rise of temperature up to 37.5 degrees, which was followed by diarrhea first with brownish watery-mucoid and later bloody stool. Afterwards the frequency of defecation increased up to one bowel movement every 5-10 minutes and only blood was noted in the stool. Remarkable was that the patient had eaten Khachapuri with raw egg the day before. CBC demonstrated: WBC count- 16.66 10<sup>9</sup>/L, Neutrophils - 75%, Relative lymphopenia 14%, increased ESR 20 mm/hr. Stool microscopy showed WBCs, RBCs and mucus in large quantities. E.coli O157:H7 Ag and Verotoxin 1 positive. No electrolyte disturbances. Abdominal ultrasound revealed thickening of the wall of ascending, descending and sigmoid colon and some effusion between intestinal loops. The patient was started with Antibiotic from the macrolide group, active infusions. Measured creatinine level was in normal ranges - 34.8 μmol/L. Despite the initial treatment the patient didn't show improvement, continued to complain about abdominal pain and nausea, had vomiting episodes and bloody-mucoid diarrhea one bowel movement each 5-10 minutes and tenesmus. Repeated CBC demonstrated worsening of the lab results: WBC 14.47 10<sup>9</sup>/L, HGB 15.2 g/dL, PLT 463 10<sup>9</sup>/L, metamyelocyte 1%, segmented neutrophils 14.44 10<sup>9</sup>/L, ESR- 2 mm/hr, glucose 70 mg/dL. In order to exclude acute surgical pathology the patient underwent abdominal CT with contrast which showed a picture of diffuse colitis. Patient continued to have abdominal pain, was irritable and developed a fever of 38.4 degrees, had repetitive vomiting episodes and bloody diarrhea once every 10-15 minutes. Glucose 60 mg/dL. Due to the severity of the condition and probable rapid worsening of the patient's vital signs, the patient was moved to the intensive care unit on the day 4 of hospital admission.

On that day repetitive renal function tests and CBC didn't show HUS findings and the patient was started with parenteral ceftriaxone. Despite the treatment, the patient's general condition worsened. Patient showed signs and the lab. finding of HUS: Creatinine 100 μmol/L, PLT -50 and decreased urine output: 780ml of urine in 24 hours 1.3ml/kg/hr. The patient required nephrologists surveillance, frequent control of renal function and in case of need renal replacement therapy so was moved to the multiprofile hospital, where underwent dialysis sessions and disease resolved with complete recovery.

**Summary and recommendations:**

Viral infections are the most common causes of gastroenteritis, from bacterial pathogens most common etiologies are Salmonella and Shigella.

In standard cases infectious gastroenteritis lasts around 6-7 days and resolves without complications.

Suspect Shigellosis in children who have high degree fever, mucoid-bloody diarrhea and tenesmus.

Empiric antibiotic treatment should be defined by the host factors and severity of illness.

As an oral antibiotic Azithromycin is usually used.

In case of treatment failure, resistant microorganism or other pathogens must be suspected and antimicrobial medication should be changed.

As the first line parenteral drug for children <18 Ceftriaxone is recommended.

With caution should be handled cases of STEC infection, especially virulent is Shiga toxin 2 producing E. Coli.

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**THE FEATURES OF EXPLORING OF MANAGEMENT OF PHARMACEUTICAL  
MARKET FROM INDIVIDUAL TO SOCIETY WELLBEING IN GEORGIA**

*Nana Gorgashidze*

*MD, PhD, Doctor of Pharmaceutical Sciences, Professor of Tbilisi State Medical University, Faculty of Pharmacy, Head of The Department of Social and Clinical Pharmacy, Tbilisi, Georgia*

*Shafiga Topchiyeva*

*Dr. Biological Sciences, Professor of Institute of Zoology, National Academy of Sciences of Azerbaijan. Baku, Azerbaijan.*

*Nodar Sulashvili*

*PhD, Doctor of Pharmaceutical Sciences, Invited Lecturer of Scientific Research-Skills Center at Tbilisi State Medical University, Tbilisi, Georgia; Associate Professor of Division of Pharmacology of International School of Medicine at Alte University; Associate Professor of Pharmacology of Faculty of Medicine at Sul Khan-Saba Orbeliani University, Associate Professor of Pharmacy Program at Shota Meskhia Zugdidi State University; Invited Professor of The School of Health Sciences, The University of Georgia, Tbilisi, Georgia.*

*ORCID ID: 0000-0002-9005-8577*

**ABSTRACT**

The well-being of consumers and the protection of the public interest depend on the social responsibility, moral side, ethical behavior and decency of employees of pharmaceutical institutions. Compliance with ethical norms and communication skills in the development of pharmaceutical activities affects the refinement of the moral norms of the consumer and society altogether. The concept of socio-ethical marketing, in turn, in one scheme combines a pharmaceutical institution, an individual patient, a customer and the public interest as a whole. The basic principle of customer orientation is recognized and marketing is defined as follows: Marketing is a type of human activity aimed at satisfying the needs and wants of customers through exchange.

The aim of the research was to study the features of exploring of management of pharmaceutical market from individual to society wellbeing in Georgia. Studying the levels of integration between employees and patients in pharmacies and their practical reflection in the Georgian pharmaceutical business, in particular, in pharmacies. Pharmacies are one of the fastest growing areas in Georgia, where the not very useful level of using modern pharmaceutical management and marketing principles is clearly visible.

As a research methodology, we used the general fundamentals of marketing, the papers and scientific articles of Georgian and foreign researchers.

To present and analyze the issue, we used the survey method through the questionnaire we have developed. We conducted this research through an anonymous survey of "Google Forms"; Presentation method of research and forecasting results. The results of the research show that pharmaceutical marketing is less customer-oriented and pharmacies have developed insignificant forms of service. Successful pharmaceutical activity uses various marketing methods. Pharmaceutical marketing is not customer-oriented. Pharmacy management is focused solely on profit. Not all customers have the same needs, they must approach the pharmacy individually and provide the appropriate service, which is an effective means of increasing loyalty.

The management of the pharmacy has not developed patient service forms. All patients are served in the same way, regardless of their financial income level. The majority of the respondents noted that the management of the pharmacy is not focused on integrated marketing. Taking into account the concept of integrated marketing creates a continuous functional chain with the customer. Obviously, the separate use of marketing communications does not give the same effect as the integrated one.

The conducted research revealed that the management of the pharmacy advertises pharmaceutical products mainly with the encouragement of consumers/patients. This includes offering discounts and gift cards, promotions, and other activities by pharmacies to attract and retain customers.

It was revealed that companies conduct marketing research and use the results of marketing research. But management does not collect scientifically based information about pharmaceutical products for selection. Also, according to the results of the research, a small part of the respondents is familiar with socio-ethical marketing. The result is probably based on the extent to which they consider social responsibility when using marketing. Cases of replacing the drug prescribed by a doctor with another drug are common, in order to increase the sale of pharmaceutical products in the pharmacy.

**Key words:** Pharmaceutical, marketing, patient, public, aspects, pharmacy, management, Georgia.

## **Introduction**

Marketing researchers often indicate that ethical norms and behaviors are a necessary condition for social marketing. Thus, this form of marketing is especially necessary and necessary for pharmacies. The management of the pharmacy shall determine the overall condition of the competitors around it and the needs of the targeted customer, which in itself will satisfy the interests of the public [1-2].

We also note that focusing solely on profits and not taking into account the interests of consumers and the public at all will hurt the institution itself. All this will be manifested by the presence and/or insecurity of the norms of ethical relations with the customer. We think that if the customer and the public are dissatisfied, thereby the pharmacy will not have a proper reputation [3-4].

The main thing in marketing is targeted orientation and complexity. Targeted orientation on the demand of a particular customer ensures the efficient operation of enterprises, since the customer is the evaluator and recruiter of their activities. The main task is to identify and satisfy the needs and interests of the targeted user in more efficient ways compared to competitors in the face of maintaining and improving the well-being of consumers and the whole community altogether [5-6].

Generally, some factors in the public-economic situation became the cause of the origin of the socio-ethical concept of marketing. In Georgia, the origin of this form of marketing is associated with a change in public form, which on the one hand was manifested by the presence of a free economic market. Changes in the market in the XXI century led to the improvement of marketing methods and ways and the development of new marketing approaches. Pharmacies began to identify the needs of customers and worry about satisfying them [7-8].

The concept of socio-ethical marketing, in turn, in one scheme combines a pharmaceutical institution, an individual patient, a customer and the public interest as a whole. The basic principle of customer orientation is recognized and marketing is defined as follows: Marketing is a type of human activity aimed at satisfying the needs and wants of customers through exchange [9-10].

**Relationships and impact forms depending on the specificity of pharmaceutical marketing are vary by level. The level of financial income of patients using the pharmacy should be taken into account. If the pharmacy has many low-income customers, it does not use the form of telephone or "service" at home when dealing with it. If the pharmacy has a high-price insolvent patient (buyer) then, full partnership relations with him are solidified [11-12].**

New technologies, new pharmaceutical products have significantly changed the relationship between patients and the pharmacy. Patients have more information about pharmaceutical news, brands and can share it with other users in different ways. We believe that not only marketing drives patient relationships, but patient-driven relationships are emerging [13-14].

The main thing in marketing is targeted orientation and complexity. Targeted orientation on the demand of a particular customer ensures the efficient operation of enterprises, since the customer is the evaluator and recruiter of their activities. The main task is to identify and satisfy the needs and interests of the targeted user in more efficient ways compared to competitors in the face of maintaining and improving the well-being of consumers and the whole community altogether. Generally, some factors in the public-

economic situation became the cause of the origin of the socio-ethical concept of marketing. In Georgia, the origin of this form of marketing is associated with a change in public form, which on the one hand was manifested by the presence of a free economic market. Changes in the market in the XXI century led to the improvement of marketing methods and ways and the development of new marketing approaches. Pharmacies began to identify the needs of customers and worry about satisfying them. Marketing researchers often indicate that ethical norms and behaviors are a necessary condition for social marketing. Thus, this form of marketing is especially necessary and necessary for pharmacies. The management of the pharmacy shall determine the overall condition of the competitors around it and the needs of the targeted customer, which in itself will satisfy the interests of the public [15-18].

### **Pharmaceutical Marketing**

The pharmacy has a multifaceted function. The first among them are: to ensure human health, pharmaceutical care, timely and quality delivery of medicines and patient care items, competent and integrated communication with the patient and the public, and full compliance with ethical norms. Pharmacy management should understand that each patient has his own needs and requirements for medicines. The consumer, in turn, chooses the pharmaceutical product he needs, and it is clear not only the influence of pharmaceutical marketing on the consumer, but also the influence of the consumer on the marketing itself. Based on consumer psychology, an important determinant of consumer behavioral marketing is the need for a pharmaceutical product. We should also mention the attitude of the user/patient towards the pharmaceutical product, which is seen as a necessity and not as a desired product. This is an important feature of pharmaceutical marketing. The lack of necessary information (evidential information) about the pharmaceutical product has a serious impact on the decision of the user/patient. We cannot ignore such an important indicator as the quality of the pharmaceutical product. We have already mentioned that one of the participants in pharmaceutical marketing is the doctor, the doctor's qualifications [19-20] (how well the doctor knows innovations, drug forms, dosage, pharmacokinetics).

### **Pharmaceutical marketing management**

Since marketing theory has been combined with management theory, it is known as "market management theory" and is based on data from applied science. Pharmaceutical marketing management process includes: formulation of goals and determination of priorities; to receive information about the object to be studied; information processing and decision-making; issuing management orders; Information support is the process of meeting the information needs of specific users, based on its acquisition, processing, filling and use of special methods and means. Qualified pharmacy management concentrates on several important points during marketing management. Among them, the main emphasis is on: the study of consumer psychology, behavior, motivation to buy; on innovative marketing, which relies on scientific and technical development in accordance with market requirements. Particular attention is paid to: pharmaceutical products, prices, sales and communication policy (integrated marketing).

### **Factors influencing patient/consumer behavior**

User behavior is influenced by various factors that are unique to each individual, content-wise, on the one hand, the individual level of analysis, and on the other, general facts that reflect the environmental level of analysis. At the individual level of analysis, the focus is on the individual characteristics of the user: his perception, attention to memory, feelings, motives, persuasive communications, etc. At the environmental level, researchers examine how the group and family influence the implementation of purchasing behavior, what are the situational factors, for example, the atmosphere of the pharmacy, what are the effects of culture, the influence of economic conditions, government regulations. Identifying the needs, demands and interests of the pharmacy on the one hand, and ensuring the well-being of the patient, consumer and society is a matter of social-ethical marketing concept. Thus, this form of marketing accurately expresses the process of pharmaceutical marketing and pharmaceutical assistance implementation [21-22].

### **The relevance of the research**

Pharmacies in the modern pharmaceutical market have a special functional load. In addition to taking care of the image and reputation of the pharmacy, it is obliged to provide competent consultation, pharmaceutical assistance and proper use of integrated activities. It becomes relevant to study the issues of pharmacy, pharmacist, doctor, patient and community relations and the methods of its implementation. This communication process is not one-way, and both society and consumers (patient, doctor) have an influence on marketing. If this interdependence is balanced, then the society and the pharmaceutical establishment itself will be in favorable conditions. The general situation of the mentioned issues determined the relevance of the research [23-24].

### **Aim and objectives of the research**

The purpose of our research is to establish the pharmacy's honest relationship with the patient and the community, taking into account the communication and ethical principles, and in turn, to study the characteristics of the feedback from the patient and the community. Studying the levels of integration between employees and patients in pharmacies and their practical reflection in the Georgian pharmaceutical business, in particular, in pharmacies. Pharmacies are one of the fastest growing areas in Georgia, where the not very useful level of using modern pharmaceutical management and marketing principles is clearly visible.

In addition, we tried to determine to what extent the awareness of pharmacy employees depends on marketing issues and management principles; Relationship between pharmacy employees and patients, communication efficiency; Pharmacy popularity - if the same customer enters the same pharmacy many times; What is the effectiveness of communication with the customer; Due to the fact that marketing communications and ethics are evolving, research analysis will allow us to formulate practical recommendations. And to find out as much as possible the effectiveness of communication with the public and the customer. As well as the norms of important communication and ethics, how correctly it is drawn up, on which the image of pharmacies depends.

### **Research Results**

The following was interestingly revealed from the mentioned data: 29 respondents from the respondents aged 19-30 work in a pharmacy; 31-40 years old - 25; 41-50 years - 9 pharmacists. It was interesting for us to continue the research according to their education and official status. According to the status of the respondents participating in the study (the position held in the pharmacy), it was revealed that 37 respondents have a higher pharmaceutical education; 16- a graduate of the College of Pharmacy; 10 respondents with higher medical education; Among the respondents with other non-medical education - 51 respondents participated; with secondary education-1; and a student - 10.

#### **Q-1. Does pharmacy management use the targeted market selection system?**

All respondents working in pharmacies answered that the management selects target markets based on its goals and resources. Obviously, without it, it will be difficult for the pharmacy to function. (See-Figure-1).

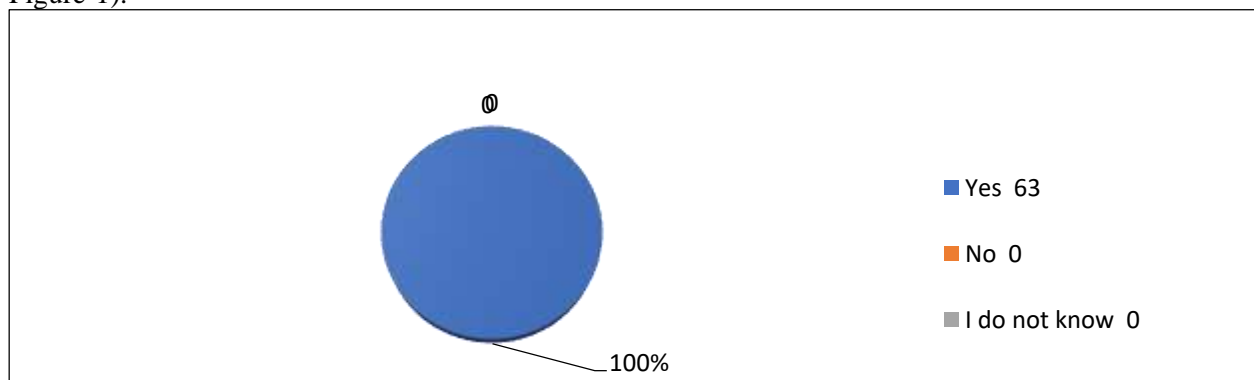


Figure-1.

Also, we received an almost identical answer about the use of marketing complex processing methods, which will help to influence the target market and get the desired result.

**Q-2. Does the pharmacy management advertise the pharmaceutical product?** (See Figure-2).

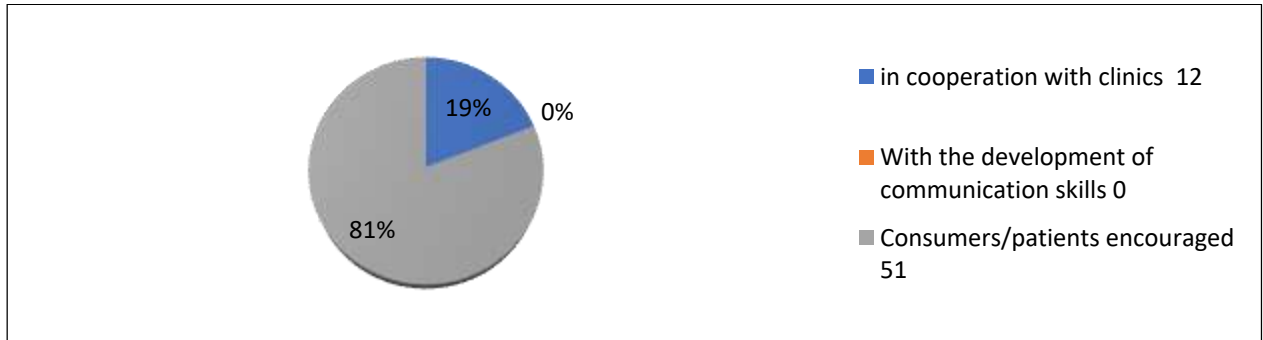


Figure-2.

The management of the pharmacy advertises the pharmaceutical products mainly with the encouragement of consumers/patients. This includes offering discounts and gift cards, promotions, and other activities by pharmacies to attract and retain customers. Also, a small part of the respondents (19%) noted that the management advertises pharmaceutical products in cooperation with clinics. Our next question was related to such an important issue of pharmacy operations as the management of demand for pharmaceutical products and their corresponding satisfaction [25-26].

**Q-3. Does the management of the pharmacy carry out the promotion of medicinal products?** (See Figure-3).

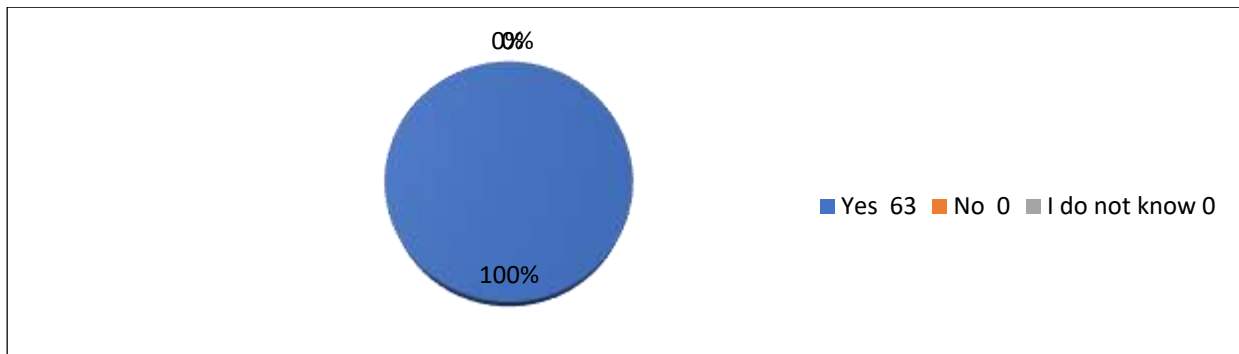


Figure-3.

100% of the respondents noted that the management promotes medicinal products.

The result is natural because, in addition to the companies that produce the pharmaceutical product themselves and promote it in their pharmacies, other pharmacies also cooperate with pharmaceutical companies.

**Q-4. Does pharmacy management study the issue of pharmaceutical product demand and unsatisfactory needs? (See Figure-4).**

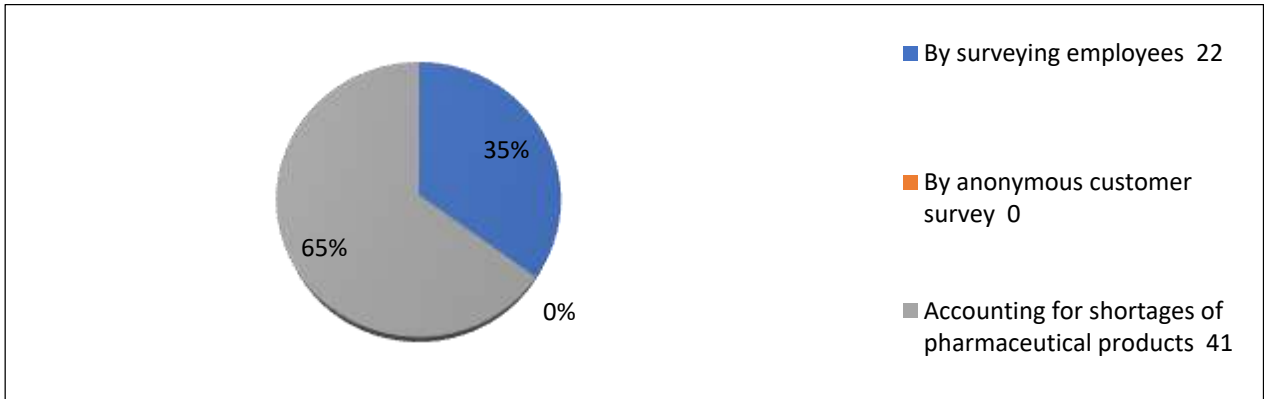


Figure-4.

Out of 63 pharmacists, 22 do not know whether the pharmacy management is studying the issue of product demand and unmet needs; 41- The respondent believes that the management keeps deficit accounting and probably they consider it a more effective way. We think that pharmacy management studies the issue of pharmaceutical product demand and unsatisfied needs mostly by accounting for pharmaceutical product shortages. They probably find it more effective. It has been observed that (100%) the pharmacy uses to improve customer satisfaction, in case of non-availability of the drug, noting the customer's need and in case of availability, informing the customer. This indicates that pharmacies are communicating properly with customers/patients, which will certainly bring positive results [27-28].

**Q-5. Are there noticeable changes in consumer behavior that affect their actions: they are not in a hurry to buy; Are they starting to look for "cheaper" products? (See Figure-5)**

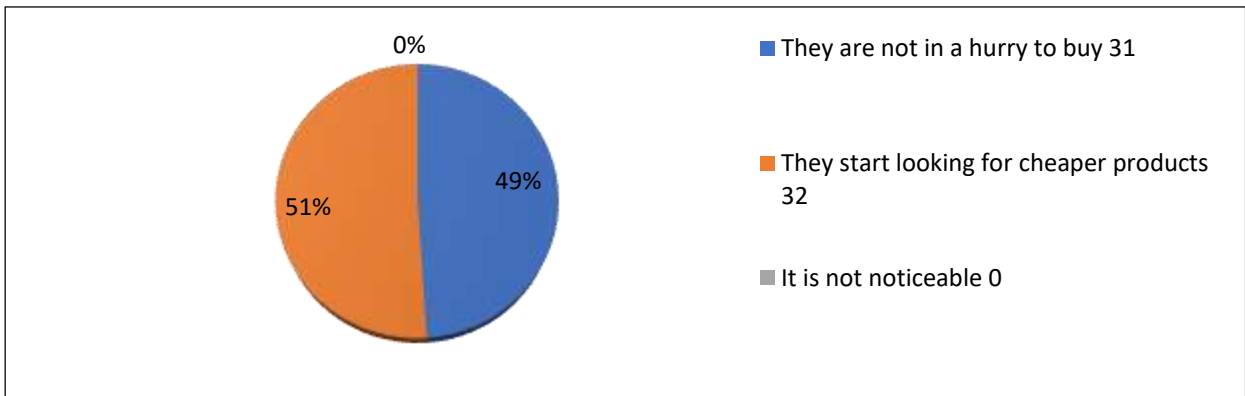


Figure-5.

This is the case when the consumer is not in a hurry to buy the product he needs due to the high price and financial situation (49%) or starts looking for a cheaper product (51%).



**Q-6. For a pharmacy, which form of system is important when interacting with the customer?**  
(See Figure-6).

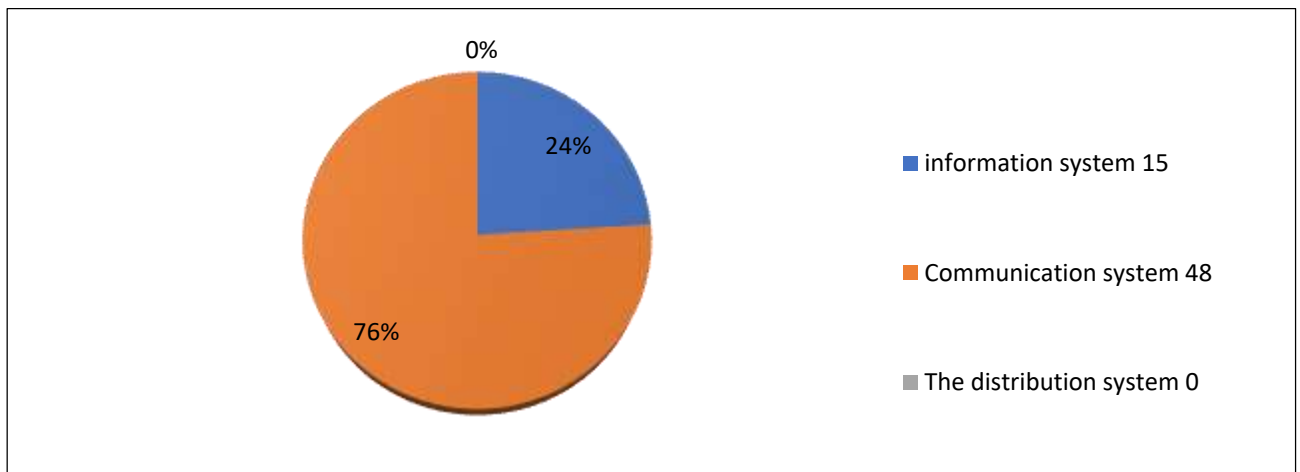
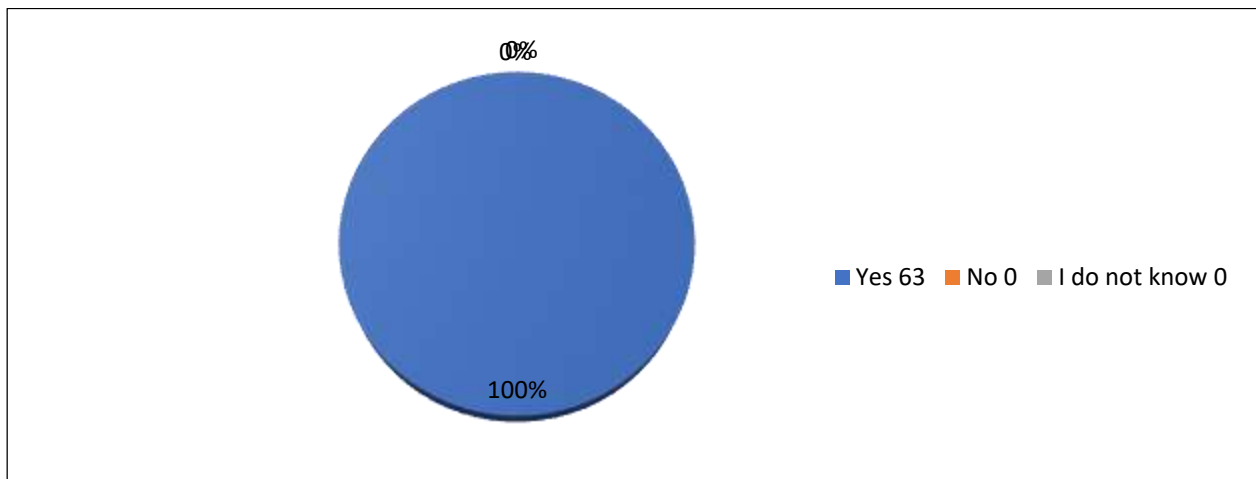


Figure-6.

From the answers to the question, it can be seen that only two forms, informational and communicative, are used during interaction with the customer. Correct and effective communication increases customer loyalty to the pharmacy.

**Q-7. Does pharmacy management conduct marketing research?** (See Figure-7).



(See Figure-7).

100% of the respondents state that the management of the pharmacy conducts marketing research. Which is an effective means of finding information about potential customers and organizing activities.

**Q-8. Does the pharmacy management search for scientifically based information about new pharmaceutical products? (See Figure-8).**

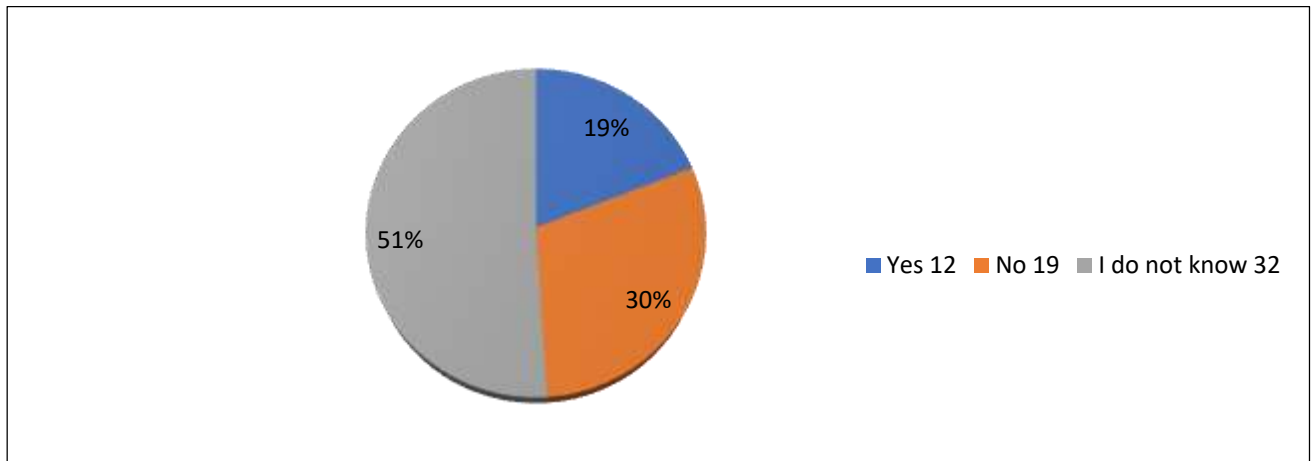
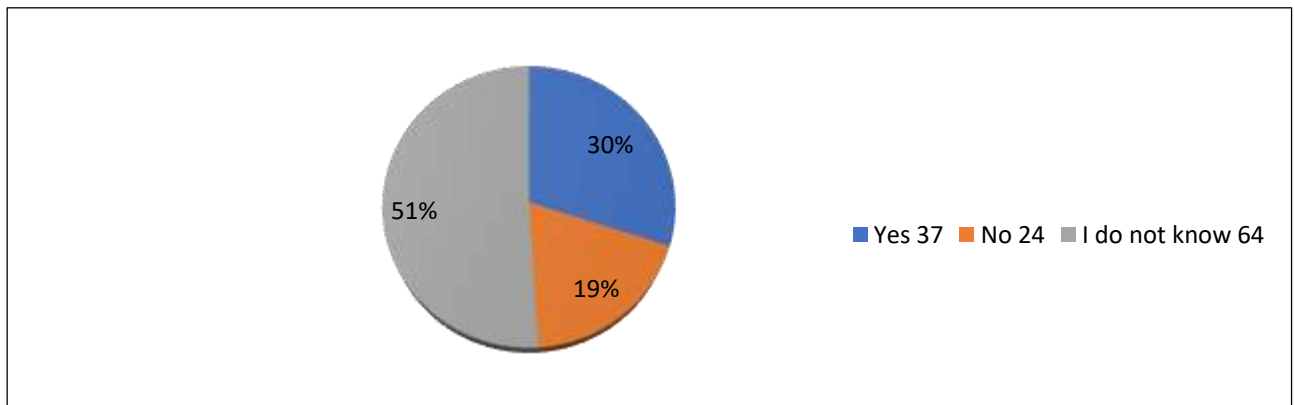


Figure-8.

This means that the management of pharmacies does not try to include new products in their assortment, the effectiveness, quality and safety of which will be scientifically substantiated. And customer/patient confidence will also be high. We consider it unfortunate when the positive answer is only 12%. 32% do not know. The questions drawn up in the second direction of the research, both considered the research of specialists and non-specialists [29-30].

**Q-9. In the pharmacy, are there cases of replacing the drug prescribed by the doctor with another drug? (See Figure-9).**



(See Figure-9).

37 out of 125 respondents indicate that there are cases of replacing one drug with another, which is 30%.

**Q-10. What is the patient's attitude towards the drugs available in the pharmacy?**

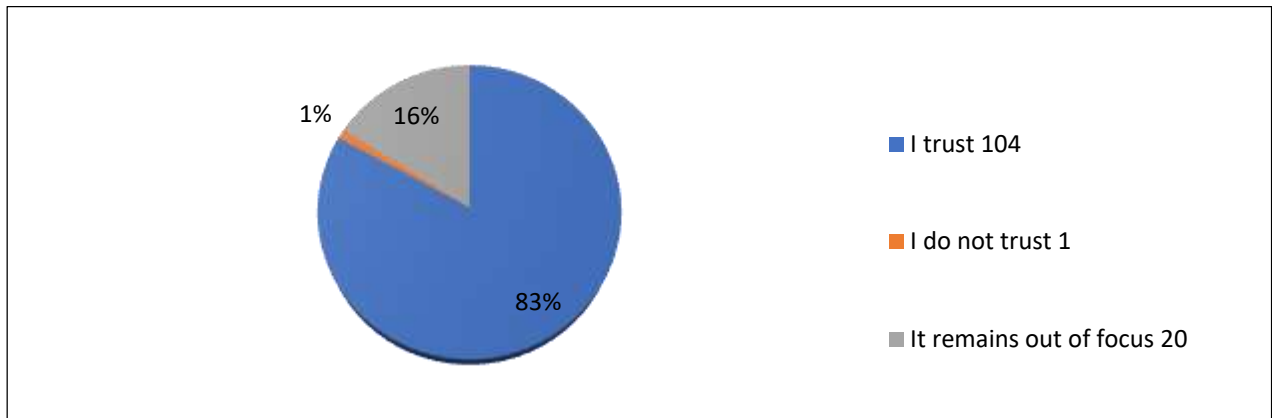


Figure-10.

Most of the respondents (83%) trust the medicines available in the pharmacy. Most likely, this result is due to effective and quality medicines.

**Q-11. Does the pharmacy fully meet the needs of customers? (See Figure-11).**

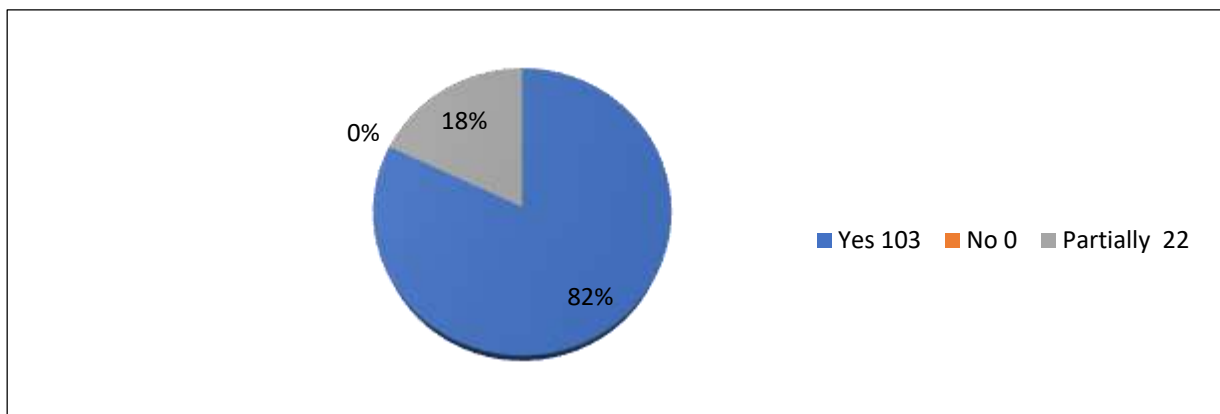


Figure-11.

**Q-12. Is the pharmacist's advice about the drug you need clear? (See Figure-12).**

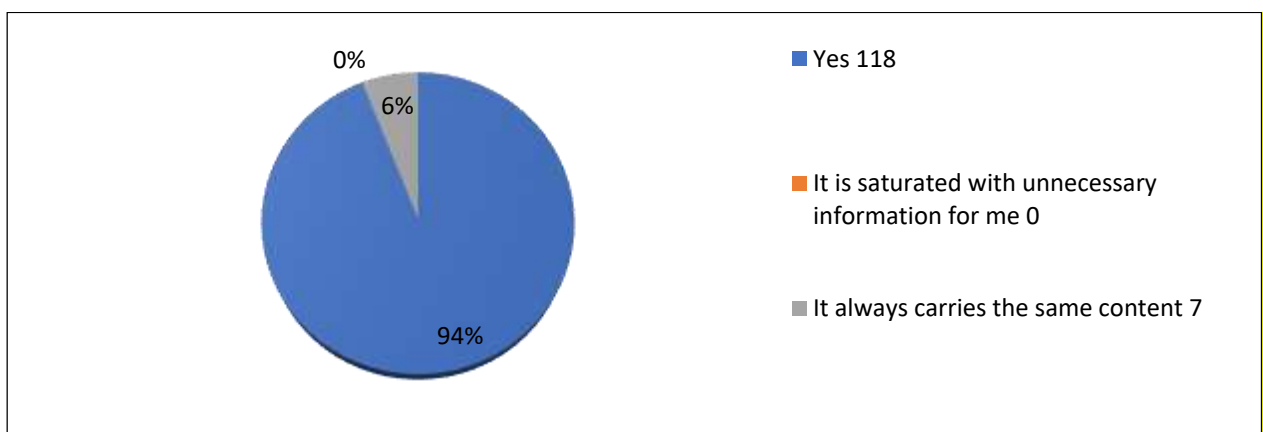


Figure-12.

Q-13. Are you familiar with the concept of social-ethical marketing? (See Fig.13).

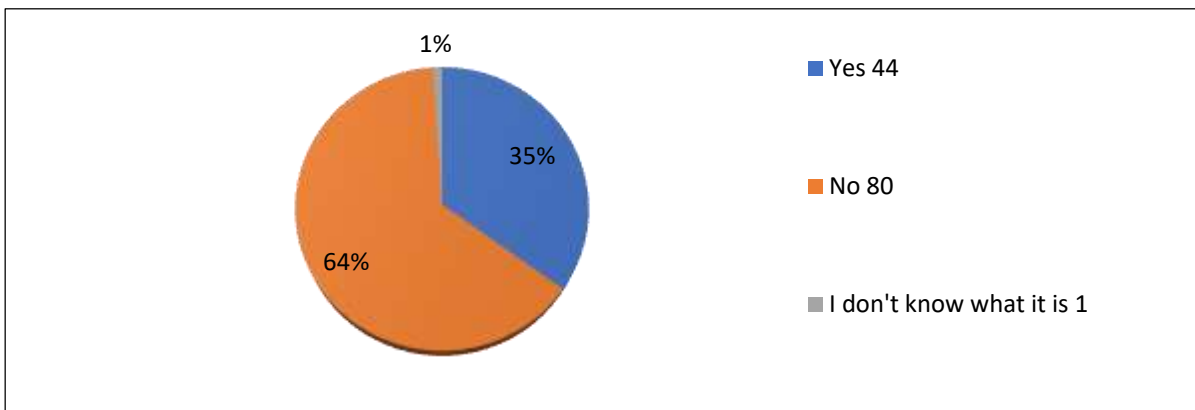


Figure-13.

Q-14. Do you think that the determining indicators when buying a drug are its effectiveness, quality and safety or price? (See Figure-14).

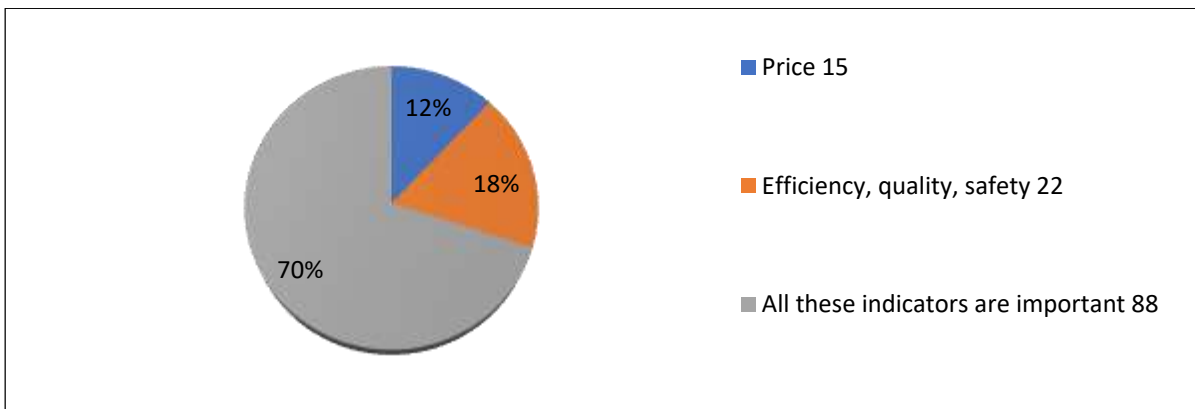


Figure-14.

Price is of primary importance for 12%, which is probably due to their financial situation.

18% consider efficiency, quality, safety as the main indicators. It turns out that for them the price is not as important as the indicators listed above. Most of the respondents (70%) attach importance to all these indicators [31-33].

Q-15. Does the customer who enters the pharmacy notice the price increase? (See Figure-15).

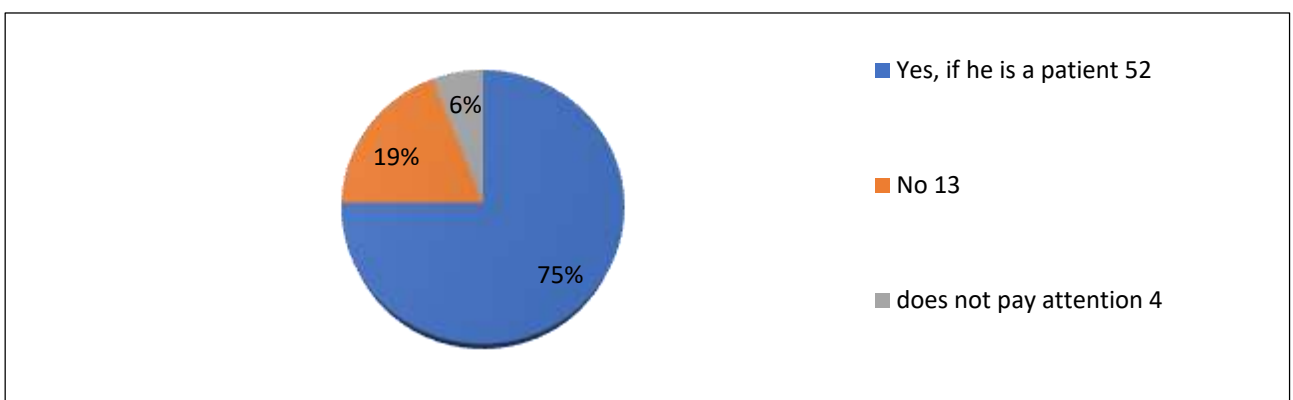


Figure-15.

75% say that patients notice the price increase immediately. Which is natural, if the patient often uses the pharmacy and is certain about the prices, he soon notices the price change. 19% reported that consumers do not notice price increases immediately. Probably, they rarely visit the pharmacy or buy

various medicines. And 6% believe that consumers do not pay attention to the increase in prices. Most likely, the priority for them is the effectiveness and quality of medicines, not the price.

**Q-16. Does the customer believe that the increased price is justified by the high quality of the product?** (See Figure-16)

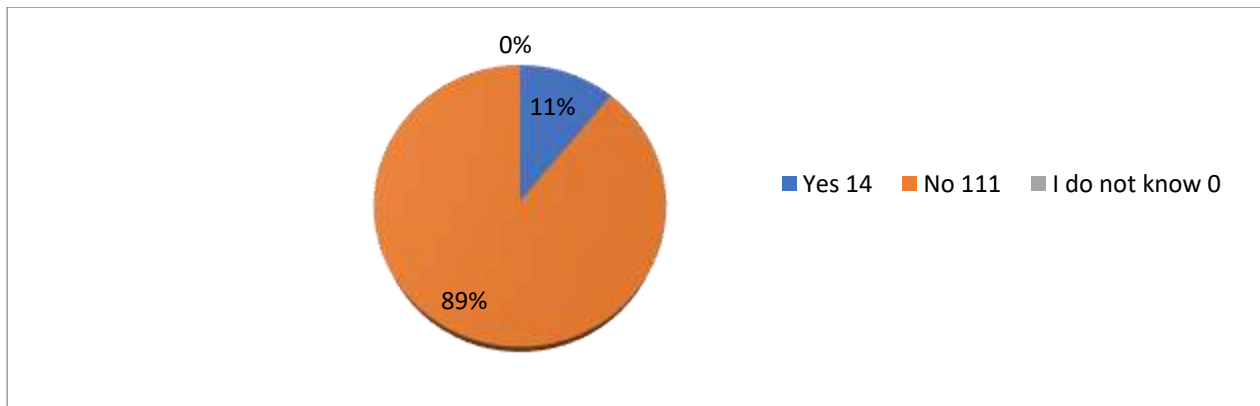


Figure-16.

A small number of respondents (11%) believe that the increased price is justified by the high quality of the product. The majority (89%) do not think so. Most likely, the reason for this is that there are many imported medicines in the Georgian pharmaceutical market, and the increase in prices is related to the increased taxes on the part of Georgian companies [28-33].

### Conclusions

1. The conducted research revealed that the management of the pharmacy advertises pharmaceutical products mainly with the encouragement of consumers/patients. This includes offering discounts and gift cards, promotions, and other activities by pharmacies to attract and retain customers.
2. It was revealed that companies conduct marketing research and use the results of marketing research. But management does not collect scientifically based information about pharmaceutical products for selection.
3. Also, according to the results of the research, a small part of the respondents is familiar with socio-ethical marketing. The result is probably based on the extent to which they consider social responsibility when using marketing.
4. Pharmaceutical marketing is not customer-oriented. Pharmacy management is focused solely on profit. Not all customers have the same needs and needs, they must approach the pharmacy individually and provide the appropriate service, which is an effective means of increasing loyalty.
5. The management of the pharmacy has not developed patient service forms. All patients are served in the same way, regardless of their financial income level.
6. The majority of the respondents noted that the management of the pharmacy is not focused on integrated marketing. Taking into account the concept of integrated marketing creates a continuous functional chain with the customer. Obviously, the separate use of marketing communications does not give the same effect as the integrated one.
7. Most of the respondents believe that the communication system is more important in dealing with the customer. Naturally, correct and effective communication increases customer loyalty to the pharmacy.
8. Cases of replacing the drug prescribed by a doctor with another drug are common, in order to increase the sale of pharmaceutical products in the pharmacy.

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ექთნების როლი პირველადი ჯანდაცვის სექტორის ინოვაციური პროექტების განხორციელებაში

**ROLE OF NURSES IN IMPLEMENTING INNOVATIVE PROJECTS IN PRIMARY HEALTHCARE SECTOR**

*მირანდა ჯანხოთელი (Miranda Jankhoteli)*

*სტუ, ბიზნესის ადმინისტრირების სადოქტორო პროგრამის დოქტორანტი*

*ნატალია ჭანტურია (Natalia Chanturia)*

*სტუ, ასოცირებული პროფესორი*

*მაკა ბულეიშვილი (Maka Buleishvili)*

*სეუ, ასოცირებული პროფესორი*

*მურთაზ თოდაძე (Murtaz Todadze)*

*სტუ, ბიზნესის ადმინისტრირების სადოქტორო პროგრამის დოქტორანტი*

**აბსტრაქტი**

ჯანდაცვის სისტემის ფუნქციონირების სამედიცინო, სოციალური და ეკონომიკური ეფექტიანობის გაუმჯობესების საფუძველია დაავადებების მკურნალობის, დიაგნოსტიკის, პრევენციისა და რეაბილიტაციის ინოვაციური ტექნოლოგიების რაციონალური დანერგვა, ჯანდაცვის დაწესებულებების ყველა დონის სამედიცინო პერსონალის მენეჯმენტისა და პროფესიული მომზადების გაუმჯობესება. ინოვაციური მიდგომები გადამწყვეტ როლს თამაშობს ეკონომიკის ნებისმიერი სექტორის, მათ შორის ჯანდაცვის სექტორის პროგრესულ განვითარებაში. საქართველოს ჯანდაცვის სექტორში მიმდინარე რეფორმებს შორის თვალსაჩინოა საშუალო განათლების მქონე სამედიცინო პერსონალის საქმიანობის ფორმირება, რაც განპირობებულია მოსახლეობის ჯანმრთელობის ნეგატიური ტენდენციებით: იზრდება ქრონიკული დაავადებების პრევალენტობა, მოსახლეობის სიკვდილიანობა და სიცოცხლის საშუალო ხანგრძლივობა გაცილებით ნაკლებია, ვიდრე განვითარებულ ქვეყნებში. ფსიქო-ემოციურ დაძაბულობას, ცხოვრების დონისა და ხარისხის დაქვეითებას თან ახლავს საზოგადოებრივი ჯანდაცვის მაჩვენებლების გაუარესება, ავადობისა და სიკვდილიანობის მატება, პათოლოგიური ხასიათის ცვლილებები, სოციალური და ინფექციური დაავადებების რაოდენობის მატება. ცხადია, არსებული ვითარება მოსახლეობასთან პრევენციული მუშაობის მნიშვნელობის და კომუნიკაციის არასაკმარისი შეფასების შედეგია, კერძოდ, სამედიცინო გამოკვლევებისადმი არასაკმარისი ყურადღების მიქცევა. იმავდროულად, პრევენცია ძალიან ეფექტური აღმოჩნდა როგორც დაავადების ადრეულ სტადიაზე იდენტიფიცირებისთვის, ასევე რისკის ჯგუფების ფორმირებისა და ჯანსაღი კონტიგენტისთვის პროფილაქტიკური ღონისძიებების ჩატარების კუთხით. საექთნო რეფორმის პირობებში, განუზომლად იზრდება მედიის როლი მოსახლეობის სამედიცინო გამოკვლევაში - ის ფუნქციონირებს როგორც დამოუკიდებელი სპეციალისტი, რომელიც ასრულებს უნიკალურ მოვალეობებს დეონტოლოგიური და სამართლებრივი პრინციპების გათვალისწინებით. პრაქტიკაში ინერგება ექთნების მუშაობის ყველაზე თანამედროვე ორგანიზაციული ფორმები. ძალიან მნიშვნელოვანია ექთნების პოტენციალის შესწავლა ცხოვრების ჯანსაღი წესის ფორმირებაში. საგულისხმოა, რომ სათანადოდ არ არის შეფასებული და დაფასებული საექთნო პერსონალის როლი კლინიკურ გამოკვლევაში და,



შესაბამისად, მისი პოტენციალი შორს არის სრულად გამოყენებისგან. საშუალო და უმცროსი სამედიცინო პერსონალის ორგანიზებული და მაღალი ხარისხის, მოქნილი და დინამიური მუშაობა ექიმის და ზოგადად, კლინიკის ეფექტიანობის მთავარი მაჩვენებელია.

სტატიაში განხილულია პირველადი ჯანდაცვის დაწესებულებებში ინოვაციური ტექნოლოგიების დანერგვისათვის საჭირო ძირითადი, ეფექტიანი და უსაფრთხო მიდგომები. დასაბუთებულია ადგილობრივი თემების საჭიროებებზე ორიენტირებული ჯანდაცვის დაწესებულებების ეფექტიანი, ინოვაციური მოდელების შემუშავება.

**საკვანძო სიტყვები:** პირველადი ჯანდაცვა, მიგრაცია, ექთნების როლი, ინოვაციური პროექტები.

## **ABSTRACT**

The basis to improve medical, social and economic efficiency of healthcare system functioning, are rational implementation of innovative technologies of treatment of diseases, diagnostics, prevention and rehabilitation; improvement of management of medical personnel of healthcare institutions at all level and professional training. Innovative approaches play a decisive role in the progressive development of every sector of economy, including the healthcare sector. Among the ongoing reforms in the healthcare sector of Georgia, formation of the activity of medical personnel with secondary education is remarkable, which is preconditioned by negative tendencies of the public health: prevalence of chronic diseases and the mortality of the population is increasing, while life expectancy is significantly shorter than in developed countries. Psycho-emotional tension, decline in level and quality of life are accompanied by worsening of the public healthcare indicators, increasing of morbidity and mortality, changes of pathological characteristics, increasing number of social and infectious diseases. It is obvious, that existing circumstances are result of inadequate assessment of the importance of preventive work with the population and communication, namely, inadequate attention paid to medical examinations. With the nursing reform, the role of a community nurse is dramatically increasing in the medical examination of the population – s/he practices as an independent specialist, who fulfills unique duties by taking into consideration deontological and legal principles. It should be noticed that the role of the nurse personnel is not adequately evaluated and appreciated in a clinical examination, and therefore, their potential is far from being fully used. Organized and high quality, flexible and dynamic work of mid and junior level medical personnel, is a main indicator of efficiency of a doctor or, in general, a clinic.

The article examines main, efficient and safe approaches of implementation of innovative technologies in the primary healthcare institutions. Elaborating of efficient and innovative models of healthcare institutions, which are oriented to the needs of local communities, is substantiated.

**Key words:** primary healthcare, migration, role of nurses, innovative projects.

## **შესავალი**

საექთნო საქმე ჯანდაცვის სისტემის, ჯანმრთელობის მრავალმხრივი დისციპლინის განუყოფელი ნაწილია. საექთნო საქმეს სამედიცინო და სოციალური მნიშვნელობა აქვს, რადგან ის მიზნად ისახავს მოსახლეობის ჯანმრთელობის მხარდაჭერას, გაძლიერებას და დაცვას, დაზარალებულთა დახმარებას და პაციენტების რეაბილიტაციას. „საქართველოში გვაქვს საექთნო პროფესიის რაობისა და ფუნქციების ცოდნის დეფიციტი როგორც საზოგადოების არასამედიცინო ნაწილში (პაციენტები), ასევე, საექიმო და საექთნო პერსონალში“. [2]

მედდის პროფესია ძალიან რთულია. მათზე მინიმუმ ოთხი ტიპის მოთხოვნაა დაწესებული: პროფესიული კომპეტენცია, ფიზიკური გამძლეობა, წესიერება და ცოდნა-უნარების უწყვეტი გაუმჯობესება. ასევე, პაციენტებთან ეფექტური კომუნიკაციის უნარი,

კომუნიკაციის ბარიერების არსის შესწავლა, მათი წარმოშობის მიზეზების იდენტიფიცირება და მათი თავიდან აცილების გზები, სამედიცინო აპარატურის ანტიინფექციური დაცვის სტანდარტიზაციის განხორციელება, ჰოსპიტალური გარემოს ინფექციური უსაფრთხოების ეპიდემიოლოგიური სტანდარტების უზრუნველყოფა ზოგადი მართვის სისტემაში მოსახლეობისთვის პრევენციული და სამკურნალო მომსახურების ხარისხის უზრუნველსაყოფად.

წარმატებული მუშაობისთვის აუცილებელია პროფესიული კომპეტენცია. უნარებისა და ცოდნის უწყვეტი გაუმჯობესება იძლევა სხვა პროფესიის წარმომადგენლებთან კომუნიკაციის შესაძლებლობას. მედისგან საჭიროა წესიერება, რადგან ის იღებს კონფიდენციალურ ინფორმაციას როგორც პაციენტისგან, ასევე მისი ოჯახისგან, ეხება ბევრ ნარკოტიკულ ნივთიერებას, აფასებს სხვა ექთნების მუშაობას, მონაწილეობს ეთიკური თვალსაზრისით რთული გადაწყვეტილებების მიღებაში; ჰქონდეს არა მხოლოდ შესანიშნავი პროფესიული ცოდნა და უნარები, არამედ ჰქონდეს თანაგრძნობის უნარი, იყოს ტაქტიანი ნებისმიერ არასტანდარტულ სიტუაციაში, ჰქონდეს მდგრადობა სტრესის მიმართ. ექთნები ყველაზე მეტ დროს ატარებენ მედიკამენტებთან და დოკუმენტაციასთან მუშაობაში. საკმაოდ დიდი დრო იხარჯება სანიტარული და ეპიდემიოლოგიური რეჟიმის უზრუნველყოფასთან დაკავშირებულ ღონისძიებებზე. ყურადღება აშკარად გასამახვილებელია უშუალოდ პაციენტის მოვლაზე დახარჯული დროის არასაკმარის რაოდენობაზე. პაციენტის ჰუმანური მოპყრობა არანაკლებ მნიშვნელოვანია, ვიდრე პროფესიული უნარები. პაციენტებში კარგი, ოპტიმისტური განწყობის შექმნა, დაავადების ხელსაყრელი კურსის რწმენა სამედიცინო პროფესიონალების მნიშვნელოვანი და საპატიო მოვალეობაა. მედდა ზედამხედველობს პაციენტის მოვლას, ეხმარება მას განახორციელოს ექიმის დანიშნულება, გეგმავს და ახორციელებს საექთნო საქმიანობის პროგრამას, რომელიც მიზნად ისახავს პაციენტის ჯანმრთელობის გაუმჯობესებას, ავადმყოფობის შემდეგ პაციენტის რეაბილიტაციას ან მძიმე შემთხვევებში მის შენარჩუნებას. ექთნები აცნობიერებენ ამ ფაქტს, თვლიან, რომ ცოდნა ძალიან მნიშვნელოვანია მათ საქმიანობაში, რაც ქმნის წინაპირობებს მათი აქტიური მონაწილეობისა საგანმანათლებლო საქმიანობაში როგორც პროფესიული ზრდის, ისე ეთიკისა და სამედიცინო სამართლის სფეროში.

საექთნო მოვლის საჭიროება უნივერსალურია და აუცილებელია ადამიანისთვის დაბადებიდან სიკვდილამდე. პაციენტის დახმარებისას მედდა უნდა შეეცადოს შექმნას მისი სულიერი ღირებულებების, წეს-ჩვეულებებისა და რწმენის პატივისცემის ატმოსფერო. მედდა ინარჩუნებს კონფიდენციალურობას, იცავს პაციენტის ინტერესებიდან გამომდინარე მიღებულ ინფორმაციას, თუ ეს ინფორმაცია არ ეწინააღმდეგება მის ჯანმრთელობას და საზოგადოების წევრების ჯანმრთელობას.

ექთნების ქცევის კოდექსის თანახმად, ექთნების ფუნდამენტურ პასუხისმგებლობას აქვს ოთხი ძირითადი ასპექტი: ჯანმრთელობის ხელშეწყობა, დაავადებების პრევენცია, ჯანმრთელობის აღდგენა და ტანჯვის შემსუბუქება.

ბრიტანულ სამედიცინო ჟურნალში (BMJ) გამოქვეყნებული კვლევის მიხედვით, რომელიც მიზნად ისახავდა, დაედასტურებინა დამოკიდებულება ჰოსპიტლებში საექთნო პერსონალის უნარ-ჩვევებსა და პაციენტების სიკვდილობას, ჰოსპიტლების რეიტინგსა და მომსახურების ხარისხის ინდიკატორებს შორის (Nursing skill mix in European hospitals: cross-sectional study of the association with mortality, patient ratings, and quality of care) დგინდება, რომ იმ ჰოსპიტლებში, სადაც ექთნებს მაღალი კვალიფიკაცია აქვთ, დაბალია სიკვდილობის კოეფიციენტი და დაბალი ხარისხის მომსახურების მიღების რისკი, ასევე, პაციენტები ამ ჰოსპიტლებს ანიჭებენ შედარებით მაღალ რეიტინგს. [2]

ძირითადი ნაწილი

მოსახლეობის ჯანმრთელობა საზოგადოების ყველაზე მნიშვნელოვანი გამოწვევა და ამავდროულად, მიღწევაა, ამიტომ მისი შენარჩუნება და გაძლიერება მნიშვნელოვანი ამოცანაა, რომელშიც ყველამ, გამონაკლისის გარეშე, უნდა მიიღოს მონაწილეობა. ამ ამოცანის შესრულებაში მნიშვნელოვანი როლი ენიჭება ჩვენს მრავალრიცხოვან, შრომისმოყვარე და ჩემი აზრით, ჯანდაცვის ერთერთ მთავარ რგოლს - ექთნებს. ბოლო ათწლეულების განმავლობაში ჩვენს ქვეყანაში საექთნო საქმეს სათანადო ყურადღება არ ეთმობოდა. ექთნის პროფესია სათანადოდ ვერ შეაფასეს და მეორეხარისხოვნად, უპერსპექტივოდ მიიჩნიეს, რამაც უარყოფითად იმოქმედა მომუშავე საექთნო პერსონალის საერთო საკვალიფიკაციო დონეზე: მედიის მუშაობის პრესტიჟი და მისი სოციალური მდგომარეობა დაკნინდა. საგულისხმოა, რომ ბოლო წლებში ჯანდაცვის სამინისტრო მიმართავს თავის ძალისხმევას ჯანდაცვის სისტემისა და სამედიცინო განათლების რეფორმირებისთვის, მნიშვნელოვან ყურადღებას აქცევს საექთნო განათლების განვითარებასა და გაუმჯობესებას, მიზანმიმართულად მუშაობს საექთნო პროფესიისა და მისი მნიშვნელობის აღორძინებისთვის. სახელმწიფო სტრუქტურების ფუნქციონირების პირობებში ცვლილებებმა, ქვეყანაში ეკონომიკური მდგომარეობის სიმძიმემ, საბაზრო ურთიერთობებზე მიმდინარე გადასვლამ წამოაყენა ჯანდაცვის სისტემის ახალი მიდგომები და ინდუსტრიის სპეციალისტების მომზადების, გადამზადებისა და მოწინავე პრაქტიკის მეთოდოლოგიური მხარდაჭერა-გაზიარება, ასევე, მათი პრაქტიკული გამოყენებისათვის საჭირო უნარ-ჩვევების დახვეწა. ეს პროცესები აქტიურად მიმდინარეობს ექთნების ჩართულობით. შეიქმნა საექთნო ასოციაცია. თვალსაჩინო და დასაფასებელია მათი ინიციატივები, მიღწევები როგორც პრაქტიკულ, ისე საგანმანათლებლო პროცესში.

საექთნო საქმიანობის პრესტიჟულობის ცვალებადობის მიზეზები შედარებით განვითარებულ ქვეყნებში, ჩემი აზრით, მრავალფეროვანია: ტრადიციულად ფორმირებული ხედვა, რომ მედდა, როგორც ექიმის თანაშემწე, ასრულებს მხოლოდ დამხმარე სამედიცინო ფუნქციებს; უცხოური გამოცდილების, სამეცნიერო პრინციპების და მართვის მიდგომების გაცნობის სიმწირე, მათი პროფესიული მომზადების დონე. რაც ცალსახად, არ შეესაბამება არსებულ რეალობას. ექთნები არ არიან მხოლოდ ექიმის თანაშემწეები, მისი ინსტრუქციების შემსრულებლები, არამედ დამოუკიდებელი სპეციალისტები ფუნქციონალური მოვალეობების ძალიან სპეციფიკური სპექტრით. ხშირია შემთხვევები, როცა კლინიკაში ექთნები პირველი აღმოჩნდებიან პაციენტის გვერდით მისი მდგომარეობის გაუარესების შემდეგ, კლინიკის გარეთ უწევთ პირველადი სამედიცინო დახმარების გაწევა როგორც უშუალოდ შემთხვევის ადგილზე, ისე აქტიური ზარებით, ასევე პაციენტებისა და მათი ნათესავების ფსიქოლოგიური დახმარება. არ არსებობს "საშუალო" სამედიცინო მუშაკები, არსებობენ ექთნები საშუალო სამედიცინო განათლებით.

რა თქმა უნდა, ჩვენი სახელმწიფოს ეკონომიკურ და პოლიტიკურ საქმიანობაში მიმდინარე ცვლილებებმა მნიშვნელოვნად იმოქმედა ჯანდაცვაზე. მოსახლეობასა და სამედიცინო პერსონალს შორის ურთიერთქმედების ახალი ფორმები ჩნდება. საჯარო სექტორის მუშაკთა უზრუნველყოფის მწირმა ფინანსურმა ჩარჩომ წარმოშვა საბაზრო ურთიერთობები მედიცინაშიც. აღმოცენდა მრავალი ფასიანი მომსახურება. მოწოდებული სამედიცინო დახმარება მოქმედებს როგორც მომსახურება და მოთხოვნადია მხოლოდ და მხოლოდ მაღალი ხარისხის, ეფექტიანი, ეკონომიკურად და გეოგრაფიულად ხელმისაწვდომი მომსახურება. სამედიცინო მუშაკების, განსაკუთრებით ექთნების მაღალი პროფესიონალიზმის საჭიროებამ გამოიწვია პირველად მომზადებაში ცვლილებების შეტანა. ამჟამად, არსებობს მრავალ დონის სისტემა: ძირითადი (სამედიცინო სკოლები),

მოწინავე (კოლეჯები) და უმაღლესი დონე (სამედიცინო უნივერსიტეტების უმაღლესი საექთნო განათლების ფაკულტეტები). შემუშავებულია პროფესიული საგანმანათლებლო პროგრამის ჩარჩო- დოკუმენტი, რომლის მიზანია უზრუნველყოს ადგილობრივ და საერთაშორისო ბაზარზე კონკურენტუნარიანი, ზოგად მოვლაზე პასუხისმგებელი ექთნის მომზადება.

ჯანდაცვის მუშაკები, როგორც წესი, მიემგზავრებიან იმ ქვეყნებში, სადაც მათ უკეთეს სამუშაო პირობებს შესთავაზებენ. მნიშვნელოვანი, მაგრამ მიგრაციის ერთადერთი სტიმული ღირსეული ხელფასია. სხვა მიზეზებში შედის უფრო მიმზიდველი სოციალური პირობები, პროფესიული ზრდის შესაძლებლობები, მართვის ეფექტიანი სისტემა და პოლიტიკური სტაბილურობა ქვეყანაში.

ჯანდაცვის მუშაკების გადაადგილებას აქვს როგორც უარყოფითი, ასევე დადებითი შედეგები. როდესაც ექიმებისა და ექთნების მნიშვნელოვანი რაოდენობა ემიგრაციაში მიდის, ქვეყნები, რომლებმაც დააფინანსეს მათი განათლება, კარგავენ ინვესტიციებს მათში. თუმცა, ფინანსური ზარალი არ არის ყველაზე დამანგრეველი. თუ ქვეყანაში არსებობს არაეფექტური ჯანდაცვის სისტემა, მისი შრომითი რესურსების გაჟონვამ შეიძლება მთელი სისტემა კოლაფსის ზღვარზე დააყენოს ადამიანის სიცოცხლის დაკარგვის ჩათლით.

დადებით მხარეს წარმოადგენს ის, რომ მიგრაციის წყალობით, ყოველწლიურად მილიარდობით დოლარის ფულადი გზავნილები მიიღება დაბალშემოსავლიან ქვეყანაში, რაც ხელს უწყობს სიღარიბის დაძლევას. გარდა ამისა, ჯანდაცვის მუშაკებს შეუძლიათ დაბრუნდნენ თავიანთ ქვეყნებში შემენილი უნარებისა და ცოდნის მნიშვნელოვანი მარაგით.

ქვეყნების წარმატებული განვითარების მხარდასაჭერად ტექნოლოგიების შექმნისა და დანერგვის აუცილებლობას ხაზს უსვამს გაერო, რაც განსაკუთრებით მნიშვნელოვანია გარდამავალი და ერთ სულ მოსახლეზე დაბალი შემოსავლის მქონე ეკონომიკის მქონე ქვეყნებისთვის. ეს სრულად ეხება სამედიცინო ინდუსტრიას, რადგან ეს არის ტექნოლოგიური გაუმჯობესება, რაც შესაძლებელს ხდის მნიშვნელოვანი პოზიტიური ცვლილებების უზრუნველყოფას მედიცინის განვითარებაში. პრაქტიკულ ჯანდაცვაში თეორიული ცოდნისა და განვითარებული ტექნოლოგიების დანერგვა გადამწყვეტი ფაქტორი ხდება მოსახლეობის ჯანმრთელობის მაჩვენებლების გაუმჯობესებისა და თანამედროვე სამედიცინო მიღწევებით პაციენტებისთვის მაქსიმალური სარგებლის მიღების მიზნით.

ინოვაციური პროცესების განხორციელების მნიშვნელოვანი საფუძველია ჯანდაცვის დაწესებულებების საქმიანობაში მოწინავე ტექნოლოგიების გამოყენების ინტეგრირებული მიდგომის შემუშავება და ინოვაციური მოდელების პრაქტიკული შედეგების ეფექტიანობის შეფასება, განსაკუთრებით ისეთ პრიორიტეტულ ჯანდაცვის სექტორში, როგორცაა პირველადი ჯანდაცვა (PHC). ეს განპირობებულია იმით, რომ მოსახლეობისთვის სამედიცინო მომსახურების ეფექტიანობის, ხარისხისა და ხელმისაწვდომობის უმაღლესი დონის მიღწევა დიდწილად განისაზღვრება პირველადი ჯანდაცვის ფუნქციონირებით, რომლის პრიორიტეტული განვითარება განისაზღვრება ჯანდაცვის სფეროში სახელმწიფო პოლიტიკის ერთ-ერთი მთავარი სტრატეგიით, სამედიცინო მომსახურების თანამედროვე სისტემის საფუძველზე. ინოვაციის კონცეფცია, როგორც სისტემური ცოდნა, რომელიც მიზნად ისახავს მომსახურების წარმოებას ან გარკვეული პროცესის პრაქტიკაში დანერგვას, განსაკუთრებულად მნიშვნელოვანია მედიცინაში.

საზოგადოებაზე ორიენტირებული პირველადი ჯანდაცვის სისტემის მოდელის ძირითადი კომპონენტები ქმნიან ერთიან ორგანიზაციულ და ფუნქციურ სტრუქტურას,

რომელიც გაერთიანებულია კონკრეტული პაციენტის, მისი ოჯახის და სახელმწიფო საზოგადოების ჯანდაცვის ძირითადი პრინციპის შესაბამისად; როდესაც პუდ სისტემის ექიმები ექთნებთან ერთად მოქმედებენ როგორც სამედიცინო დახმარების კოორდინატორები, ყველა საჭირო სპეციალისტის, დაწესებულებისა და ორგანიზაციის აქტიური ჩართულობით, ამისათვის შესაბამისი მომზადებით, საჭირო ლოგისტიკური და ადამიანური რესურსებით [3, გვ 193]

ბოლო წლებში მუდმივად იზრდება მოსახლეობისთვის გაწეული სამედიცინო მომსახურების მოცულობა, რაც იწვევს პოლიკლინიკის ექთნების დატვირთვას, რასაც ამძიმებს რიგ განყოფილებებში საექთნო პერსონალის ნაკლებობა. ამ პირობებში, პოლიკლინიკის ექთნების პროფესიული აქტივობა, არსებული მაღალი ფსიქო-ემოციური სტრესით და მნიშვნელოვანი ფიზიკური დატვირთვით, უარყოფითად მოქმედებს მათ ჯანმრთელობის მდგომარეობაზე - ექთნების უმეტესობას ქრონიკული დაავადებები აქვს. გარდა ამისა, ფიზიკური და ფსიქო-ემოციური სტრესი სამსახურში უარყოფითად მოქმედებს ექთნების ოჯახურ ცხოვრებაზე, რამაც შეიძლება შეცვალოს მათი ემოციური ფონი და უარყოფითად იმოქმედოს სამუშაო გარემოში პაციენტებთან ურთიერთობაზე.

ჩვენს ქვეყანაში სამედიცინო ინოვაციების განვითარების ძირითადი წყაროა უმაღლესი სამედიცინო საგანმანათლებლო დაწესებულებები, კვლევითი დაწესებულებები, რომელთა ინოვაციური საქმიანობა შეფასებულია პატენტების, გამოგონებების, პუბლიკაციების რაოდენობით. ამასთან, აღსანიშნავია, რომ პრაქტიკული ჯანდაცვისთვის უფრო მნიშვნელოვანი მაჩვენებლებია კლინიკურ პრაქტიკაში ახალი სამედიცინო ტექნოლოგიების დანერგვის შესრულების მაჩვენებლები, ტექნოლოგიური სამედიცინო ინოვაციების განმახორციელებელი ჯანდაცვის დაწესებულებების პროპორცია, ანუ ახალი ან გაუმჯობესებული სამედიცინო პროდუქტების, სამუშაოების, მომსახურების, ტექნოლოგიური პროცესებისა და სხვა სახის ინოვაციური აქტივობების შემუშავება და განხორციელება.

ამის გათვალისწინებით, პრაქტიკული ჯანდაცვის დაწესებულებების რეალური ინოვაციური განვითარების შესაფასებლად, მიზანშეწონილია არ გავამახვილოთ ყურადღება ფუნდამენტური კვლევის ეფექტურობის შეფასების ზოგადად მიღებულ ინდიკატორებზე (გაცემული საპატენტო განაცხადებისა და პატენტების რაოდენობა, პუბლიკაციის საქმიანობის ინდექსი თანამშრომლები და ა.შ.), ვინაიდან მათი რაოდენობა გავლენას არ ახდენს მოსახლეობის ჯანმრთელობის მაჩვენებლებზე და გათვალისწინებულია რეგიონის ინოვაციური განვითარების ზოგად ინდექსში. ამავდროულად, პრაქტიკული ჯანდაცვისთვის, უპირველეს ყოვლისა, მნიშვნელოვანია სამედიცინო და დემოგრაფიული მაჩვენებლები, რომელთა დინამიკაზე გავლენა უნდა მოახდინოს ინოვაციების დანერგვამ, ასევე სამედიცინო ტექნოლოგიების კლინიკურ პრაქტიკაში დანერგვის ეფექტურობის რაოდენობრივმა და ეკონომიკურმა მახასიათებლებმა.

მედდას შეუძლია დამოუკიდებლად აკონტროლოს, უმკურნალოს (შეინახოს საექთნო სამედიცინო ჩანაწერები) პაციენტების გარკვეული ჯგუფებს (მაგალითად, ჰოსპისებში) და გამოიძახოს ექიმი მხოლოდ კონსულტაციისთვის. „ზოგადად ითვლება, რომ „რაც არ არის დოკუმენტირებული - არ გაკეთებულა“. ამიტომ სამედიცინო პერსონალი (ექთანი, ექიმი) თვითონ წყვეტს რისი დოკუმენტირება უნდა მოხდეს“. [6]

გარდა ამისა, იქმნება და ფუნქციონირებს ექთნების საზოგადოებრივი ორგანიზაციები, ჯანდაცვის სისტემაში საექთნო პრობლემების გათვალისწინებით, პროფესიის პრესტიჟის გაზრდით, ორგანიზაციის წევრების მოზიდვით საექთნო სფეროში სამეცნიერო კვლევებზე, კონფერენციების ჩატარებით, სემინარებით აქტუალურ საკითხებზე საექთნო საქმეში,

ექთნების სამართლებრივი უფლებების დაცვა და ა.შ. თუმცა, პრობლემა ის არის, რომ ექთნების მრავალფეროვანი მოვალეობები და ამბულატორიული კლინიკებისთვის დამახასიათებელი აქტივობების დიდი მოცულობა ხშირად ხელს უშლის ექთნების მუშაობის ეთიკური და დეონტოლოგიური ასპექტების სრულ განხორციელებას სამართლებრივ პრინციპებთან შესაბამისობაში. იმავდროულად, მათმა უფულებებელყოფამ შეიძლება გამოიწვიოს ძალიან სერიოზული უარყოფითი შედეგები პაციენტის ჯანმრთელობაზე. ექთნებს, უახლესი ცოდნით, შეუძლიათ შეასრულონ თავიანთი სამუშაო უფრო ხარისხიანად და ეფექტურად, რაც გავლენას მოახდენს არა მხოლოდ პაციენტების კეთილდღეობაზე, არამედ ექთნების კმაყოფილების ხარისხზე.

დასკვნა

ამრიგად, ჯანდაცვაში სერვისებისა და მომსახურების ხარისხის აუცილებელი დონის უზრუნველყოფა უნდა განხორციელდეს ჯანდაცვის სისტემის ყველა დონეზე ურთიერთდაკავშირებული ღონისძიებებით რესურსების გამოყენების ოპტიმიზაციის, მოდერნიზაციის, ინოვაციების, მართვის თანამედროვე ტექნოლოგიების გამოყენებით, მიღებული შედეგების ეფექტურობის შემდგომი შეფასებით.

ჯანდაცვის დაწესებულებების ეფექტური ინოვაციური მოდელების დანერგვა, რესურსების რაციონალური გამოყენება, საექთნო ინფორმატიზაცია და აქტიური ჩართულობა, რომლებიც ორიენტირებულია ადგილობრივი მოქალაქეების საჭიროებებზე როგორც ქალაქებში, ისე სოფლად. მნიშვნელოვანია სახელმწიფოს მხრიდან სამედიცინო პერსონალის თვითრეგულირებადი საშუალო ხელფასის გადახედვა, სამოტივაციო სისტემების შემუშავება, რაც გააუმჯობესებს სამედიცინო მომსახურების ხელმისაწვდომობისა და ხარისხის დონეს, დაავადებათა პრევენციას და ცხოვრების ჯანსაღი წესის პოპულარიზაციას.

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გადამოწმების თარიღი 05.12.2022

**MAIN ASSESSMENT ISSUES OF THE FEATURES OF THE PHARMACEUTICAL SAFETY  
COMPLEX QUESTIONS REFLECT ON PHARMACEUTICAL ORGANIZATIONS IN  
GEORGIA**

***Nana Gorgaslidze***

*PhD, Doctor of Pharmaceutical Sciences, Professor of Tbilisi State Medical University, Faculty of Pharmacy, Head of The Department of Social and Clinical Pharmacy, Tbilisi, Georgia*

***Nodar Sulashvili***

*PhD, Doctor of Pharmaceutical Sciences, Invited Lecturer of Scientific Research-Skills Center at Tbilisi State Medical University, Tbilisi, Georgia; Associate Professor of Division of Pharmacology of International School of Medicine at Alte University; Associate Professor of Pharmacology of Faculty of Medicine at Sulkhan-Saba Orbeliani University, Associate Professor of Pharmacy Program at Shota Meskhia Zugdidi State University; Invited Professor of The School of Health Sciences, The University of Georgia, Tbilisi, Georgia.*

*ORCID ID: 0000-0002-9005-8577.*

***Marina Giorgobiani***

*MD, PhD, Doctor of Medical Sciences, Professor of Tbilisi State Medical University, Faculty of Public Health; Department of Hygiene and Medical Ecology, Tbilisi, Georgia;*

*ORCID ID: 0000-0003-0686-5227*

**ABSTRACT**

Occupational safety is a broad commandment and encompasses in itself a safe environment saturated with sanitary norms, primarily the safe use of medicines, subject to all conditions. This determines not only the quality, but also the prevention of a dangerous environment for the population and employees. The all the requirements are necessary for working conditions including normalized working hours, temperature regime, degree of pollution, fire condition, as well as other unforeseen cases, must be lawfully observed. The aim of the research was to study the features of the pharmaceutical safety complex questions reflect on pharmaceutical organizations in Georgia and to identify their strengths and weaknesses, pros and cons, for to reflect a specific problem and to find ways to solve, eliminate and resolve it. In order to achieve the above-mentioned goal, we considered it necessary to determine the quality and compliance of the work space safety of the research facilities with the Organic Law of Georgia on Labor Safety. Assessing the risk of harm to personnel and consumers was considered an existing epidemic. Regarding safety - according to the data of the study period. The information source of the paper is the materials of the survey of pharmacists and its statistical collections, Georgian laws, laws and other legal acts. In general, the subject of research was the Georgian pharmaceutical market, which creates a danger not only for consumers but also for employees. The objects of research are pharmacies operating in the market, pharmaceutical companies, regulatory bodies and employees working there. Based on the existing theoretical foundations of occupational safety, we considered it necessary to identify the methodological and practical issues, the set of materials from which we selected the goal of research.

Healthcare is the area of activity that is most strictly regulated by the state. Today, the health care system, which includes all departmental and sectoral levels of the state economy, is not only a combination of medical-prophylactic, rehabilitation and recovery institutions, but also it is closely connected with ecology, labor protection, social programs, etc. One of the most important functions of health is to promote and restore the balance and harmony of individual and public health. According the study results was found nesesitys and demands of: Expand the scope of the draft law on labor safety and extend it to all places of employment, without exception; Equip the labor inspectorate with an unconditional and free access to the places of employment, which implies the authority of the



mechanism by its own decision, to carry out inspections of the places of employment without the prior permission of the court.

The law of Georgia on labor safety envisages an appropriate system of sanctions, including the proper rules for the application of sanctions and adequate amounts of fines, which will have both preventive and responsive effects. The state should create an appropriate legislative and institutional framework; We think this will help transform the existing department into an effective labor inspectorate. The possibility will be created of the institutional capacity of its independence and efficiency and the law will also provide guarantees for the individual independence inspectors. Also, the draft law should explicitly indicate the labor inspectorate as the body responsible for law enforcement.

**Key words:** Issues, challenges, occupational, safety, pharmacists, pharmaceuticals, organizations, Georgia.

## **INTRODUCTION**

The purpose of the labor legislation in Georgia is to regulate the relationship between the employer and the employee through clearly defined legal regulation that excludes the exploitation of the employee and creates the possibility of work based on human dignity, freedom and self-development. Accordingly, the purpose of labor legislation is to regulate private legal relations at the normative level to the extent that it is necessary for the proper social protection of workers. The employer is obliged to provide the candidate with information about the work to be performed, working conditions, contract form, remuneration and legal status of the employee during the employment relationship. The performance of the assigned work is usually subject to organizational regulation and the daily and/or weekly hourly work schedule set by the employer. Under such organizational arrangements, it is important to classify time into work, break, and leisure time [1-2].

Working time includes the time that an employee must use to fulfill a contractual obligation. Break time is the period of time between working hours, while break time is defined by labor law as leave periods and days off. Overtime work is voluntary, although the Labor Code provides for exceptional cases where overtime work becomes mandatory for an employee. These cases are:- To prevent natural disasters and/or to eliminate their consequences;-Unpaid; To prevent an industrial accident and/or to liquidate its consequences with appropriate compensation. The Labor Code establishes the right of the employer to take paid leave of 24 working days and unpaid leave of 15 calendar days. Depending on the specifics of the work, the Labor Code provides for additional leave for those working in heavy, harmful or hazardous work in the amount of 10 calendar days a year. The list of such works is approved by the order of the Minister for Internally Displaced Persons from the Occupied Territories of Georgia, Labor, Health and Social Protection [3-4].

The International Labor Organization has developed international labor standards, which are set out in the Declaration of Fundamental Principles and Rights, which are widely recognized and of particular importance. They are widely used regardless of a country's level of development or ratification of cultural property and related conventions [5-6].

These standards are composed of qualitative rather than quantitative standards and do not define specific levels of working conditions, wages, or occupational safety and health standards. They are not intended to measure comparative advantage. The main labor standards are human rights, they are recognized in internationally ratified international human rights instruments, including the Convention on the Rights of the Child [7-8].

Employees' rights in the UK include the right to work, a paid disciplinary process during which they are eligible for escort, daily breaks, paid leave and more. Safety and social resilience include: protecting employees' rights and safe working conditions, preventing human trafficking and eliminating child labor. In pharmaceutical institutions, hygiene standards are required and adhered to. Pharmacy institutions are all institutions in which pharmaceutical activities are carried out. When carrying out pharmaceutical activities under the influence of high-risk factors, possible cases of occupational diseases of an employee may develop [9-10].

An occupational disease (acute or chronic) develops under the influence of factors that threaten the working environment and the production process, causes a deterioration in his health and/or restriction of his professional ability to work in the short or long term, and is determined by the legislation of Georgia. Therefore, the specifics of pharmaceutical activities should be taken into account, in particular: the development of a new pharmaceutical product (molecule), the use of various chemicals and technologies, which, in turn, require special precautions. Also, one cannot ignore the necessary characteristics during storage, transportation, delivery, consumption of finished products, and, as a result, the need to comply with sanitary and hygienic working conditions [11-12].

The International Labor Organization (ILO) was formed in 1919 as part of the League of Nations to protect workers' rights. Later, the ILO joined the United Nations. The UN itself protects the rights of workers.

1. Everyone has the right to work, free choice of work, fair and favorable working conditions and protection from unemployment;
2. Everyone has the right to equal pay for equal work without any discrimination;
3. Everyone who works has a just and favorable standard of living that ensures the dignity of himself and his family and, if necessary, provides other means of social protection;
4. Everyone has the right to form trade unions and join trade unions to protect their interests.
5. Everyone has the right to rest, including reasonable limitations of working hours and paid vacation.

Related to the pharmaceutical industry: measures related to waste collection, processing, waste disposal, pollution control and other waste management processes. Therefore it is necessary to consider:

1. Sanitary-hygienic characterization of working conditions - physical, chemical, biological factors of the production and/or working environment and the labor process;
2. The permissible norms of chemical substances in the air of the working zone of the pharmaceutical institution shall be used for the hygienic assessment of the working conditions for the following purpose: A) To determine the conformity with the hygienic norms to check the working conditions of the employees and to make a hygienic conclusion; B) To determine the priority direction during the implementation of remedial measures and to determine its effectiveness; C) To create a database at the level of enterprise, field, region, republic; D) To determine the level of occupational risk, to take preventive measures and to justify social protection measures; E) To investigate cases of occupational diseases and poisoning [13-15].

ISO – The normative act of the International Organization for Standardization provides:

1. The purpose of labeling and marking hazardous chemicals is to inform the contact persons and the user about the harmful effects of these substances on health and the environment, in order to ensure their safe use;
2. In order to safely treat a hazardous chemical and maintain its consumer properties, the creator/manufacturer shall classify the substance / preparation according to the hazard before submitting it to the state examination and registration application, as well as develop a draft of the mark and label;
3. Each category of hazard classification shall be abbreviated, accompanied by the relevant risk phrase or phrases;
4. If the substance is classified as flammable, sensitizing or hazardous to the environment, only the phrase risk shall be used;
5. If a substance is classified as carcinogenic, mutagenic or toxic, the appropriate abbreviation is used to indicate the category (eg 1,2,3) [16-18].
6. Hazard classification categories are expressed by the following abbreviations: a) Explosive: E b) Oxidizing: O c) Particularly flammable: F + d) Highly flammable: F flammable: R10 f) Highly toxic: T + g) Toxic: T h) Harmful: Xn i) Corrosive: C j) Irritant: Xi l) Sensitizing: R42 and / or R43 m)

Carcinogenic: Carc. Cat. (1) n Mutagenic: Muta. Cat. (1) n For toxic reproduction: Repr. Cat. (1) o for hazardous environment: N and / or R52, R53, R59.

7. Hazard classification categories are represented by symbols with risk R-phrases and safety S-phrases.

8. The user who carries out the use of hazardous chemicals is obliged to ensure the maintenance of the label and mark on the container.

In order to investigate and study the possible danger, the data are important, in particular the information on the label, which is emphasized in the mentioned normative act. Required:

A) For the substance - trade name, chemical name, synonyms common according to IUPAC and CAS number; B) For the drug - trade name, chemical names of the constituents according to IUPAC, CAS numbers and concentrations; C) State registration number; D) Scope of application; E) Complete information about the manufacturer, importer or distributor of the substance / preparation: name, surname, address, telephone; F) Date of manufacture, expiration date, batch or series number, storage conditions, net, mass; G) Symbols and signs of the relevant classification of danger; H) R-phrases indicating a specific hazard; I) S-phrases denoting security measures; J) Information on first aid.

The same document defines:

1. How to provide the required information on the label: A) For hazardous chemicals used within the country - in Georgian; B) For export chemicals in several foreign languages (English, Russian, German, French, Spanish, etc.); C) The inscription should be easy to understand for the carrier and the professional user.

2. The label shall indicate the prohibition of re-use of packaging or material, as well as recommendations for its disposal and decontamination;

3. The label must be firmly affixed to the packaging container or material as soon as the chemical is packaged;

4. The dimensions of the label are determined according to the volume of the container. The size of the label should not exceed: a) in case of volume up to 3 liters - 52X74 mm; B) in case of volume more than 3 liters and not more than 50 liters - 105X148 mm; C) in case of volume more than 50 liters and not more than 500 liters - 148X210 mm;

5. Each symbol on the label should occupy 1/10 of the surface of the container and at the same time should not be less than 1 cm;

6. Danger symbols shall be displayed in accordance with Annex 3. If the danger is indicated by more than one symbol, then on the label: A) When displaying the necessary E symbol, it is not necessary to display the F, F + and O symbols; B) It is not necessary to display the symbols Xn, Xi, C when the necessary T + or T symbol is displayed; C) it is not necessary to display the symbols Xn, Xi when displaying the necessary C symbol; D) Necessary Xn, display of the symbol Xi is not required when displaying the symbol;

7. Symbols should be drawn in a square on a black, orange-yellow background;

8. Risk phrases for the label are selected according to the hazard criteria. A maximum of six phrases are used to describe the risk. Mixed risk phrases are used when necessary. If a substance is characterized by several categories of hazard the standard phrases should cover all of them;

9. Safety S-phrases for the label are selected according to the risk phrases. A maximum of six S-phrases are usually sufficient to form security measures [19-21].

From a safety point of view, special importance is attached to the transportation of a pharmaceutical product, which is set out in the same Act as follows:

1. In case of transportation of a chemical substance, the label of the transport container shall include additional information on the number of packed container places placed in the transport container, the net and gross mass of each place, an indication on the normative-technical documentation;

2. If it is practically impossible to label and mark the container of a hazardous chemical due to the size of the container or the nature of the packaging, the relevant information must be reflected in the attached documentation;

3. Requirements for marks include: A) The markings on the label must reflect accurate information about the hazardous chemical; B) The label must be firmly attached to the container. Its size must comply with the requirements set by the norms. The inscription should be clear and easy to understand; (C) Labels with signs and symbols depicted on them must be uniform, including the R-phrases of risk and the S-phrases of safety used in the colors used [22-23].

This document addresses the safety issues of the pharmaceutical product in pharmaceutical establishments, as well as the cases when the patient uses the pharmaceutical product. The Ministry of Labor, Social Affairs, and the Ministry of Internally Displaced Persons from the Occupied Territories of Georgia (hereinafter referred to as the Ministry) is the Labor Safety Supervision Authority in Georgia. Protecting the health of the employed population, preventing occupational and occupational diseases, promoting a safe environment in the workplace. The beneficiaries of the program are citizens of Georgia. The program provides state-sponsored occupational health research for various services, including state-owned enterprises [24-25].

The employer is obliged to provide the employee with the safest working environment for health. The need for individual measures to protect and maintain the health of employees is particularly high in some areas of employment. In order to protect the health of employees in the workplace, as well as the importance of the work performed, national legislation provides for cases and rules for mandatory periodic medical examination of an employee at the expense of the employer. Periodic and regular medical examinations are required depending on the content of the activity. With the exception of cases provided for by a regulatory enactment, the employer has the right to determine additional conditions for a medical examination [26-27].

Working conditions. An important prerequisite for the rational use of employees' working time and, in general, for increasing the efficiency of their work are normal working conditions and the establishment of rational internal rules for work and rest at the enterprise. Work should be carried out in normal, favorable conditions, and when planning a workplace and its technological equipment, it is necessary to take into account the latest advances in technology and technology [36-39]. This significantly helps to reduce staff fatigue, save time, improve staff efficiency and ultimately improve work efficiency and success. Quite common in the West is the so-called. "The theory of human capital". According to this theory, the knowledge and skills of employees are considered to belong to their organization, which generates income. And the costs of acquiring this knowledge (personnel recruitment, selection, salary, adaptation, training, certification, improvement of working conditions) are considered an investment. Although the efficiency of such investments is the highest and, in addition, people are the most important resource for them, there are still records in the educational and scientific literature of these countries that seem to be the least developed, for example, finance, manufacturing, , marketing, materials Management of technical supply. In the Georgian realities, only the first steps are being taken in this direction against a very poor background of economic development, wages, employment and living standards. Thus, when it comes to the successful management of an organization, it should in principle be said that limiting investments in human resources, ignoring the factor of trust and respect, inadequate staff motivation, reducing concern and social insecurity by boomerangs return to the development of the company [28-29].

By the decree of the Government of Georgia, the state program for monitoring the working conditions was approved, the implementation of which was entrusted to the central office of the Ministry. The target group of the program includes employers who give their prior consent to the monitoring. In addition, under this program, employers receive a notification about the inspection 5 working days before the monitoring procedure. Within the program, the target group is selected and the monitoring sequence is determined. The program does not establish the rules for conducting monitoring and its regulation is linked to the issuance of an individual act of the Minister. Violation of labor safety norms is controlled by a labor safety specialist - a person with appropriate qualifications appointed/ invited by

the employer, who ensures the introduction and management of labor safety measures to prevent violations of labor safety norms [30-32].

According to the Georgia-EU Association Agenda for 2014-2016, Georgia has committed itself to establishing a labor inspection mechanism and institution that would have adequate potential to test working conditions and meet International Labor Organization standards. This issue is also defined in Chapters 13 and 14 of the Georgia-EU Association Agreement, the implementation of which is a future perspective.

Among the main tasks and functions of the mentioned department, the implementation of state supervision is defined:

- Implementation of technical regulations and labor safety mechanism for compliance with working conditions in the field of labor safety requirements, observance of safety rules during the production process and other work environment safety control, in case of violation of which the department is authorized to use the sanctioning mechanism;
- Supervise the observance of labor legislation and the investigation and registration of accidents at the place of employment;
- Take preventive measures against human trafficking in order to prevent forced labor;
- Analysis of labor law, violations of labor and health safety and the causes of industrial injuries, development of proposals and recommendations for their elimination and prevention;
- Review of applications, complaints and proposals within the scope of authority granted by the legislation of Georgia.
- Other rights provided by the statute [33-35].

#### **AIM AND OBJECTIVES OF THE RESEARCH**

The aim of the research was to study the legal-normative basis of labor safety, equipment and sanitary-hygienic requirements of activities in pharmaceutical institutions, to identify their strengths and weaknesses, pros and cons, to reflect a specific problem and to find ways to solve, eliminate and resolve it. In order to achieve the above-mentioned goal, we considered it necessary to determine the quality and compliance of the work space safety of the research facilities with the Organic Law of Georgia on Labor Safety. Assessing the risk of harm to personnel and consumers was considered an existing epidemic. Regarding safety - according to the data of the study period.

#### **MATERIALS AND METHODS**

The information source of the paper is the materials of the survey of pharmacists, international economic journals, reports of the Ministry of Internally Displaced Persons from the Occupied Territories, Labor, Health and Social Affairs, statistical collections of the State Department of Statistics, Georgian laws, bylaws and other legal acts.

In general, the subject of research was the Georgian pharmaceutical market, which creates a danger not only for consumers but also for employees. The objects of research are pharmacies operating in the market, pharmaceutical companies, pharmaceutical companies, regulatory bodies and employees working there.

Based on the existing theoretical foundations of occupational safety, we considered it necessary to identify the methodological and practical issues, the set of materials from which we selected the objects of research.

The 2 types of questionnaires for pharmacists were selected. The questionnaire, on the one hand, considers whether there is a regulatory legal framework on labor safety in Georgia and, on the other hand, whether all the requirements provided by the legal framework are met, to what extent they comply with the requirements and standards.

Through this questionnaire, we focused on the following key issues:

- What information do pharmacists have about occupational safety, including sanitation?
- Is labor safety in pharmaceutical institutions regulated in Georgia;
- Is there a legal normative basis for sanitary requirements;
- If regulated, then how much is actually done in pharmaceutical establishments;
- Whether employees are provided with information on safety rules when hired and whether there is an appropriate entry in the employment contract.

As a research method, we used specific quantitative and qualitative studies, based on the results of which we drew some conclusions and developed recommendations.

**RESULTS AND DISCUSSION:**

The target segment of the research was 5 objects,

- 2 of them were pharmaceutical factories:
  - GMP Ltd;
  - Neopharm Ltd.
- 2 Drugstores
  - Pharmacy PSP Ltd
  - Aversi-Pharma Ltd
- And the regulatory body

Ministry of Internally Displaced Persons from the Occupied Territories, Labor, Health and Social Affairs of Georgia, LEPL Agency for Regulation of Medical and Pharmaceutical Activities.

The answers to each question from each of the five objects are presented in summary form (we did not consider it necessary to present the results separately at this stage). With this we tried to present an overall picture of the data actually available. The survey was conducted with a pre-compiled questionnaire, the anonymity of the respondents was protected.

Table №1

Q 1. Is there a dezo-barrier in the pharmaceutical facility / pharmacy?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	63.4	36.5	Yes	99.9
No	36.6	36.5	No	0.1
I do not know	-	-	I do not know	-

It is noteworthy that before the pandemic, 36.6% of respondents reported that there were no dezo barriers in pharmacies. The results of the survey differ significantly from the data obtained during COVID-19 infection. 99.9% of respondents confirm that there are dezo barriers in pharmacies. See Table №1.

Table №2

Q 2. Are there safety / separation glasses at pharmacy counters?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	75.2	23.5	Yes	98.7
No	24.8	23.5	No	1.3
I do not know	-	-	I do not know	-

In this case, the protective glasses at the pharmacy counters, or the specialist and patient separating glasses mentioned above, were significantly increased during the pandemic. But more than 23% of respondents think they do not know. See Table №2.

The start date of the study was October 2019, which lasted until May 2020. Thus, the data were collected, which we conditionally divided before the Covid-19-related contraction (February) and during the Covid-19 activation period. In both cases, due to the current situation, we used the same topical questions. Accordingly, an average of 142 respondents (from all five facilities) were interviewed. The answers are presented with two data. All the first diagrams presented are data up to Covid-19. Second, even the data obtained during Covid19 [36-39].

Table №3

Q 3. Is labor safety regulated in Georgia?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	30.7	43.9	Yes	74.6
No	25	5.5	No	19.5
I do not know	44.3	38.4	I do not know	5.9

The data show that 44.3% of respondents were not informed about labor safety regulations in Georgia. And, 25% thought that security was not regulated at all. However, it should be noted that during the pandemic, the survey was conducted again and 74.6% of respondents believe that occupational safety is regulated by law. We also note that the need for labor safety regulation is growing, accounting for 43.9%. See Table №3

Table №4

Q 4. Do you know the law on labor safety?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	34.8	33.8	Yes	68.6
No	65.8	43.4	No	31.4
I do not know	-	-	I do not know	-

The answers to this question show that if 34.8% knew about the Labor Law of Georgia before the pandemic, the developed situation necessitated knowledge with a difference of 33.8%. See Table №4.

Table №5

Q 5. Is labor safety regulated in pharmaceutical institutions?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	30.3	40.0	Yes	70.3
No	33.1	11.9	No	21.2
I do not know	36.6	28.1	I do not know	8.5

The data show that 30.3% of the respondents did not know about the regulation of occupational safety in a pharmaceutical facility before the pandemic. In the conditions of the pandemic, the interest in this direction increased by 40.0% and also the number of respondents who were unaware decreased from 36% to 28.1% from 8.5%, which somehow indicates a necessary tendency for self-development. See Table №5.

Table №6

Q 6. Do you know the legal normative based on sanitary requirements?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	41.8	31.9	Yes	73.7
No	58.2	31.9	No	26.3
I do not know	-	-	I do not know	-

The answers to the question about the degree of informativeness about the sanitary requirements of the legal normative base in pharmaceutical institutions do not look very good. The data show that it seems that all respondents are familiar with this issue, but it seems that the current situation also played a role here and the degree of improvement of knowledge amounted to - 31.9%. See Table №6.

Table №7

Q 7. Are sanitary requirements regulated in pharmaceutical facilities?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	32.4	45.6	Yes	78
No	34.5	17.6%	No	16.9
I do not know	33.1	28	I do not know	5.1

Unfortunately, 31.1% of respondents did not have information about the regulation of sanitary requirements. In this regard and 34.5% believed that it was not regulated. But in a re-survey, informatics increased by 45.6%, with 78% believing it to be regulated. The number of those who did not know decreased by 28% to 5.1%. See Table №7.

Table №8

Q 8. On the territory of Georgia, is there any registration of occupational disease at work with the existing high-risk, severe, harmful hazardous conditions?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	41.8	9.0	Yes	50.8
No	25.5	0.8	No	26.3
I do not know	32.6	9.7	I do not know	22.9

On this question, we think that the level of informatics is low and it should also be noted that before the pandemic and during the pandemic, interest in this area changed by only 9.0%. There are small gaps between the responses of respondents who do not know whether accounting is taking place. See Table №8.

Interest in hiring employers to learn about occupational safety rules increased from 49.3% to 72% to 22.7%. Respondents who did not know and were not informed when hiring accounted for 50.0% which decreased by 22.7% and amounted to 28%. It should be noted that a high rate would be high on all of the above questions to maintain a high degree of information on all occupational safety regulations when hiring. We think that this information is important and should be taken into account.

Table №9

Q 9. Is there occupational safety at your workplace?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	48.9	30.8	Yes	79.7
No	51.1	30.8	No	20.3
I do not know	-	-	I do not know	-

It is noteworthy that 48.9% of respondents in the workplace believe that occupational safety is protected and 51% state that it is not protected, which changed significantly during the pandemic and increased by 30%. We think more attention is needed in this direction. See Table №9.

Table №10

Q10. Is the essence of your job a labor safety specialist?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	39.4	12.3	Yes	51.7
No	28.2	4.9	No	33.1
I do not know	32.4	17.1	I do not know	15.3

The urgency of this question has increased during the pandemic, but the respondents' answers are not in full compliance and a shortcoming has been identified. It is estimated that 51.7% of the institutions are security specialists. And the difference between pandemic and pandemic time is only 12.3%. See Table №10.

Table №11



Q 11. Are you aware of the health risk factors in your workspace?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	49.6	37.6	Yes	87.2
No	50.4	37.6	No	12.8
I do not know	-	-	I do not know	-

It is unfortunate that 50% were unaware of the existence of health hazards in the workplace and the degree of interest in information during the pandemic changed by 37.6% to 87.2%. It should definitely be noted that pharmaceutical activity is associated with life-threatening substances. And especially if the touch is long. See Table №11.

Table №12

Q 12. Is the compliance of the production environment and the physical, chemical and biological factors of the labor process with the hygienic norms of your facility?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	44.7	11.2	Yes	55.9
No	22.7	6.1	No	28.8
I do not know	32.6	17.3	I do not know	15.3

According to the answers to this question, there is no favorable situation in the pharmaceutical facility in this regard, the need for permanent identification of health hazards in the workplace has been identified. See Table №12.

Table №13

Q 13. Is there an evacuation board/drawing in your workspace?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	62.4	32.5	Yes	94.9
No	37.6	32.5	No	5.1
I do not know	-	-	I do not know	-

Before the pandemic, 62.1% said that during the pandemic - 94.9%, according to the survey results, during the pandemic, the number of medical institutions where the evacuation board was posted increased by 32.5%. It is known that the evacuation board is a plan of the floors of a building (pharmacy), which shows the evacuation exits, rescue facilities and their locations, etc. The spread of the evacuation board in the pharmacy was due to the sharply increased number of patients in pandemic conditions and the stressful environment created by the situation caused the pharmacists to lose attention, thus increasing the risk of harmful events (flammable substance ignition, fire hazard, etc.). See Table №13.

Table №14

Q 14. Do you think that all workplaces should have the appropriate safety requirements? (Fire extinguisher, hood, alarm, etc.)?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	73.2	20.8	Yes	94
No	26.8	20.8	No	6
I do not know	-	-	I do not know	-

Prior to the pandemic, 26.8% of respondents thought that appropriate safety precautions were not necessary in the facility, however, the current situation changed the majority view on this issue and 94% of respondents after the pandemic noted the need for appropriate security equipment, which was completely logical. The quarantine and isolation declared during the pandemic led to a change in the usual rhythm of life before adapting to the existing situation, people had to deal with a situation that was foreign and unusual to them, and mistakes were often made at high risk of adverse events. There has been an increase in rescue services, fire and emergency medical services and, consequently, continuous

work in a busy schedule. All this made it necessary to place appropriate safety equipment in the workplace to be able to respond in a timely manner to the situations created. See Table №14.

Table №15

Q 15. Do you think the institution should take into account psycho-social factors (stress, communication, post-traumatic stress)?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	66.2	16	Yes	82.2
No	19	2.1	No	16.9
I do not know	14.8	13.9	I do not know	0.9

Almost all respondents to this question state that psycho-social factors should be taken into account in the institution. And positive responses, i.e. necessity before pandemic and pandemic time difference was 16%. Difference (66.2% before pandemic and 82.2% during pandemic). But it should also be noted that 33.8 (19 + 14.8) does not know the psycho-social factors should be taken into account in the institution. See Table №15.

Table №16

Q 16. Do you think if it is necessary to teach labor safety rules as a discipline?

Before Covid-19 (%)		Differences (%)	During Covid-19 (%)	
Yes	84.5	13	Yes	97.5
No	15.5	13	No	2.5
I do not know	-	-	I do not know	-

Quite interesting answers to the question of whether safety rules need to be learned. In both cases, the difference between the responses of the respondents is small and 13%. Nearly 90% believe that occupational safety needs to be taught. And as far as I know to date this issue is included in the Pharm Case and Organization and Economics curriculum. See Table №16.

## DISCUSSION

Evaluation and analysis of the data obtained from our research suggest that there is a need to tighten and control safety regulations in the pharmaceutical facility; 44.3% of respondents are not informed about labor safety regulations in Georgia; More than 33% of respondents are unaware of the regulation of occupational safety in a pharmaceutical facility; Low legal-normative base and level of awareness on sanitary requirements in pharmaceutical institutions; 50% of respondents were unaware of the presence of potential or existing health hazards in the workplace.

Healthcare is the area of activity that is most strictly regulated by the state. Today, the health care system, which includes all departmental and sectoral levels of the state economy, is not only a combination of medical-prophylactic, rehabilitation and recovery institutions, but also it is closely connected with ecology, labor protection, social programs, etc. One of the most important functions of health is to promote and restore the balance and harmony of individual and public health. We think we need: Expand the scope of the draft law on labor safety and extend it to all places of employment, without exception.

Equip the Labor Inspectorate with an unconditional and free access to the places of employment, which implies the authority of the mechanism, by its own decision, to carry out inspections of the places of employment without the prior permission of the court; The Law of Georgia on Labor Safety envisages an appropriate system of sanctions, including the proper rules for the application of sanctions and adequate amounts of fines, which will have both preventive and responsive effects.

The state should create an appropriate legislative and institutional framework; We think this will help transform the existing department into an effective labor inspectorate. The possibility will be created of the institutional capacity of its independence and efficiency, and the law will also provide guarantees for the individual independence of inspectors; Also, the bill should directly refer to the Labor Inspectorate as the body responsible for law enforcement. At present, the legal-normative base of labor safety, equipment and sanitary-hygienic requirements in Georgia creates a safe environment for

activities in pharmaceutical establishments, the permanent control of compliance with the norms of which guarantees full protection for those in contact with the pharmaceutical product.

We believe that the right, legal approach, strict control and state policy in the field of drug trafficking are a prerequisite for creating a safe environment. Most importantly, despite the interests of the owners of the Georgian pharmaceutical industry and modern marketing approaches, the safety of the population and employees remains a priority.

## **CONCLUSIONS**

Based on the study of the problems of this issue and the results of the research, we can draw the following conclusions:

- Most pharmaceutical establishments (50-60%) do not have a fire board with appropriate equipment, evacuation exit and scheme. Also has no person responsible for the matter;
- Disobedience and specialist protection / separation facility prior to pandemic were minimal (increased by 99%) during pandemic;
- 97% of respondents believe that labor safety should be taught in all its characteristics.
- Pharmaceutical establishments do not comply with the hygienic norms of the internal and external environment, physical, chemical and biological factors of the labor process. The facility also does not take into account psychosocial factors related to safety (stress, communication, post-traumatic stress, etc.);

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**PREVALENCE OF *Microsporium canis* FROM STRAY KITTENS AND PET CATS IN GANJA, AZERBAIJAN**

*Narmin Alasgarova*<sup>1</sup>

<sup>1</sup>*Azerbaijan State Agrarian University, department of Veterinary Epidemiology, Microbiology and Parasitology, Ganja, Azerbaijan*

*Asaf M. Omarov*<sup>2</sup>

<sup>2</sup>*ADA University, associate professor, Baku, Azerbaijan*

**Keywords:** cat, *M. canis*, dermatophytosis

### **Introduction**

Dermatophytosis is a disease caused by *Microsporium canis* is a pathogenic dermatophyte that usually colonizes animals, and secondary infection of humans comes from pets (Maya Hariu, Yuji Watanabe et al., 2021).

Since *M. canis* is a zoonotic disease that is a common infection in pet cats, it places veterinarians, animal care staff, and owners at risk of infection (by Alex Moskaluk, Lauren Darlington et al., 2022). Cats, which live very close to humans, may expose humans to this pathogen (Vena Chupia, Jirapat Ninsuwon et al., 2022).

Infection with *M. canis* is usually associated with alopecia, and infection has been diagnosed by isolation of fungus, which has characteristic hyphae or arthroconidia, from the patients' hair lesions (Hsiao YH, Chen C, Han HS, et al., 2018). *M. canis* cause lesions to the glabrous skin (*tinea corporis*) and to the head (*tinea capitis*) (by Mario Pasquetti, Anna Rita Molinar Min et al., 2017).

The infected patients show hair loss with erythema and are diagnosed as having dermatophytosis, but the transmission routes of *M. canis* from animals to others are sometimes unclear, although they are critical to the treatment of patients and infection control (Maya Hariu, Yuji Watanabe et al., 2021).

Asymptomatic animal carriers of *M. canis* are regarded a critical factor in the epidemiology of the disease (Sebastian Gnat, Dominik Lagowski et al., 2018). In asymptomatic cases, both Wood's lamp examination and microscopic analyses of suspected areas are highly recommended (Maya Hariu, Yuji Watanabe et al., 2021).

### **Materials and Methods**

This research focused on the epidemiology of *M. canis* found in cats.

A cross-sectional survey was conducted for stray kittens and pet cats in Ganja city from October 2021 to March 2022. 5% confidence level, 1000 population size, 5% expected prevalence were selected for sample size. The needed sample size for the detection of diseases was 57 tasters. Kittens and dogs were selected randomly and 57 hair samples and skin lesions were collected from stray kittens and domestic cats belonging to veterinary students of Azerbaijan State Agrarian University. The samples have been processed in the Laboratory of the Department of Veterinary Epidemiology, Microbiology and Parasitology of Azerbaijan State Agrarian University Ganja, Azerbaijan and the Laboratory of a Veterinary clinic of the faculty of veterinary medicine of Azerbaijan State Agrarian University Ganja, Azerbaijan.

Different mycological examinations (including a culture obtained by hair brushing and Wood's lamp examination) were performed on 57 cats. Sample size 57, Number positive 28, Test sensitivity 0.9, Test specificity 0.99, Confidence level 0.95, CI type for AP Normal approx., CI type for TP Normal approx.

Sabouraud Dextrose Agar (SDA) was used for *Microsporium canis* isolation and cultivation.

Samples were examined with 10% KOH preparation.

The face-to-face interview was conducted by the dermatologist of Ganja International Hospital dr. Sikar Huseynov

### **Results**

1. The source of infection (SOI) was demonstrated to be stray kittens that had been adopted.
2. *M. canis* isolated from 17 stray kittens and 11 domestic cats.
3. 13 cats were asymptomatic infected animals presenting discrete Wood's-positive lesions disseminated on the whole body.

	<b>Estimate</b>	<b>Lower 95 % CL</b>	<b>Upper 95 % CL</b>
Apparent Prevalence (Normal approx.CL)	0.4912	0.3614	0.621
True Prevalence (Normal approx.CL)	0.5407	0.3949	0.6865
Positive predictive value	0.9907		
Negative predictive value	0.8937		
Likelihood ratio +ve	90		
Likelihood ratio -ve	0.101		

4. 20 years old veterinary student Sevinc Hasanova presented with pruritic, erythematous lesions on the head with alopecia. The dermatologist of Ganja International Hospital dr. Sikar Huseynov diagnosed dermatophytosis caused by fungal infection, and *M. canis* was suspected as the pathogen because of the morphologic characteristics.

### **Outcomes**

1. *M. canis* was detected among the carnivores in Ganja city
2. *Apparent prevalence was 0.4912 CI95% [0,36; 0.62]*
3. *True prevalence was 0.5407 CI 95% [0.3949;0.6865]*
4. *M. canis* was detected among humans

**ADÖLESAN GEBELİKLER VE EBELİK YAKLAŞIMLARI  
ADOLESCENT PREGNANCY AND MIDWIFERY APPROACHES**

*Sümeyye ALTIPARMAK<sup>1</sup>*

<sup>1</sup> İnönü Üniversitesi, Sağlık Bilimleri Fakültesi, Ebelik Bölümü, Malatya, Türkiye.

<sup>1</sup>ORCID ID: 0000-0002-4759-1210

*Ayşe Nur YILMAZ<sup>2</sup>*

<sup>2</sup> Fırat Üniversitesi, Sağlık Bilimleri Fakültesi, Ebelik Bölümü, Elazığ, Türkiye.

<sup>2</sup>ORCID ID: 0000-0003-0489-7639

**ÖZET**

Adölesan çağı, çocukluktan erişkinliğe geçiş dönemini ifade etmekle birlikte 10-19 yaşlar arası kapsamaktadır. Adölesan gebelikler de bu yaşlar arasında gerçekleşen gebelikler olarak tanımlanmakta, tıbbi ve sosyal sorunları da beraberinde getiren riskli gebelikler olarak kabul edilmektedir. Bu derlemenin amacı, adölesan gebelikler ve ebeler yaklaşımı hakkında bilgi vermektir. Adölesanlar, toplumun önemli bir kısmını oluşturmakta, aynı zamanda büyük ölçüde ihmale de uğramaktadırlar. Türkiye gibi gelişmekte olan ülkelerde gelenekler ve kültürel yapının etkisiyle erken yaşta evlilikler ve devamında adölesan gebelikler daha fazla görülmektedir. Adölesan gebeliklerde beslenme yetersizliği, adölesan dönemin hızlı büyümeye bağlı artmış vitamin ve mineral gereksinimi, bu gereksinimin yeterli karşılanmaması sonucu kemik kitlesi kaybı ve anemi, gebelikte normalden daha az kilo alımı, gebelikte oluşan hipertansiyon, preeklampsi, abortus, erken doğum riski, inrauterin gelişme geriliği, erken membran rüptürü, baş-pelvis uygunsuzluğu, doğum öncesi bakımın (DÖB) yetersiz olması ve bunlara bağlı olarak gelişen obstetrik komplikasyonlar daha fazla meydana gelmektedir. Bu olası komplikasyonları önlemek için ilk yapılması gereken adölesan gebeliklerin oluşmasını önlemektir. Bunun için de; cinsel ve üreme sağlığı hizmetlerinin adölesanlar arasında yaygınlaştırılması sağlanmalı, ülkelerin özelliklerine uygun olarak sorunlar ve çözümler belirlenmelidir. Adölesanlara ebeler tarafından güvenli cinsel yaşam konusunda bilgilendirme yapılmalıdır. Ergen kızların eğitim hayatlarına devam etmelerini sağlamak ve kadınlara çalışma hayatında daha fazla yer açmak da önemlidir. Eğer adölesan gebelik oluşmuş ise; DÖB’de rutin kontrollerin yanında anne adayının psikolojik açıdan doğuma hazırlanması ve eğitilmesi de önemlidir ve bu ebelerin sorumlulukları arasındadır. Adölesan gebelik deneyimleyen kadınların, DÖB süresince sağlığı ebeler tarafından en üst düzeyde sürdürülmeli, sağlıkla ilgili karşılaşılabilecekleri sorunlar en aza indirilmelidir. Adölesan anneler ebeveynlik ile ilgili sorumlulukları yönetmede ve sorunlarla baş etmede yeterli olamayabilirler ve kendini çaresiz hissedebilirler. Özbakım ve yenidoğana bakımında teşvik ve destek verilmelidir. Adölesan anneye problemleriyle başa çıkma becerisi kazandırılırken, doğum sonrası dönemde karşılaşılabilecek psikolojik sorunların engellenmesine yardımcı olunmalıdır. Mevcutsa zararlı alışkanlıkları bırakması konusunda desteklenmelidir.

**Anahtar Kelimeler:** Adölesan gebelik, ebe, anne.

**ABSTRACT**

Adolescence refers to the transition period from childhood to adulthood, and covers the ages of 10-19. Adolescent pregnancies are also defined as pregnancies occurring between these ages, and are considered as risky pregnancies that bring along medical and social problems. The purpose of this review is to give information about adolescent pregnancies and midwifery approaches. Adolescents constitute an important part of the society, but they are also neglected to a great extent. In developing countries such as Turkey, early marriages and subsequent adolescent pregnancies are more common due to the influence of traditions and cultural structure. Nutritional deficiency in adolescent pregnancies, increased vitamin and mineral requirement due to rapid growth in adolescence, bone mass loss and anemia as a



result of insufficient fulfillment of this requirement, less weight gain than normal during pregnancy, hypertension during pregnancy, preeclampsia, abortion, premature birth risk, intrauterine growth retardation, Premature rupture of membranes, cephalopelvic incompatibility, inadequate prenatal care (PC) and related obstetric complications occur more frequently. The first thing to do in order to prevent these possible complications is to prevent the occurrence of adolescent pregnancies. For this, too; sexual and reproductive health services should be expanded among adolescents, problems and solutions should be determined in accordance with the characteristics of the countries. Adolescents should be informed about safe sexual life by midwives. It is also important to enable adolescent girls to continue their education and to make more room for women in working life. If adolescent pregnancy has occurred; In antenatal care, besides routine controls, psychological preparation and training of the expectant mother for birth is also important and this is among the responsibilities of midwives. The health of women experiencing adolescent pregnancy should be maintained at the highest level by midwives during antenatal care, and health-related problems should be minimized. Adolescent mothers may not be able to manage parental responsibilities and cope with problems, and they may feel helpless. Encouragement and support should be given in self-care and newborn care. While gaining the ability to cope with the problems of the adolescent mother, it should be helped to prevent psychological problems that may be encountered in the postpartum period. If available, they should be supported to quit harmful habits.

**Keywords:** Adolescent pregnancy, midwife, mother.

## **GİRİŞ**

Adölesan dönemi bireyin biyolojik, psikolojik ve sosyal değişimlerle birlikte çocukluktan erişkinliğe geçiş dönemi olup, 10-19 yaşlar arası olarak kabul edilmektedir (Şen ve Kavlak 2011; Aydın 2013). Dünya nüfusunun %30'nu oluşturan adölesanların %95'i gelişmekte olan ülkelerde bulunmaktadır. Hem gelişmiş hem gelişmekte olan tüm dünya ülkelerinde adölesan gebelikler çok önemli bir sağlık sorunu yaratmaktadır (Aydın 2013). Türkiye Nüfus ve Sağlık Araştırması (TNSA) 2018 verilerine göre, Türk toplumunun %16.0'ını adölesan yaş grubu bireyler oluşturmaktadır. Ülkemizde 15-19 yaşları arasındaki adölesanların %5'i evlidir ve anne olma oranı %3,5 olmakla birlikte yaşla artış göstermektedir (TNSA 2018).

Günümüzde gelişmiş ve gelişmekte olan ülkelerde sağlık sorunlarından biri olan adölesan gebelikler hem anne hem de bebek sağlığını olumsuz açıdan etkilemektedir. Adölesan gebelikler, riskli gebelikler arasında yer almaktadır ve anne ile bebek açısından önemli sosyal ve sağlık problemlerine neden olabilmektedir (Aydın 2013). Bu derlemenin amacı, adölesan gebelikler ve ebelik yaklaşımları hakkında bilgi vermektir.

### **1. ADÖLESAN GEBELİĞİN VE ANNELİĞİN KADININ SAĞLIĞINA ETKİLERİ**

Gelişmekte olan ülkelerde adölesanların %30'u 18 yaş altında, %14'ü 15 yaş altında evlenmekte ve 15-19 yaş arasında bulunan adölesanlar kendilerinden yaşça büyük partnerler ile evliliğe ya da cinsel ilişkiye zorlanmaktadır (Aydın 2013). Adölesan dönemde karşılaşılan doğurganlık, sağlık ve sosyal açıdan sonuçları dikkatle incelendiğinde önemli bir sorun teşkil etmektedir. Adölesan bireylerin yaşadığı anneliğin, demografik ve sosyal açıdan birçok olumsuz sonucu bulunmaktadır (Şen ve Kavlak 2011). Adölesan gebelikler yüksek riskli gebelikler olarak kabul edilmekte, tıbbi ve sosyal sorunları da beraberinde getirmektedir. Yapılan çalışmalarda doğurganlık yaşı azaldıkça annelerde komplikasyon görülme oranının yükseldiği saptanmıştır (Edirne ve ark. 2010; Aydın 2013). Adölesan gebelerde sigara ve bağımlılık yapıcı madde tüketimi ile HIV ve diğer cinsel yolla bulaşan enfeksiyonlarla daha fazla karşılaşıldığı bildirilmektedir (Mason 2011). Beslenme yetersizliği, gebeliğin başlangıcında boy ve kilonun azlığı, gebelikte beklenenden daha az kilo alımı karşılaşılan problemlerdir. Ayrıca bu gebelik ile bir sonraki gebelik arasındaki sürenin kısalığı, fazla sayıda gebelik yaşama, evlilik dışı gebelik deneyimleme, prenatal izlem sayısındaki yetersizlik, gebelikte ve postpartum dönemde kanama, zor doğum eylemi ve fistül oluşumu görülen diğer komplikasyonlardandır (Şen ve Kavlak 2011).

Adölesanlarda diğer gebeliklerden daha az olmakla birlikte, anemi, gebelik hipertansiyonu ve preeklampsi-eklempsi gibi komplikasyonlar da görülmektedir. Ayrıca adölesan gebeliklerde perinatal morbidite ve mortalitenin arttığı saptanmıştır (Şen ve Kavlak 2011). Beklenenden daha erken yaşta

evlenen adölesan kadınlarda maternal ölümlerle yüksek oranda karşılaşmaktadır. Erken yaşta evlenen adölesanlar, özellikle de kontraseptif yöntem kullanımının çok az olması veya hiç olmaması nedeniyle daha uzun süre gebelik yaşama riski taşımaktadır. Bunun bir sonucu olarak da erken yaşlarda doğurganlığın bailaması, ileriki yaşlarda başlamasına kıyasla çok çocuklu ailelerin oluşmasına neden olmaktadır (TNSA 2018). Adölesanların erken yaşlarda cinsel ilişkiye girmeye başladığı ve aile planlaması yöntemi kullanımının düşük oranda olduğu saptanmıştır (Aydın 2013).

Gençlerin genellikle kendi vücutlarına ve karşı cinsiyete ait üreme özellikleri hakkında bilgi sahibi olmadıkları bilinmektedir (Mason 2011). Yeterli olmayan bilgi düzeyi ile deneyimlenen cinsel ilişki sonucu adölesan bireylerde cinsel yolla bulaşan hastalıkların görülme sıklığı, istenmeyen bir gebelik yaşama, yasal olmayan koşullarda abortuslar ve bu durumlara bağlı gelişen komplikasyonlar giderek artış göstermektedir (Öner ve Yapıcı 2010). Erken yaşta çocuk sahibi olmak, kadınların ekonomik faaliyetlere katılmasını önlemekte, uzun vadede anneye, bebeğe, aileye ve ülke ekonomisine büyük ölçüde yükler yüklemektedir (Demiröz ve Canbulat 2008).

Literatür incelendiğinde adölesan dönemde doğum yapan kadınların gebelik döneminde kontrollerinin yeterli düzeyde olmadığı ve bu durumun olumsuz obstetrik sonuçlarla karşılaşma riskini arttırdığı belirtilmektedir. Biyolojik, psikolojik ve sosyal gelişimi tamamlanmayan adölesan bireyin gebe kalması, eğitim almasını ve meslek sahibi olmasını engellemekte, sorumluluklarını arttırmakta ve resmi nikâh yapılmasına engel olmaktadır (Letourneau ve ark. 2004; Öner ve Yapıcı 2010; Aydın 2013). Bireylerin adölesan dönemde gebe kalması annenin çalışma hayatına katılmasına engel olmakta ve kadını ekonomik açıdan diğer kişi/kişilere bağımlı hale getirmektedir (Öner ve Yapıcı 2010).

Adölesan çağda yapılan evlilikler, bireyin kendine olan güveninin azalmasına neden olurken, bireyin kendine özgü bir kimlik oluşturmasını da güçleştirmektedir. Tüm bu durumlara ek olarak adölesan annelerde doğum sonrası karşılaşılabilecek problemlerle baş etmede güçlükler ve benlik saygısında düşme meydana gelmektedir (Letourneau ve ark. 2004).

## **2. ADÖLESAN GEBELİĞİN VE ANNELİĞİN ÇOCUK SAĞLIĞINA ETKİLERİ**

Adölesan dönemdeki kadınların cinsel ilişki, aile planlaması yöntemleri, abortus, gebelik, annelik ve bebek bakımı gibi konularda bilgi ve tecrübeleri daha ileri yaştaki kadınlara göre yetersizdir. Bu nedenle gebe kalmak sadece adölesanların kendi hayatlarına yük getirmekle kalmaz, aynı zamanda doğacak olan bebeğe ve aileye de ciddi problemler getirmektedir (Demiröz ve Canbulat 2008).

Prematüre, düşük doğum ağırlıklı bebek ve asfiksi gibi yenidoğanın mortalite riskini arttıran ve ileriki hayatında sağlık problemi yaşamasına neden olan sorunlar adölesan annelerin bebeklerinde daha fazla görülmektedir. Adölesan dönemde doğan bebeklerin diğer bebeklere oranla daha düşük kiloda doğdukları saptanmıştır. Bunun nedeninin sigara ve alkol tüketiminin fazla olması söylenebilir (Aydın 2013). Ayrıca bebeğin boyunun kısa olması sık görülen komplikasyonlar arasında sayılabilir (Aydın 2013). Literatür incelendiğinde, yenidoğanlarda doğum travması, konjenital anomali, enfeksiyon, mekonyum aspirasyonu, umbilikal kordon transpozisyonu, respiratuar distres ve oligohidroamnios gibi problemlerin de gözlemlendiği saptanmaktadır (Keskinöglü ve ark. 2007).

Adölesan dönemde anne olan kadınların, çocuklarının sağlığı ve gelişimi konusunda, gebelikte sigara tüketmek, bebeği emzirmemek ve çocuğunu okul öncesi eğitime göndermemek gibi riskli davranışlar sergilediği belirlenmiştir (Keskinöglü ve ark. 2007). Literatür incelendiğinde adölesan annelerin diğer annelere kıyasla postpartum ilk iki ayda bebeklerinin bakım sorumluluğunu daha geç aldıkları ve sağlık hizmetlerine ulaşmada daha fazla problem yaşadıklarını bildirilmiştir (Letourneau ve ark. 2004). Adölesan anne bebeklerinin erişkin anne bebeklerine kıyasla beslenme sorunu yaşadıkları, fiziksel gelişimde geri kalma riskini daha fazla yaşadıkları ve bilişsel fonksiyonlarının daha geri olabileceği vurgulanmaktadır (Bulut ve ark. 2008; Şen ve Kavlak 2011). Ayrıca hayatın ilerleyen dönemlerinde öğrenme zorlukları ile karşılaşma, düşük okul performansına sahip olma, davranış problemleri ile suç işleme potansiyellerine sahip olma ve sorunlu akran ilişkileri yaşama gibi problemler adölesan ebeveynlerin çocukları arasında daha yaygın olarak saptanmıştır (Breheny ve Stephens 2010; Aydın 2013).

### **3. ADÖLESAN GEBELİKTE EBELİK YAKLAŞIMLARI**

Adölesan dönemde anneliği deneyimleyen kadına, olası problemlerle başa çıkma becerisi kazandırılmalı ve postpartum dönemde ortaya çıkabilecek psikolojik sorunların engellenmesine yardımcı olunmalıdır. Kadınların zararlı alışkanlıkları varsa (sigara, alkol vb.) gebelikten itibaren postpartum dönem de dâhil olmak üzere bebeğe vereceği zararlar anlatılmalı ve bırakması konusunda desteklenmelidir. Adölesan dönemde anne olan kadınlar ebeveynlik ile ilgili sorumluluklarla ve problemlerle baş etmede etkin olamayabilirler ve kendilerini çaresiz hissedebilirler. Aynı zamanda maddi olarak da desteğe ihtiyaçları vardır. Kendi ve bebeklerinin bakımında yardım gereksinimleri bulunmaktadır. Gebelik dönemindeki kontrollerde ve bakımlarda rutin izlemlerin yanı sıra anne adayının psikolojik açıdan doğum eylemine hazırlanması ve doğum eylemi konusunda eğitim alması da önemlidir. Gebelik süresince adölesanın sağlığı en yüksek düzeyde devam ettirilmeli, sağlıkla ilgili sorunları en aza indirilmelidir. Ebeler tarafından aile planlaması yöntemleri ile ilgili bilgi verilmeli kadınla işbirliği yapılarak kullanabileceği yöntemlere karar verilmelidir. Postpartum döneme ve anneliğe sosyal adaptasyonu konusunda yardımcı olunmalıdır. Ebeler tarafından bebeğin babası da eğitimlere dahil edilmeli ve ebeveynlik konusunda cesaretlendirilip desteklenmelidir (Lifer 2012; Çınar 2017).

### **SONUÇ**

Adölesan gebeliklerin önlenmesi, ülkelerin ekonomik seviyelerinin yükseltilmesi ve etkili danışmanlık hizmetlerinin sunulması açısından önemlidir. Ayrıca adölesan dönemde meydana gelebilecek gebelikleri engelleyebilmek adına, okullaşma ve eğitim hayatına devamın teşvik edilmesi önem arz etmektedir. Kadınların çalışma hayatında daha fazla yer edinmesi sağlanarak hem kadının sosyal statüsü artırılmalı hem de erken yaşta olası evlilikten ve bu evlilik sonucu ortaya çıkabilecek gebelikler ile komplikasyonlarından korumaya yardımcı olunmalıdır. Adölesan bireyler arasında cinsel sağlık ve üreme sağlığı hizmetlerine erişimin artırılması için ülkelere ve sağlık sistemlerine özgü modellerin kararlaştırılması, olası problemlerin belirlenip çözümler üretilmesi de faydalı olacaktır. Genç bireylerin güvenli cinsel yaşam konusunda bilgilenmesini sağlamak için, eğitim müfredatı içinde cinsel sağlık bilgileri verilmelidir. Okula gitmeyen adölesan bireylere ise kitle iletişim araçları kullanılarak ve eğitim kampanyaları ile ulaşılmalıdır. Bu önerilere ek olarak eğitim ve danışmanlık almak isteyen bireylerin yargılama ve sorgulama olmadan sağlık birimlerine kolayca ulaşabilmesi sağlanmalıdır.

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**HEMŞİRELİK BAKIMI VE MİZAH  
NURSING CARE AND HUMOR**

*Süreyya BULUT*

*Aydın Adnan Menderes Üniversitesi, Hemşirelik Fakültesi, Hemşirelik Bölümü, Aydın, Türkiye.*

*ORCID ID: 0000-0002-3813-8203*

**ÖZET**

Mizah, yaşanan olay ya da durumların komik ve eğlenceli tarafını görebilme yeteneği, başka bir ifade ile kendisine gülünebilme, başkalarını güldürebilme, komik olma özelliği olan ruh hali olarak tanımlanmaktadır. Gülünç olan bir şeyi görebilme, algılayabilme ve anlatabilme yeteneği, gülünç bulunan şeylerin türü, mizahı yaşayış ya da ifade ediş tarzı ve günlük yaşamda verilen mizahi tepkilerin sıklığı, mizah duygusu olarak adlandırılır. Bu duygu bireyden bireye farklılık gösterir.

Mizah duygusu, yaşanan negatif olaylarda bile çoğu zaman pozitif bakış açısı geliştirmeyi sağlayan, beden ile ruhu birbirine bağlayan bir enerji olarak değerlendirilmiştir. Olumlu mizah anlayışlarının bireyleri daha mutlu birer birey haline dönüştürmesi beklenirken olumsuz mizah anlayışlarının da mutsuz ve zorlukları rahat bir şekilde aşamayan bireyler olması beklenir.

Mizahın fizyolojik mekanizması incelendiğinde, endorfin ve dopamin üretilmesini sağlar. Mizah zor durumları kolaylaştırır, mizah bağlılık yaratır, mizah etkili bir terapötik iletişim tekniği olabilir, mizah planlanabilir veya kendiliğinden olabilir, mizahı paylaşmak kalıcı etkiler yaratır. Sağlık bakımında mizah ve kahkaha, tedavi sırasında hastaların ve sağlık hizmeti sunucularının öznel iyi oluşlarını ve çevreleri ile ilgili olma potansiyelini artırır, hastanın ruh halini ve yaşam kalitesini iyileştirmeyi amaçlamaktadır. Stres ve tehdit durumunda mizah yoluyla olumsuz duygu yükü hafifleyerek stres azalır, gerilimi azaltır bunun yanında, tehdit, baskı sıkıntı oluşturan durumlar karşısında kendini güçlü ve yeterli hissettirir ve daha olumlu duygularla yer değiştirir.

**Anahtar Kelimeler:** Hemşirelik, bakımı, mizah

**ABSTRACT**

Humor is defined as the ability to see the funny and funny side of the events or situations, in other words, to be able to laugh at oneself, to make others laugh, and to be funny. The ability to see, perceive and describe something that is funny, the type of things that are funny, the way of living or expressing humor, and the frequency of humorous reactions in daily life are called sense of humor. This feeling differs from individual to individual.

The sense of humor has been evaluated as an energy that connects the body and the soul, which often enables to develop a positive perspective, even in negative events. While it is expected that positive sense of humor will transform individuals into happier individuals, negative sense of humor is expected to be individuals who are unhappy and cannot easily overcome difficulties.

When the physiological mechanism of humor is examined, it provides the production of endorphins and dopamine. Humor facilitates difficult situations, humor creates commitment, humor can be an effective therapeutic communication technique, humor can be planned or spontaneous, sharing humor creates lasting effects. Humor and laughter in health care increase the subjective well-being of patients and health care providers during treatment and their potential to be relevant to their environment, aiming to improve the patient's mood and quality of life. In the event of stress and threat, the negative emotional load is alleviated through humor, reducing stress, reducing tension. In addition, it makes one feel strong and competent in the face of threatening, pressure and distressing situations, and replaces it with more positive emotions.

**Key Words:** Nursing, care, humor

**KARDİYOPULMONER BYPASS SIRASINDA KULLANILAN PRİME SOLÜSYONLARININ  
OKSİDATİF STRES ÜZERİNE ETKİSİ  
EFFECT OF PRIME SOLUTIONS USED DURING CARDIOPULMONARY BYPASS ON  
OXIDATIVE STRESS**

***Bişar AMAÇ***

*Department of Cardiovascular Surgery, Division of Perfusion, University of Health Sciences,  
Sanliurfa Mehmet Akif Inan Research and Training Hospital, Sanliurfa, Turkey.*

*ORCID ID:0000-0003-0320-4239,*

**ÖZET**

**Giriş:** Kardiyopulmoner bypass (KPB) eşliğinde gerçekleştirilen kardiyak cerrahide ekstrakorporeal dolaşım sistemindeki (Kalp-akciğer makinesinde kullanılan oksijenatör ve tubing set hatları vs) havayı boşaltmak ve hemodilüsyonu sağlamak için çeşitli prime solüsyonları kullanılmaktadır.

**Amaç:** Bu çalışmada KPB sırasında prime solüsyon olarak kullanılan dengeli isolayt ile ringer laktat solüsyonunun oksidatif stres üzerine etkisini karşılaştırmak amaçlanmaktadır.

**Yöntem:** Bu çalışmaya KPB eşliğinde koroner arter bypass greft (KABG) replasmanı uygulanmış benzer demografik ve tanımlayıcı verilere sahip toplam 40 hasta dahil edildi. Hastaların 20'sinde prime solüsyonu olarak dengeli isolayt solüsyonu, 20'sinde ise ringer laktat solüsyonu kullanıldı. Hastaların preoperatif ve postoperatif 1. ve 5. gün kan numunelerinden total antioksidan seviye (TAS), total oksidatif seviye (TOS) ve oksidatif stres indeksi (OSİ) düzeyleri ölçüldü ve sonuçlar istatistiksel olarak değerlendirildi.

**Bulgular:** Prime solüsyonu olarak dengeli isolayt solüsyonu kullanılan grubun preoperatif ve postoperatif (1. ve 5 gün) TAS, TOS ve OSİ düzeyleri arasında anlamlı fark vardı ( $p<0,05$ ). Prime solüsyonu olarak ringer laktat solüsyonu kullanılan grubun da preoperatif ve postoperatif (1. ve 5 gün) TAS, TOS ve OSİ düzeyleri arasında anlamlı fark vardı ( $p<0,05$ ). İki grubun karşılaştırılmasında ise dengeli isolayt solüsyonu kullanılan gruba kıyasla ringer laktat solüsyonu kullanılan grubun postoperatif (1. ve 5 gün) TOS ve OSİ düzeyleri anlamlı olarak daha yüksek, TAS düzeyi ise anlamlı olarak daha düşüktü ( $p<0,05$ ).

**Sonuç:** KPB sırasında kullanılan bu iki prime solüsyonundan dengeli isolayt solüsyonu kullanılan hasta grubunun postoperatif oksidatif stres düzeyinin daha düşük olması, dengeli isolayt solüsyonunun prime solüsyonlarında kullanımının daha güvenli olacağını düşündürmektedir.

**Anahtar Kelimeler:** Kardiyopulmoner Bypass, Prime Solüsyonu, Oksidatif Stres.

**ABSTRACT**

**Introduction:** In cardiac surgery performed with cardiopulmonary bypass (CPB), various prime solutions are used to evacuate the air in the extracorporeal circulatory system (Oxygenator and tubing set lines etc. used in heart-lung machine) and to provide hemodilution.

**Aim:** In this study, it is aimed to compare the effects of balanced isolate and ringer lactate solution used as a prime solution during CPB on oxidative stress.

**Method:** A total of 40 patients with similar demographic and descriptive data who underwent CPB-guided coronary artery bypass graft (CABG) replacement were included in this study. Balanced isolate solution was used as the prime solution in 20 of the patients and Ringer's lactate solution was used in 20 of the patients. Total antioxidant level (TAS), total oxidative level (TOS) and oxidative stress index (OSI) levels were measured from the preoperative and postoperative 1st and 5th day blood samples of the patients, and the results were evaluated statistically.

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**Results:** There was a significant difference between preoperative and postoperative (1st and 5th day) TAS, TOS and OSI levels of the group in which balanced isolate solution was used as the prime solution ( $p < 0.05$ ). There was a significant difference between preoperative and postoperative (1st and 5th days) TAS, TOS and OSI levels in the group that used Ringer's lactate solution as the prime solution ( $p < 0.05$ ). In the comparison of the two groups, postoperative (1st and 5th days) TOS and OSI levels were significantly higher and TAS levels were significantly lower in the group using ringer lactate solution compared to the group using balanced isolate solution ( $p < 0.05$ ).

**Conclusion:** The lower postoperative oxidative stress level of the patient group in which balanced isolate solution was used from these two priming solutions used during CPB makes us think that the use of balanced isolate solution in priming solutions would be safer.

**Keywords:** Cardiopulmonary Bypass, Prime Solution, Oxidative Stress.

**COMPETITIVE STUDY OF THE DIFFERENT VACCINE EFFECTIVENESS OF COVID-19 INFECTION**

*Hasanzade Dinara<sup>1</sup>, Suada Najafova<sup>1</sup>, Elvin Allahverdiyev<sup>1</sup>, Asaf M.Omarov<sup>2</sup>*

*<sup>1</sup>Azerbaijan State Agricultural University, Ganja, Azerbaijan*

*<sup>2</sup>ADA University*

*ORCID ID:0000-0002-2286-5510*

**ABSTRACT**

The study was conducted to investigate the difference in vaccine effectiveness of COVID-19 infection. The survey was conducted among Veterinary faculty staff and students at ASAU in Ganja city. The population size is 1356, the expected frequency is 20%, the acceptable margin of error is 5%, the confidence level is 95%, the design effect is 1,0 and the software was given us 208 respondents for simple random sampling. Out of 238, respondent 151 were vaccinated, and 87 were not vaccinated. Out of 151 vaccinated respondents, 37 were infected, and 114 were not infected. Out of 87 unvaccinated 24 were infected, and 63 were not infected. Odds ratio 0.85 95%CI [0.46;1.5], Risk Ratio 0.88 CI 95%[0.57;1.38].

**Key words:** survey, respondent, vaccine, confidence level

**Introduction**

Coronaviruses are a large family of viruses that are known to cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). [1] Coronavirus disease 2019 (COVID-19) is a highly contagious viral illness caused by severe acute respiratory syndrome SARS-CoV-2. It has had a devastating effect on the world's demographics resulting in more than 5.3 million deaths worldwide. It has emerged as the most consequential global health crisis since the era of the influenza pandemic of 1918.[2] The outbreak of COVID-19 has proven to be a world wide unprecedented disaster. The virus has inflicted billion of lives across the globe in many ways eg physically, psychologically, socially. Compared to MERS and SARS, COVID-19 has had: significantly higher transmissibility; worst post-recovery implications; frequent mutations (from the initial SARS-CoV-2 strain) leading to higher mortalities and uncontrolled virulence. The clinical manifestations of this particular virus has exhibited deleterious impacts on systems other than the respiratory system (primary target organ) eg brain, hematological system, liver, kidneys, endocrine system, etc. with no promising curatives to date. Lack of emergency treatments and shortage of life-saving drugs has promoted the repurposing of existing therapeutics along with the emergence of vaccines with the combined efforts of scientists and industrial experts in this short span.[3]

As of 6 December 2021, there have been approximately 266 000000 confirmed cases of COVID-19, including approx. 5 300 000 deaths, reported to WHO.[4]

**Material and methods**

The survey was conducted among Veterinary faculty staff and students at Azerbaijan State Agricultural University (ASAU) in Ganja city. The veterinary faculty has 1268 students and 88 teaching staff. 238 respondents were involved to face to face study. 208 are students, 1 is an assistant, 1 laboratory assistant, 15 is a professor assistant, and 13 didn't say profession. Out of 238 respondents, 101 were male, and 137 were female. Statcal was used for the detection of sample size and power. The population size is 1356, the expected frequency is 20%, the acceptable margin of error is 5%, the confidence level is 95%, the design effect is 1,0 and the software was given us 208 respondents for simple random sampling. EpiInfo 7 was used for statistical purposes.



### **Results**

Out of 238, respondent 151 were vaccinated, and 87 were not vaccinated. Out of 151 vaccinated respondents, 37 were infected, and 114 were not infected. Out of 87 unvaccinated 24 were infected, and 63 were not infected. Odds ratio 0.85 95%CI [0.46;1.5], Risk Ratio 0.88 CI 95%[0.57;1.38]. 117 (72 female, 45 male) were vaccinated with Sinovac, 23 (11 female 12 male) Pfizer, 10 (4 female 6 male) Biontech, 1 Diniva, 1 Sputnik, 14 (7 female, 7 male) don't know. 61(40 female, 21 male) were infected COVID-19, 26 were confirmed by PCR, and 17 were contacted by an infected man. 37 infected after vaccination, 31 Sinovac, 1 Pfizer, 1 biotech, 1 Divina. Out of 117 Sinovac immunization 31 were infected, 86 were not infected, Out of 34 other vaccines 6 were infected, and 28 were not infected. Odds ratio 1.6 CI95% [0.63; 4.4], Risk ratio 1.5 CI 95% [0.68;3.2]

### **Outcomes**

Odds ratio 0.85 less than unvaccinated,

Risk Ratio 0.88 less than unvaccinated

Sinovac was widely held vaccine among veterinary faculty staff

Sinovac vaccine Odds ratio 1.6, risk ratio 1.5

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**RADYOAKTİF İYOT TEDAVİSİ ALAN DİFFERANSİYE TİROİD KANSERLİ HASTALARDA TEDAVİYE KOMPLET YANITI PREDİKTE ETMEDE TEDAVİ ÖNCESİ TİROGLOBULİN SEVİYESİNİN ROLÜ**

**THE ROLE OF PRE-THERAPY THYROGLOBULIN LEVEL IN PREDICTING COMPLETE RESPONSE TO TREATMENT IN PATIENTS WITH DIFFERENTIAL THYROID CANCER REQUESTING RADIOACTIVE IODINE THERAPY**

**Ferat KEPENEK<sup>1</sup>**

<sup>1</sup> SBÜ. Gazi Yaşargil Eğitim ve Araştırma Hastanesi, Nükleer Tıp Kliniği, Diyarbakır, Türkiye.

<sup>1</sup>ORCID ID: 0000-0002-5631-7643

**ÖZET**

**Amaç:** Tiroid kanseri en yaygın endokrin malignitedir ve insidansı son birkaç on yılda artmaktadır. Diferansiye tiroid kanseri (DTC), tüm tiroid kanserlerinin yaklaşık %90'ını oluşturur ve genel olarak, yaklaşık %95'e varan mükemmel 10 yıllık hastalığa özgü sağ kalıma sahiptir. Tiroid hormonunun kesilmesiyle desteklenen RAI (radyoaktif iyot) tedavisinden önce yüksek düzeyde stimüle tiroglobulin (Tg)'in kötü prognozu öngördüğü bildirilmiştir. Bu çalışmada RAI tedavisi alan DTC'li hastalarda tedaviye komplet yanıtı predikte etmede tedavi öncesi tiroglobulin seviyesinin rolünü araştırmayı amaçladık.

**Yöntem:** Bu retrospektif çalışmaya Ocak 2010-Ocak 2014 tarihleri arasında opere DTC tanısı ile RAI tedavisi için kliniğimize yönlendirilen 143 hasta dahil edildi. Tüm hastaların tedavi ve takibi ATA (American Thyroid Association) risk sınıflamasına göre yapıldı. Tüm hastaların TSH (Thyroid stimulant hormone) ve Tg değerleri (hem RAI tedavisi öncesi hem de 6. Ay RAI taraması öncesi) kaydedildi. Ayrıca tüm hastaların tedavi sonrası ve 6. ay I-131 tüm vücut tarama (TVT) görüntüleri değerlendirildi. Tedavi sonrası 6. ayda yapılan TVT görüntülerinde tirid lojunda tutulum saptanmayan ve stimüle Tg değeri 2 ng/ml'nin altında olan hastalar komplet yanıtı olarak değerlendirildi. Tedaviye komplet yanıtı değerlendirmede hesaplanan cut-off (kestirim) değerinin ayırdığı sınıflama ile gerçek sınıflama arasındaki ilişki için duyarlılık ve özgüllük oranları ROC (Receiver Operating Curve) eğrisi analizi ile incelendi.

**Bulgular:** Çalışmaya katılan 143 hastanın yaş ortalaması 44,43 (15-81) olarak hesaplanmış olup 119 (% 82,6) hasta kadındı. Hastaların subtiplerine bakıldığında 135 hastada Papiller karsinom 7 hastada foliküler karsinom ve 1 hastada Hurthle hücreli karsinom saptandı. Hastaların tedavi öncesi Tg değerleri 42,94 (0,04-1000) ng/ml olarak bulunmuş olup 6. Ay TVT öncesi Tg 25,47 (0,04-1000) ng/ml değerleri olarak bulundu. Ayrıca Hastaların tedavi öncesi TSH değerleri 83,98 (30-137) mIU/L olarak bulunmuş olup 6. Ay TVT öncesi TSH değeri 85,11(31,7-100) mIU/L olarak bulundu. ROC eğrisi ile tedavi öncesi Tg'nin cut-off değeri  $\leq 11,97$  ng/ml olarak bulunmuş olup %84,8 duyarlılık ve % 85,5 özgüllük ile tedaviye komplet yanıtın öngörülebilir olduğu bulundu.

**Sonuç:** Sonuç olarak RAI tedavisi alan DTC'li hastalarda tedavi öncesi tiroglobulin seviyesinin tedaviye komplet yanıtı predikte etmede önemli bir rolünün olduğunu bulduk.

**Anahtar Kelimeler:** Tiroglobulin, Radyoaktif iyot, Diferansiye tiroid kanseri

**ABSTRACT**

**Aım:** Thyroid cancer is the most common endocrine malignancy and its incidence has been increasing over the past few decades. Differentiated thyroid cancer (DTC) accounts for approximately 90% of all thyroid cancers and overall has an excellent 10-year disease-specific survival of approximately 95%. It has been reported that highly stimulated Thyroglobulin (Tg) predicts poor prognosis before RAI (radioactive iodine) therapy supplemented by discontinuation of thyroid hormone. In this study, we

aimed to investigate the role of pre-treatment thyroglobulin level in predicting the complete response to treatment in patients with DTC who received RAI.

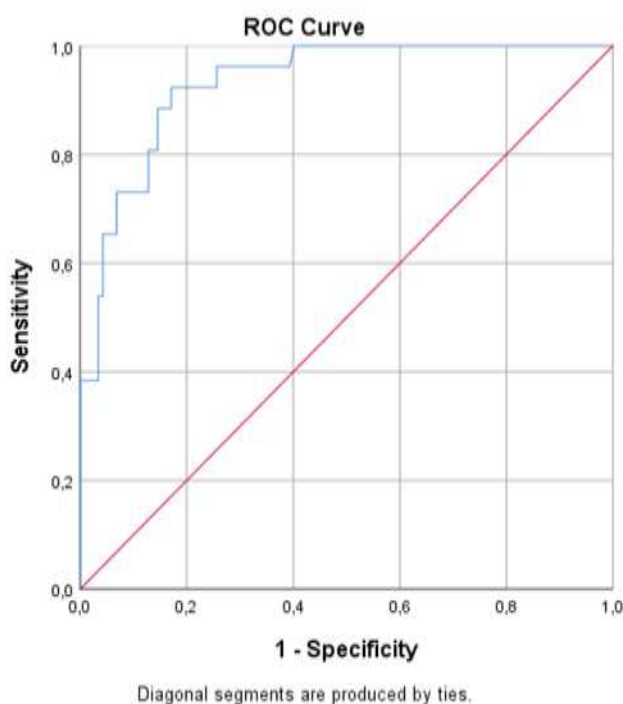
Methods: In this retrospective study included 143 patients who were referred to our clinic for the treatment of RAI with the diagnosis of operated DTC between January 2010 and January 2014. All patients were treated and followed up according to the ATA (American Thyroid Association) risk classification. TSH (Thyroid stimulating hormone) and Tg values of all patients (both before RAI treatment and before 6th month RAI screening) were recorded. In addition, post-treatment and 6-month I-131 whole body scan (TVT) images of all patients were evaluated. Patients who did not show involvement in the thyroid region in the TVT images performed at the 6th month after the treatment and whose stimulated Tg value was below 2 ng/ml were evaluated as having a complete response. Sensitivity and specificity ratios were analyzed by ROC (Receiver Operating Curve) curve analysis for the relationship between the classification calculated by the cut-off value calculated in the evaluation of the complete response to treatment and the actual classification.

Results: The mean age of 143 patients participating in the study was calculated as 44.43 (15-81), and 119 (82.6%) patients were women. When the subtypes of the patients were examined, papillary carcinoma was found in 135 patients, follicular carcinoma in 7 patients, and Hurthle cell carcinoma in 1 patient. The pre-treatment Tg values of the patients were found to be 42.94 (0.04-1000) ng/ml, and the Tg values before the 6th month TVT were found to be 25.47 (0.04-1000) ng/ml. In addition, the pre-treatment TSH values of the patients were found to be 83.98 (30-137) mIU/L, and the TSH value before the 6th month TVT was found to be 85.11 (31.7-100) mIU/L. The cut-off value of Tg before treatment with the ROC curve was found to be  $\leq 11.97$  ng/ml, and complete response to treatment was predictable with 84.8% sensitivity and 85.5% specificity.

Conclusion: In conclusion, we found that pre-treatment thyroglobulin level has an important role in predicting the complete response to treatment in patients with DTC receiving RAI treatment.

**Keywords:** Thyroglobulin, Radioactive iodine, Differentiated thyroid cancer.

Şekil 1: ROC eğri analizi



**GÜVENLİ ANNELİK VE EBELİK UYGULAMALARI  
SAFE MOTHERHOOD AND MIDWIFERY PRACTICES**

*Ayşe Nur YILMAZ<sup>1</sup>*

<sup>1</sup> *Fırat Üniversitesi, Sağlık Bilimleri Fakültesi, Ebelik Bölümü, Elazığ, Türkiye.*

<sup>1</sup> *ORCID ID: 0000-0003-0489-7639*

*Sümeyye ALTIPARMAK<sup>2</sup>*

<sup>2</sup> *İnönü Üniversitesi, Sağlık Bilimleri Fakültesi, Ebelik Bölümü, Malatya, Türkiye.*

<sup>2</sup> *ORCID ID: 0000-0002-4759-1210*

**ÖZET**

Güvenli annelik; anneye gebelik öncesi, anne ve bebeğe gebelik boyunca, doğumda ve sonrasında gerekli tüm bakım, takip ve tedavi hizmetlerinin verilmesidir. Aynı zamanda bütün bu dönemlerde risklerin ve komplikasyonların tanımlanması, önlenmesi ve yönetimini kapsayan bütüncül yaklaşımdır. Güvenli annelik, her kadının temel anne sağlığı hizmetlerinden yararlanabilmesini, üreme ve cinsel sağlık konusunda çiftleri bilinçlendirmeyi ve toplumsal cinsiyet eşitliğini sağlamayı amaçlamaktadır. Anne sağlığı kapsamında doğum öncesi ve sonrası bakım hizmetleri ile doğum hizmetlerini, gebelik ve doğumdaki acil hizmetleri, yenidoğan bakımını ve aile planlamasını içermektedir.

İlk defa 1987’de Nairobi’de Birleşmiş Milletler Nüfus Fonu (UNFPA), Birleşmiş Milletler Uluslararası Çocuklara Yardım Fonu (UNICEF), Dünya Sağlık Örgütü (DSÖ), Dünya Bankası ve birçok ülkeden çeşitli kuruluşlar toplanmış ve güvenli annelik girişimini başlatmıştır. 2000 yılına dek güvenli annelik girişimiyle anne ölümlerinin %50 oranında azaltılmasını hedeflenmiştir. 1995’te Pekin’de yapılan Dördüncü Dünya Kadın Konferansında kadın sağlığına özellikle de anne ölümü ve uzun dönem sekelleri konularına küresel anlamda dikkat çekilmiş, Türkiye de dahil olmak üzere pek çok gelişmekte olan ülke bu hareketi tanımış ve içinde yer almıştır. Güvenli annelik hareketinin hedeflerinin başında; anne ölümlerinin ve yenidoğan bebek ölümlerinin azaltılması, temel sağlık hizmetlerinin yeterli düzeyde verilmesi ile gebeliğe bağlı komplikasyonlar ve ölümlerin önlenmesi, her kadının güvenli bir gebelik süreci yaşama ve güvenli bir doğum yapma hakkına erişmesi bulunmaktadır. DSÖ’nün güncellenen 2017 verilerine göre ise gebelik, doğum ve doğum sonrası dönemdeki komplikasyonlardan kaynaklanan ölümler son yirmi yılda %38 oranında azalmıştır, ancak yine de ortalama yılda yaklaşık %3 azalma ile bu iyileşme hızı hala çok yavaş kalmaktadır. Aynı zamanda anne ölüm oranlarında ülkeler arasında büyük farklar da devam etmektedir. 2017 yılı anne ölümlerinin %86’sı Sahra Altı Afrika ve Güney Asya bölgesinden bildirilmiştir. DSÖ anne sağlığı için sürdürülebilir kalkınma hedefleri (SKH) kapsamında 2030 yılına kadar 100.000 doğumda 70’in altında anne ölümü hedeflemektedir.

Türkiye’de ve Dünya’da “Güvenli Annelik bakımı” almamayı etkileyen faktörler, kadının eğitim durumu, toplumsal konumu, sosyokültürel ve ekonomik durumu, sağlık güvencesi varlığı, sağlık hizmetlerine ulaşamama, sağlık çalışanı ile yaşanan iletişim sorunları, sağlık çalışanlarının yetersizliği gibi nedenlerdir. Güvenli annelik, sağlıklı annelik demektir. Güvenli annelik girişimlerinin sağlanması ve sürdürülmesi için ebelerin yetkinliğine, bakıma uygun eğitim ve beceriye sahip olmasına ihtiyaç vardır. Bu derlemenin amacı, güvenli annelik girişimine, etkileyen faktörlere, Dünya’da ve Türkiye’de yapılan ebelik uygulamalarına dikkat çekerek önerilen stratejileri sunmak ve bu stratejiler ışığında kadın sağlığını koruma ve geliştirmede ebelerin rol ve sorumluluklarına yönelik önerilerde bulunmaktır.

**Anahtar Kelimeler:** Güvenli, Anne, Ebelik.

## **ABSTRACT**

Safe motherhood is the provision of all necessary care, follow-up and treatment services to the mother before pregnancy, to the mother and the baby during pregnancy, at birth and after. It is also a holistic approach that covers the identification, prevention and management of risks and complications in all these periods. Safe motherhood aims to ensure that every woman can benefit from basic maternal health services, to raise awareness of couples on reproductive and sexual health, and to ensure gender equality. Within the scope of maternal health, it includes prenatal and postnatal care services and delivery services, emergency services in pregnancy and birth, newborn care and family planning.

For the first time in Nairobi in 1987, the United Nations Population Fund (UNFPA), the United Nations International Children's Fund (UNICEF), the World Health Organization (WHO), the World Bank and various organizations from many countries gathered and started the safe motherhood initiative. Until 2000, it was aimed to reduce maternal mortality by 50% with the safe motherhood initiative. At the Fourth World Conference on Women held in Beijing in 1995, global attention was drawn to women's health, especially maternal mortality and its long-term sequelae, and many developing countries, including Turkey, recognized this movement and took part in it. At the beginning of the goals of the safe motherhood movement; reducing maternal and neonatal deaths, providing adequate basic health services, preventing pregnancy-related complications and deaths, and ensuring that every woman has the right to a safe pregnancy and a safe delivery. According to WHO's updated 2017 data, deaths from complications in pregnancy, childbirth and postpartum period have decreased by 38% in the last two decades, but this rate of recovery is still very slow with an average decrease of 3% per year. At the same time, large differences in maternal mortality rates remain between countries. 86% of maternal deaths in 2017 were reported from Sub-Saharan Africa and South Asia. Under the WHO sustainable development goals (SDGs) for maternal health, by 2030 it aims to have less than 70 maternal deaths per 100,000 births.

Factors affecting not receiving "Safe Maternity care" in Turkey and in the world are reasons such as women's educational status, social position, socio-cultural and economic status, presence of health insurance, inaccessibility to health services, communication problems with health workers, inadequacy of health workers. Safe motherhood means healthy motherhood. In order to provide and maintain safe motherhood initiatives, midwives need to have the competency, education and skills appropriate for care. The aim of this review is to present the recommended strategies by drawing attention to the safe motherhood initiative, the factors affecting it, midwifery practices in the world and in Turkey, and to make suggestions on the roles and responsibilities of midwives in protecting and improving women's health in the light of these strategies.

**Keywords:** Safe, Mother, Midwifery.

## **GİRİŞ**

Güvenli annelik kavramı, 1987 yılında gündeme geldiğinde, tahmini olarak dünyada her dakikada 380 kadının gebe kaldığı, bu gebeliklerin 190'ının istenmeyen gebelikler olduğu, 110 kadının gebelik ile ilgili komplikasyon yaşadığı, 40 kadının sağlıksız düşük yaptığı ve 1 kadının gebelik ve gebeliğe bağlı nedenler ile öldüğü saptanmıştır (Demirbağ, 2018).

Dünya Sağlık Örgütü, 1987 yılında Nairobi'de düzenlenen bir konferansta, uluslararası kuruluşların ve yüze yakın ülkenin temsilcilerinin ortak karar ve desteğiyle Güvenli Annelik programı başlatılmıştır. Programın ana hedefi, yetersiz hizmet alan ve önlenemez nedenlerden kaynaklanabilecek anne ve bebek ölümlerini ve sakatlıklarını 2000 yılına kadar %50 oranında azaltmaktır. Ancak aradan geçen 35 yıla rağmen dünyada, özellikle gelişmekte olan ve az gelişmiş ülkelerde anne ölüm oranları ideal seviyelere ulaşmış değil. Gelişmekte olan ülkelerde yapılan araştırmaların sonuçlarına göre; anne ölümlerinin başlıca nedenleri şiddetli kanama, toksemi, enfeksiyon, engellenen doğum ve sağlıksız koşullarda kürtajdır. Yenidoğan ölümlerinin önde gelen nedenleri gebelikte yetersiz antenatal bakım, doğum sırasındaki yanlış uygulamalar, hipotermi ve enfeksiyonlardır (Demirbağ, 2018).

## **GÜVENLİ ANNELİK**

15-49 yaş arası olan doğurganlık dönemi, kadın sağlığında gebelik ve doğumla ilgili olay ve komplikasyonların en yoğun yaşandığı dönem olarak bilinmektedir. 1987 yılında DSÖ öncülüğünde Dünya Bankası, Birleşmiş Milletler Nüfus Fonu ve 55'ten fazla ülkenin katılımı ile Nairobi'de yapılan uluslararası toplantının temel amacı doğurganlık dönemi sorunlarına yönelik anne ve yenidoğan ölümlerini azaltmak için Güvenli Annelik programının başlatılması yönünde olmuştur.

Güvenli Annelik; anneler için gebelik öncesi, anne ve bebeğe antenatal, intrapartum ve postpartum bakım ve tedavi hizmetlerinin sağlanması, istenmeyen ve yüksek riskli gebeliklerin önlenmesi, gebelik, doğum ve doğum sonrası komplikasyonların tanımlanması, önlenmesi ve yönetimini kapsayan anne ve bebek ölümleri ve komplikasyonlarını azaltmaya yönelik bütüncül yaklaşım olarak tanımlanmıştır. Bu toplantıda güvenli annelik tanımından yola çıkarak ülkeler 2000 yılına kadar anne ölüm ve hastalıklarını yarı yarıya azaltmak, çocuk ve anne sağlığını en üst düzeye çıkarmak için hedefler koymuşlardır (Sağlık Bakanlığı, 2009; Karakaya ve Coşkun, 2013).

Güvenli annelik uygulamasının kısa vadedeki hedefleri; bakım kalitesini geliştirmek, hizmetlere erişimi artırmak, bu hizmetin önemi ve nasıl kullanılacağı konusunda toplumu eğitmek, aile planlaması ve anne sağlığı hizmetlerini daha etkin hale getirmektir. Uzun vadedeki hedefleri; sosyoekonomik durumunu iyileştirmek için sağlık, eğitim ve diğer faktörleri kapsamlı bir şekilde ele almaktır (Coşkun ve Kaya, 2016).

### **DÜNYADA GÜVENLİ ANNELİK**

1994'te Birleşmiş Milletler konferans serisinde yer alan Kahire Uluslararası Nüfus ve Kalkınma Konferansı ile 20 yıllık bir eylem planı yapılmıştır. Katılımcı ülkeler, toplum sağlığının ve iyilik halinin geliştirilmesi ve nüfus büyüme hızının azaltılması konusunda görüş birliği sağlamışlardır. 1995 yılında Pekin Dördüncü Dünya Kadın Konferansında kadın sağlığına özellikle de anne ölümü ve uzun dönem sekelleri konularına küresel anlamda dikkat çekilmiş, Türkiye ve bir çok gelişmekte olan ülke bu hareketi tanımış ve içinde yer almıştır (Artıran İğde ve ark., 2008).

Güvenli annelik hareketinin hedeflerinin başında; anne ölümlerinin ve yenidoğan bebek ölümlerinin azaltılması, temel sağlık hizmetlerinin yeterli düzeyde verilmesi ile gebeliğe bağlı komplikasyonlar ve ölümlerin önlenmesi, her kadının güvenli bir gebelik süreci yaşama ve güvenli bir doğum yapma hakkına erişmesi bulunmaktadır.

DSÖ 2008 yılında gerçekleşen yaklaşık 358.000 anne ölüm nedenlerinin %60'ının doğum sonrası dönemde meydana geldiğini raporunda ifade etmiştir. Bu ölümlerin %45'inin doğumdan sonraki ilk 24 saat içerisinde, %65'inin bir hafta içerisinde olduğu saptanmıştır. Anne ölümlerin en sık olduğu bölgelerin Afrika ve Güney-doğu Asya ülkeleri gibi gelişmekte olan ya da az gelişmiş ülkelere olduğuna dikkat çekmektedir (Demirbağ, 2018).

DSÖ'nün güncellenen 2017 verilerine göre ise gebelik, doğum ve doğum sonrası dönemdeki komplikasyonlardan kaynaklanan ölümler son yirmi yılda %38 oranında azalmıştır, ancak yine de ortalama yılda yaklaşık %3 azalma ile bu iyileşme hızı hala çok yavaş kalmaktadır. Aynı zamanda anne ölüm oranlarında ülkeler arasında büyük farklar da devam etmektedir. 2017 yılı anne ölümlerinin %86'sı Sahra Altı Afrika ve Güney Asya bölgesinden bildirilmiştir. DSÖ anne sağlığı için sürdürülebilir kalkınma hedefleri (SKH) kapsamında 2030 yılına kadar 100.000 doğumda 70'in altında anne ölümü hedeflemektedir (WHO, 2019).

### **TÜRKİYE'DE GÜVENLİ ANNELİK**

Güvenli annelik programı Türkiye'de 1994 yılında pilot uygulamalarla başlatılmıştır. Güvenli annelik programının müdahale alanlarının başında gebenin doğum öncesi, doğumda ve doğum sonrası bakım alması bulunmaktadır. 2013 Türkiye Nüfus ve Sağlık Araştırması (TNSA) verilerine göre çalışmadan önceki son beş yılda Türkiye'deki gebelerin %97'si doğum öncesi bakım almış, %97,4'ü doğum sırasında tıbbi eğitim almış kişilerce yardım almış, %93,1'i ise doğum sonrası 41 gün içinde doğum sonrası bakım almıştır (TNSA, 2013).

Güvenli annelik programının en etkili olduğu göstergelerden bir diğeri, anne ölümlerinin belirlenmesine yönelik çalışmalardır. 1973-1983 yılları arasında yapılan bir çalışmada, anne ölümleri değerlendirilmiş

ve anne ölüm oranı (AÖO) yüz bin canlı doğumda 119 olarak saptanmıştır. Aynı çalışmada kanama %58 ile anne ölümlerinin en sık nedeni olarak saptanmıştır.

1997-1998 yılları arasında Sağlık Bakanlığı, DSÖ, UNFPA ve Hacettepe Üniversitesi Tıp Fakültesi Halk Sağlığı Anabilim Dalı iş birliği ile seçilmiş 53 ilin doğum yapılan bütün hastanelerinde “Anne Ölüm Nedenleri Araştırması” yapılmıştır. Bu çalışmada AÖO 100.000 doğumda 49.2 olarak bulunmuştur.

2006 yılında ise Türkiye Üreme Sağlığı Programı kapsamında Ulusal Anne Ölüm Araştırması yapılmıştır. Bu araştırmayla ülkemizin AÖO 100.000 canlı doğumda 28,5 olarak, gebeliğe bağlı ölüm oranı (GBÖO) ise 100.000 canlı doğumda 38,3 olarak saptanmıştır. Araştırmada asıl çarpıcı sonuç ise bölgeler arasında ölüm oranlarının büyük farklılıklar göstermesidir. Araştırma sonuçlarına göre AÖO kent ortalaması 100.000 canlı doğumda 20,7 saptanırken, kırsal kesimde ortalama 100.000 canlı doğumda 40,3 olarak saptanmıştır. Araştırmada elde edilen sonuçlara göre Türkiye’de anne ölümleri nedenleri arasında ilk sırada %24,9 ile kanama gelmektedir. Doğrudan anne ölüm nedenleri arasında ikinci sırada ise anne ölümlerinin %18,4’ünü oluşturan ödem, proteinüri, hipertansiyon ve konvülsiyon ile desteklenen eklampsi bulunmaktadır. Dolaylı nedenler %21,2 olarak saptanmıştır.

Türkiye TNSA verilerine detaylı bakıldığında yıllara göre Anne Ölüm Oranı (100.000 Canlı Doğumda); 2004’de 50,2; 2005’de 39,3; 2006’da 28,5; 2007’de 21 2008’de 19,4; 2009’da 18,4; 2010’da 16,4; 2011’de 15,5; 2012’de 15,4; 2013’de 15,9; 2014’de 15,2; 2015’de 14,7; 2016’da 14,7 olduğu görülmektedir (Demirbağ, 2018).

Bu çalışmayla elde edilen sonuçlara göre Türkiye’de gözlenen anne ölümleri ekonomik geçiş yaşayan ülkelere benzerlikler göstermektedir. Anne ölümü oranının yüksek olduğu kırsal bölgelerin acil obstetrik bakım hizmetleri veren sağlık kurumlarına ulaşımında sorunlar yaşadığı belirlenmiştir. Bu çalışma sonucunda ölüm oranlarının azaltılmasında hastanelerin ölümle sonuçlanan ya da ölümün kıyısından dönülen vakaları değerlendirmesi ve olumsuz sonuçlara götüren olaylar zincirini anlayabilmek amacıyla izleme komitesi kurmasının faydalı olacağı düşünülmüştür (Demirbağ, 2018).

Tüm bu araştırmalar ışığında anne ölümlerinin önlenmesinde en önemli faktörlerin annenin doğumda, doğum öncesinde ve sonrasında iyi kalitede sağlık hizmetine ulaşılabilirliğinin sağlanması, yüksek riskli gebeliklerin yakın takip edilmesi, acil durumların etkili şekilde yönetilmesi, aile planlama hizmetlerinin sunulması olduğu düşünülmektedir. Bunun yanında yoksulluk, eğitimsizlik ve cinsiyet ayrımcılığıyla savaşılmaması da anne ölümlerinin önlenmesinde büyük önem taşımaktadır. Aynı zamanda bu sonuçlar anne ölümlerini önlemeyi amaçlayan programlar arasında en etkin yaklaşımı sağlayan “Güvenli Annelik” programının uygulamanın gerekliliğini göstermektedir. Ülkemizde anne ölüm oranlarındaki düşüş dikkat çekicidir. Bu sonuç ülke politikalarının anne ve çocuğa yönelik sağlık hizmetine gerekli önemi verdiğini göstermektedir. Ancak bu sonucun daha iyiye gelebilmesi için güvenli anneliğe yönelik programların devamının ve geliştirilmesinin gereği de görülebilmektedir.

## **GÜVENLİ ANELİK YAKLAŞIMIYLA ANNELİK GÜVENLİĞİ**

Güvenli annelik, kadınlara ve ailelerine gebeliklerin zamanlamasını, sayısını ve aralığını uygun şekilde düzenlemek ve hamile kadınlara temel obstetrik bakım sağlamak için gerekli hizmetlerin sağlanması anlamına gelir. Yeni doğmuş bir bebeğin yaşaması ve sağlığı, ancak ve ancak son derece önemli olan yaşamının ilk dakikalarında ihtiyaçlarının anlaşılması ve gerekli hizmetlerin sağlanmasıyla mümkündür. Anneliği güvenli hale getirmek anlamına gelmektedir. Güvenli annelik yaklaşımı, istenmeyen yüksek riskli gebelik sayısını, obstetrik komplikasyonları, komplikasyonlu kadınlarda ölüm riskini, anne ve yenidoğan ölümlerini ve hastalıkları azaltabilen, basit, uygulanabilir, uygun maliyetli müdahaleleri bir araya getirir. Bu hedeflere ulaşmada temel konular, aile planlaması, anne ve yenidoğan için doğum öncesi, doğum ve doğum sonrası bakım, komplikasyonlar için temel obstetrik bakım ve yenidoğan için özel bakımdır.

### **Anne-Bebek Paketi**

Anne-bebek paketi, antenatal, intrapartum ve postpartum dönemde anne ve bebek sağlığına yönelik gerekli müdahaleleri yaparak ölümcül olabilecek komplikasyonları ortadan kaldırarak güvenli annelik programının kısa sürede başarılı olabilmesini amaçlamaktadır. Güvenli annelik yaklaşımında anne-

bebek paketlerinin uygulanmasıyla, anne ve yenidoğan ölümlerinde önemli azalmalar meydana gelmektedir. Yapılan çalışmalara göre; annede kanamaya bağlı ölümlerde %55, sepsise bağlı olanlarda %75, eklampsiye bağlı olanlarda ise %80 azalma olduğu saptanmıştır. Yenidoğan da ise, doğum asfiksisine bağlı ölümlerde %40-60, tetanosa bağlı ölümlerde %80, doğum travmasına bağlı olan ölümlerde ise %40-60 azalma bulunmuştur.

## **GÜVENLİ ANNELİK PROGRAMINDA MÜDAHALE ALANLARI**

### **Doğum Öncesi Bakım Hizmetleri**

Doğum öncesi bakım hizmetleri gebeliğin saptanması, sağlıklı şekilde sürdürülmesi, patolojik durumların belirlenmesi ve yönetilmesi açısından önem taşır. Antenatal bakım hizmetlerinin kapsam, kalite ve niteliğinin artırılması hem anne-bebek hem de aile ve toplum açısından çok önemlidir. Doğum öncesi bakım anne ve bebek sağlığında risk oluşturabilecek faktörlerin saptanıp giderilmesi için çiftlere verilmesi gereken gebelik öncesi danışmanlıkla başlar (Kısa, 2021). Aile planlaması danışmanlığı ve uygulama hizmetlerinin artırılması ile istenmeyen ve planlanmayan gebeliklerin engellenmesi, cinsel yolla bulaşan hastalıkların (CYBE), hepatit ve HIV enfeksiyonunun önlenmesi ve tedavisi, portpartum birinci ayda karşılaşılabilecek maternal ve neonatal tetanozun önlenmesi için gebelikte tetanoz bağışıklamaşının yapılması, mevcut hastalıkların tedavisinin planlanarak sürdürülmesi gerekir. Kaliteli bir gebelik yaşanması için ilgili danışmanlık hizmetinin verilmesi, gebelik sırasında yeterli beslenmesinin sağlanması, demir ve fosfat ilavesi ile aneminin azaltılması, gebelikten kaynaklanan komplikasyonların tanınması, erken tanı ve tedavisi (preeklampsi/eklampsi, anemi) yapılmalıdır.

### **Doğum**

Temiz ve güvenli bir doğum sağlamak, komplikasyonları tespit etmek, erken tanılamak ve yönetmek (eklampsi ve uzamış doğum eylemi vb.) önemlidir.

### **Doğum Sonrası Bakım Hizmetinin Verilmesi**

Postpartum dönemde anneye ve bebeğe verilen bakımın amacı; anne ve bebeğin fiziksel ve psikolojik sağlığını korumak, anne sütü ve emzirme ile ilgili anneyi bilgilendirmek, anne-bebek ilişkisinin gelişimini sağlamak, annenin sosyal çevresi içinde annelik konumunu benimseyebilmesine ve kendine güvenini kazanmasına yardım etmek olmalıdır. Anneye doğum sonu komplikasyonların (kanama, sepsis, eklampsi gibi) erken tanınması ve tespiti ile sağlık kuruluşunda gerekli önlem ve yaklaşımların uygulanması, doğum sonrası bakım (emzirme komplikasyonlarına uygun yaklaşım) ve aile planlaması ile ilgili bilgilendirme hizmetinin verilmesi gerekir. Bebek için ise, gerekli hallerde resüsitasyon yapılması, hipotermisinin önlenmesi ve yönetimi, emzirmenin teşvik edilmesi, yenidoğan enfeksiyonlarının önlenmesi ve yönetilmesi gerekir (Kısa, 2021).

### **Anne-Bebek Paketinin Ülkemizde Uygulanmasında İzlenmesi gereken Basamaklar**

1. Ulusal standartlar, stratejiler ve politikaların saptanarak tanımlanması
2. İhtiyaçların belirlenmesi
3. Ulusal aksiyon planının hazırlanması
4. Maliyetin hesaplanması
5. Mevcut ve ulaşılabilir kaynakların belirlenmesi
6. Aktivitelerin toplum düzeyinde uygulanması
7. Sağlık hizmetlerinin güçlendirilmesi
8. İnsan kaynaklarının geliştirilmesi
9. Araç-gereç sağlanması
10. Hizmetlerin niteliğinden emin olunması
11. Bilgilendirme, eğitim ve iletişimin sağlanması
12. Sosyal Mobilizasyon



13. Tüm programın izlenmesi ve değerlendirilmesi (Demirbağ, 2018).

### **TÜRKİYE'DE VE DÜNYA'DA “GÜVENLİ ANNELİK BAKIMI” ALMAYI ETKİLEYEN FAKTÖRLER**

Türkiye’de ve dünya’da “güvenli annelik bakımı” almayı etkileyen Nedenler arasında kadınların eğitim düzeyi, sosyal statüsü, sosyokültürel ve ekonomik durumu, sağlık sigortasının varlığı, sağlık hizmetlerine ulaşamaması, sağlık çalışanları ile iletişim sorunları, sağlık çalışanı eksikliği sayılabilir (Karakaya ve Coşkun, 2008; Demirbağ, 2018).

Kadınların gebelik, doğum ve doğum sonrası dönemde sağlık hizmetlerden etkin bir şekilde yararlanamaması üç aşamada özetlenebilir. Gebe veya yeni doğum yapmış bir kadında gecikme, ailesinin komplikasyonları anlamaması ve yardım istememesi, kadının komplikasyonlar için gerekli sağlık ve tedavi hizmeti almak üzere uygun bir sağlık hizmeti veren merkeze gitmekten çekinmesi ve sağlık merkezine gidilmesinden sonra uygun sağlık ve tedavi hizmetinin alınmasında gecikmedir.

### **GÜVENLİ ANNELİK PROGRAMINDA EBENİN ROLÜ**

Ebeler, birinci basamak sağlık hizmetleri sunumunda kadınların en fazla karşılaştığı profesyonel sağlık personelidir. Evlilik öncesi dönemden başlayarak genital hijyen sağlığı, kadın organlarının ve fonksiyonları/üreme sağlığı, evliliğe hazırlık, gebeliğe hazırlık, gebelik süresi, doğum, doğum sonrası ve yenidoğan dönemi boyunca anne ve bebek sağlığını korumaya yönelik önlemleri alınması, anneye öğretilmesinin planlanması ve uygulanması ebelerin rol ve sorumluluklarıdır. Ebeler, anneye yönelik sorun ve çözümlerinde danışmanlık rolünü üstlenmektedir. Ayrıca ebe annenin haklarına yönelik yaptığı girişimlerle de annenin savunuculuk rolünü üstlenmektedir. Güvenli annelik girişimlerini sağlamak ve sürdürmek için ebelerin yetkinliğine, bakıma uygun eğitim ve beceriye sahip olmalarına ihtiyaç vardır.

### **SONUÇ**

Güvenli annelik, anne ve bebeklerde hastalık ve ölümü azaltmaya yönelik geliştirilmiş dünyanın gelişim hedeflerinden biridir. Bu kapsamda esas sorumluluk sağlık profesyonellerine düşmektedir. Özellikle güvenli annelik girişimlerini sağlamak ve sürdürmek için ebelerin yetkinliğine, bakıma uygun eğitim ve beceriye sahip olmalarına ihtiyaç vardır. Güvenli annelik girişimine, etkileyen faktörlere, Dünya’da ve Türkiye’de yapılan ebelik uygulamalarına dikkat çekerek önerilen stratejileri sunmak ve bu stratejiler ışığında kadın sağlığını koruma ve geliştirmede ebelerin rol ve sorumluluklarındandır. Ülkeler kendilerine ait durum analizi doğrultusunda geliştirilmiş güvenli annelik programı uygulamasıyla, yetersiz beslenmeden, ayrımcılıktan, kendilerine yönelik hakların eksikliğinden ve anne olma özelliklerinden kaynaklanan her türlü konularda, annenin ve bebeğinin güvenliğini sağlayarak anne ve çocuk ölümlerini azaltmış olacaklardır.

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**KRONİK CİVA KLORÜR UYGULANAN RATLARDA BÖBREKDEKİ OKSİDATİF HASAR ÜZERİNE NARINGENİNİN KORUYUCU ETKİSİ**

**PROTECTIVE EFFECT OF THE NARINGENIN ON OXIDATIVE DAMAGE IN THE KIDNEY IN RATS WHICH APPLIED TO CHRONIC MERCURY CHLORIDE**

***Merve KAHRAMANOĞULLARI***

*Fırat Üniversitesi, Veteriner Fakültesi, Biyokimya AD. Elazığ, TÜRKİYE*

*ORCID NO: 0000-0002-5283-829X*

***Mine ERİŞİR***

*Fırat Üniversitesi, Veteriner Fakültesi, Biyokimya AD. Elazığ, TÜRKİYE*

*ORCID NO: 0000-0001-6209-4792*

***Mine YAMAN***

*Fırat Üniversitesi, Veteriner Fakültesi, Histoloji AD. Elazığ, TÜRKİYE*

*ORCID NO: 0000-0001-6209-4792*

**ÖZET**

Cıva endüstriyel, farmakolojik ve tarımsal alanlarda sıklıkla kullanılan en yaygın çevre kirlertici ağır metallere biridir. Cıva klorür, proteinlerle kolayca organo-cıva kompleksleri oluşturabildiğinden cıvanın en toksik formları arasında yer almaktadır. Cıva zehirlenmesi, bu tipteki komplekslerin oluşumu yoluyla böbrek yetmezliğine sebep olur. Cıva klorür gibi inorganik cıva tuzlarının birincil hedef organı böbreklerdir. Cıva zehirlenmesinde, böbrek bozukluklarının patogenezinde etkili olan serbest radikaller artmaktadır. Böbrekte inorganik cıva birikimine, endojen tiyol içeren glutatyon gibi moleküllerle bağlanması sebep olmaktadır. Naringenin ise oksidatif strese karşı direnci artıran bir flavonoiddir. Doğal bir flavonoid olan naringenin, turuncgil meyvelerinde, domateste, çilekte, greyfurtta ve kakaoda yaygın olarak bulunmaktadır. Naringenin farmakolojik olarak potansiyel bir antioksidan kabul edilmiş olup, reaktif oksijen türleri ve serbest radikalleri azaltıcı etkisi halkasının hidroksil grubunun elektron verici özelliğinden kaynaklanmaktadır. Bu çalışmada ratlarda cıva klorürün nefrotoksitesine karşı naringenin (50 ve 100 mg/kg/gün) koruyucu etkisini araştırmak amaçlanmıştır. Deneme; Kontrol, Naringenin-100, Cıva klorür (0.4 mg/kg/gün), Cıva klorür + Naringenin-50, Cıva klorür + Naringenin-100 olmak üzere beş gruba ayrılan erkek Wistar-Albino ratlarda (n=41) gerçekleştirildi. Cıva klorür i.p yolla, naringenin gavaj yoluyla 20 gün boyunca uygulandı. Kronik cıva klorüre maruz kalan ratların böbrek dokusunda oksidatif stres belirteçlerinden olan, malondialdehide (MDA), süperoksit dismutaz (SOD), glutatyon-S-transferaz (GST), glutatyon peroksidaz (GSH-P<sub>x</sub>) seviyelerinde önemli bir artış tespit edilirken, glutatyon (GSH) seviyesinde ise önemli bir düşüş saptandı (p<0,001). Naringenin ilavesinin böbrek dokusundaki azalmış olan glutatyonu artırdığı, yükselmiş olan MDA, SOD, GST ve GSH-P<sub>x</sub> seviyelerini ise azalttığı tespit edildi. Katalaz aktivitesinde ise deneme grupları arasında önemli bir fark saptanmamıştır. Cıvaya maruz kalan ratlarda naringenin ilavesi GSH düzeylerini artırmış, bu artış Naringenin-100 grubunda kontrol değerlerinin üzerinde bulunmuştur. Cıva uygulanan ratlarda serumda artan üre ve kreatinin seviyelerinin naringenin ilavesi ile azaldığı görülmüştür (p<0,001). Sonuç olarak naringenin hem antioksidan özelliğinden dolayı hem de GSH düzeylerini artırarak böbrekte cıva klorürün sebep olduğu oksidatif hasarı önlemektedir. Bu nedenle naringenin nefroprotektif etkiye sahip olduğu sonucuna varılmıştır.

**Anahtar Kelimeler:** Cıva Klorür, Naringenin, Oksidatif Stres, Böbrek

**ABSTRACT**

Mercury is one of the most common environmental polluting heavy metals that is frequently used in industrial, pharmacological and agricultural fields. Mercury chloride is among the most toxic forms of mercury, as it can easily form organo-mercury complexes with proteins. Mercury poisoning causes kidney failure through the formation of this type of complex. The primary target organ of inorganic mercury salts such as mercury chloride is the kidneys. Free radicals, which are effective in the pathogenesis of kidney disorders, increase in mercury poisoning. The accumulation of inorganic mercury in the kidney is caused by its binding with molecules such as endogenous thiol-containing glutathione. Naringenin is a flavonoid that increases resistance to oxidative stress. Naringenin, a natural flavonoid, is commonly found in citrus fruits, tomatoes, strawberries, grapefruit, and cocoa. Naringenin has been accepted as a potential antioxidant pharmacologically, and its reducing effect on reactive oxygen species and free radicals is due to the electron donating feature of the hydroxyl group of the ring. In this study, it was aimed to investigate the protective effect of naringenin (50 and 100 mg/kg/day) against the nephrotoxicity of mercury chloride in rats. Experimental groups were performed in male Wistar-Albino rats (n=41) divided into five groups as Control, Naringenin-100, Mercury chloride (0.4 mg/kg/day), Mercury chloride + Naringenin-50, Mercury chloride + Naringenin-100. Mercury chloride was administered i.p. and naringenin was administered by gavage for 20 days. A significant increase was detected in the levels of Malondialdehyde (MDA), superoxide dismutase (SOD), glutathione-S-transferase (GST), glutathione peroxidase (GSH-Px), which are oxidative stress markers in the kidney tissue of rats exposed to chronic mercury chloride. However, a significant decrease in glutathione (GSH) level was detected ( $p < 0.001$ ). It was determined that the addition of naringenin increased the decreased glutathione in the kidney tissue and decreased the elevated MDA, SOD, GST and GSH-Px levels. There was no significant difference in catalase activity between the experimental groups. The addition of naringenin increased GSH levels in rats exposed to mercury, which was above the control values in the Naringenin-100 group. It was observed that the increased urea and creatinine levels in the serum of rats administered mercury decreased with the addition of naringenin. As a result, naringenin prevents oxidative damage caused by mercury chloride both due to its antioxidant properties and increasing GSH levels. Therefore, it was concluded that naringenin has a nephroprotective effect.

**Keywords:** Mercury Chloride, Naringenin, Oxidative Stress, Kidney

İSTANBUL İLİ PALYATİF BAKIM MERKEZLERİNDE ÇALIŞAN HEMŞİRELERİN  
YAŞADIKLARI ZORLUKLAR  
CHALLENGES FACED BY NURSES WORKING IN ISTANBUL PALLIATIVE CARE  
CENTERS

*Sibel ÖZDEMİR ÖZMEN<sup>1</sup>*

<sup>1</sup>*Tev Ezel Gülen Kıray Meslekî ve Teknik Anadolu Lisesi, İstanbul, Türkiye.*

<sup>1</sup>*ORCID ID: 0000-0002-9099-527X*

*Alev YILDIRIM KESKİN<sup>2</sup>*

<sup>2</sup>*Selçuk Üniversitesi, Akşehir Kadir Yallagöz Sağlık Yüksekokulu, Hemşirelik, Konya, Türkiye.*

<sup>2</sup>*ORCID ID: 0000-0003-0981-5364*

## ÖZET

**Giriş:** Bu çalışma, palyatif bakım merkezlerinde çalışan hemşirelerin yaşadıkları zorlukları belirlemek amacıyla yapılmıştır. **Materyal ve Metot:** Veriler, araştırmacı tarafından hazırlanan tanımlayıcı veri toplama formu ve Palyatif Bakım Zorlukları Ölçeği (PBZÖ) kullanılarak toplanmıştır. Verilerin değerlendirilmesinde; sayı, yüzde ve ortalamalar, Independent t testi, One Way ANOVA testi, Mann Whitney U testi, Kruskal-Wallis testi, Spearman Korelasyon testi, basit doğrusal regresyon analiz testi kullanılmıştır. İstatistiksel testlerin anlamlılık düzeyi  $p < 0.05$  olarak kabul edilmiştir. **Bulgular:** Çalışmaya katılan hemşirelerin %92,5'i kadın, %49,1'i 31-40 yaş arasında, %75,5'i lisans mezunu, %82,1'inin palyatif bakım hastalarıyla çalışma süresi 0-5 yıl olduğu belirlenmiştir. Hemşirelerin PBZÖ toplam puan ortalaması  $42,82 \pm 7,69$ , ölçek alt boyutlarından “*multidisipliner ekiplerde iletişim*”  $8,60 \pm 2,38$ , “*hasta ve aile ile iletişim*”  $9,44 \pm 2,29$ , “*uzman desteği*”  $7,44 \pm 2,35$ , “*belirtilerin azaltılması*”  $8,83 \pm 2,55$  ve “*iletişim koordinasyonu*” alt boyutu puan ortalamaları  $8,50 \pm 2,59$  olarak orta düzeyin üzerinde bulunmuştur. Çalışmaya katılan hemşireler iş ortamı koşullarının uygunsuzluğunu, iş yükü fazlalığını, mobbingi, kurum kültürü yetersizliğini, birebir karar verememeyi, fiziksel, ekonomik ve sosyo kültürel etkenleri palyatif bakım engeli olarak gördükleri belirlenmiştir. PBZÖ toplampuanı ve alt boyutları arasında anlamlı bir farklılığın olduğu saptanmıştır ( $p < 0.05$ ). Hemşireler, yara bakımı, trakeostomi bakımı, pozisyon verme ve solunum desteği uygulamalarında ekip iletişimi ve uzman desteğine ihtiyaç duyduklarını ve zorlandıklarını belirtmişlerdir. **Sonuç ve Öneriler:** Palyatif bakımda çalışan hemşireler birçok zorlukla karşılaşmakta ve yaşadıkları bu engellerin kaldırılmasına yönelik sağlık hizmetleri ve politikaların güçlendirilmesinin önemli olduğu düşünülmektedir.

**Anahtar Kelimeler:** Palyatif, palyatif bakım, palyatif bakım hemşiresi.

## ABSTRACT

**Introduction:** This study was conducted to determine the difficulties experienced by nurses working in palliative care centers. **Material and Method:** Data were collected using the descriptive "Personal and Professional Introductory Information Form" prepared by the researcher and the "Palliative Care Difficulties Scale (PCDS)". In the evaluation of the data; numbers, percentages and means, Independent t test, One Way ANOVA test, Mann Whitney U test, Kruskal-Wallis test, Spearman Correlation test, simple linear regression analysis test were used. The significance level of statistical tests was accepted as  $p < 0.05$ . **Results:** It was determined that 92.5% of the nurses participating in the study were women, 49.1% were between the ages of 31-40, 75.5% had a bachelor's degree, and 82.1% worked with palliative care patients for 0-5 years. The total mean score of nurses' PCDS was  $42.82 \pm 7.69$ , sub-dimensions of the scale “communication in multidisciplinary teams”  $8.60 \pm 2.38$ , “communication with patient and family”  $9.44 \pm 2.29$ , “expert support”  $7.44 \pm 2.35$ . The mean score of  $44 \pm 2.35$ , “reducing symptoms”  $8.83 \pm 2.55$  and “communication coordination” sub-dimension was  $8.50 \pm 2.59$ , which was above the medium level. It was determined that the nurses participating in the study considered the inconvenience

of work environment conditions, excessive workload, mobbing, inadequacy of corporate culture, inability to make one-to-one decisions, and physical, economic and socio-cultural factors as palliative care barriers. Nurses stated that they needed team communication and expert support in wound care, tracheostomy care, positioning and respiratory support practices and they had difficulties. It was determined that there was a significant difference between the PCDS total score and its sub-dimensions ( $p < 0.05$ ). **Conclusions and Recommendations:** Nurses working in palliative care face many difficulties and it is thought that it is important to strengthen health services and policies to remove these obstacles.

**Keywords:** Palliative, palliative care, palliative care nurse.

**MONITORING OF ZOONOSIS DISEASES IN "GARABAGH" AND "DILBAZ" HORSES**

*Asaf Omarov<sup>1</sup>, Siala Rustamova<sup>2</sup>, Shalala Zeynalova<sup>2</sup>, Kubra Yusifova<sup>2</sup>, Saida Aliyeva<sup>3</sup>, Aygun Azizova<sup>2</sup>, Kamran Karimov<sup>4</sup>*

<sup>1</sup>ADA University

ORCID ID: 0000-0002-2286-5510

<sup>2</sup>Scientific Research Veterinary Institute

<sup>3</sup>ADA University

<sup>4</sup>The Azerbaijan Equestrian Federation

**ABSTRACT**

The study was conducted to investigate brucellosis and chlamydiosis in horse farms located in Aghstafa and Agjabadi regions of Azerbaijan. Blood samples were taken from 171 horses and tested using Rose-Bengal (platelet-agglutination) and Enzyme-Linked Immunosorbent Assay (ELISA) tests. Apparent and true prevalence levels were calculated. The apparent prevalence (Wilson CI) for Chlamydiosis was 0.0256% CI95[0.0071;0.0888]; for Brucellosis Apparent prevalence (Wilson CI) 0.0058% CI95[0.001;0.0324]. Infected animals were quarantined, and preventive measures were taken.

**Key words:** monitoring, apparent, prevalence, seromonitoring

**Introduction**

Infectious diseases are a threat caused by the complex interaction of humans, animals, and the environment and seriously affect health. Preventive measures are applied to reduce these threats, and seromonitoring is an example of these actions<sup>1</sup>. Seromonitoring programs are carried out with the aim of observing threatening diseases, early detection of disease events, increasing the effectiveness of precautionary measures and monitoring the result of vaccination<sup>2</sup>.

**Material and methods**

283 Garabagh horses are kept in the Garabakh equestrian complex. 14 of them are stallions, 50 mares, and 31 foals. To determine the incidence of zoonosis in farms, the number of samples to be taken was first determined. For this purpose, the measurement and observation power module of the Epiinfo 7 program was used. The population was divided into 5 clusters with a confidence interval of 95% for observation, an expected minimum prevalence of the disease of 10%, an acceptable margin of 5%, and a design effect is one. At that time, the program required a total of 93 samples, 19 in each cluster.

The Dilbaz Equestrian Complex was keeping 180 Dilbaz horses. Among them are 25 stallions, 35 mares, and 35 foals. Same approached was implemented

**Result**

In general, a positive result was found in 1 out of 171 samples against brucellosis in "Dilbaz" Equestrian farm. For confirmation, the sample was tested by ELISA and the result was negative. Specific antibodies were detected in 2 (3.7%) (S/P% - 58 and 94) AP is 0.0256 95% CI [0.0071; 0.0888], samples in "Dilbaz" Equestrian farm against chlamydiosis

Calculation of Estimated true prevalence for Chlamydiosis were taken sample size 78, number positive 2, test sensitivity 0.95, test specificity 0.88, confidence level 0.95 CI type for AP Wilson, CI type for TP Blaker.

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Prevalence of brucellosis, Sample size 171, number positive 1, test sensitivity 0.98, test specificity 0.7, confidence level 0.95, CI type for AP Wilson, CI type for TP Blaker

### **Discussion**

Brucellosis disease is widespread all over the world, especially in the Middle East, it is one of the main problems for humans and animals<sup>3</sup>. In Azerbaijan, brucellosis disease is considered an endemic disease of large and small horned animals<sup>4</sup>. The researched areas are not located close to each other, however, the movement of people, animal migration, etc. factors increase the likelihood of the disease spreading to other farms.

### **Outcomes**

1. Zoonosis was observed on the farms;
2. The Apparent and true prevalence calculated for brucellosis and chlamydiosis;
3. Apparent prevalence of Chlamydiosis is higher than brucellosis
4. True prevalence level is negative probably it is the related amount of positive results
5. The small number of positive results does not allow for correctly estimate the PPV indicators

### **Acknowledgment**

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**DENEYSEL ÇALIŞMALARDA STEREOLOJİK HACİM ANALİZLERİ: CAVALIERİ YÖNTEMİ**

**STEREOLOGICAL VOLUME ANALYSIS IN EXPERIMENTAL STUDIES: CAVALIERI METHOD**

**Ömür Gülsüm DENİZ**

*Bolu Abant İzzet Baysal Üniversitesi, Tıp Fakültesi, Histoloji ve Embriyoloji Anabilim Dalı,*

*Bolu, Türkiye*

*ORCID ID: 0000-0001-9254-175X*

**ÖZET**

Stereoloji; üç boyutlu biyolojik yapılardan elde edilen kesitlerin iki boyutlu düzlemde analiz edilmesi neticesinde elde edilen verilerin kullanımı ile, bu yapıların üç boyutlu özellikleri ile ilgili çıkarımlar ve yorumlar yapılmasını sağlayan bilim dalıdır. Bu sayede stereoloji, oldukça karmaşık ve farklı büyüklüklerde olan biyolojik elemanların yapısal özellikleri ile ilgili araştırma imkânı vermektedir. Dokudan kesitler alınması neticesinde; ilgili yapıların boy, şekil, hacim ve yönelimleriyle ilişkili olarak iki boyutlu düzlemde içerdiği bileşenler hakkında bilgi sağlayan kesit izdüşümleri elde edilir. Kesit doğrultusundaki değişim, eğer ilgili doku içindeki partikül dağılımı izotropik değilse farklı izdüşümlerin oluşumuna neden olmaktadır. Histolojik kesitlerdeki kantitatif çalışmalarda bu durum oldukça yanıltıcı ve taraflı sonuçların ortaya çıkmasına neden olmaktadır. Bu sebeple, dokulardan elde edilen histolojik kesitler dokuyu oluşturan yapıların hacmi veya sayısı hakkında kesin bir bulgu sunamaz. Bu bağlamda; morfometrik düzeyde yürütülen araştırmalarda, bir dokunun veya dokuya ait herhangi bir bölümünün genel doku hacmine oranı veya gruplar arası kendi hacimlerine oranı gibi birçok hacim değerlendirmesi kantitatif veri elde etmek amacıyla sık sık tercih edilmektedir. Bu doğrultuda; verilerin güvenilirliğini ve doğruluğunu artırmak amacıyla Cavalieri prensibi olarak bilinen stereolojik yöntem en çok tercih edilen hacimsel analiz yöntemlerinden birisidir. Cavalieri prensibini uygulamak için hacmi hesaplanacak olan yapı baştan sona sistematik rastgele örnekleme kurallarına göre kesilerle dilimlere ayrılır. Ardından tüm dilimlerin aynı yöne bakan yüzeylerinin alanı uygun bir yöntem kullanılarak hesaplanır. Tüm dilimlerden elde edilen yüzey alanları toplanarak ortalama dilim kalınlığı ve örnekleme katsayısı ile çarpılır ve yapının hacmi tarafsız bir hesaplama ile elde edilmiş olur. Biyolojik yapılardan uygun metotlar kullanılarak elde edilmiş nicel ve tarafsız veriler klinikte kesin teşhise gidilmesinde oldukça önemlidir. Bu bağlamda; Cavalieri yönteminin en önemli özelliğinden biri iş yükünü azaltarak istatistiksel doğruluk çerçevesinde tarafsız ve kesin sonuçlar elde edilebilmesine imkân sağlamaktır. Bu yöntemin çok yönlülüğü, tarafsızlığı ve uygulamadaki basitliği doğrultusunda yeni yaklaşımların geliştirilebilmesine olanak sağlaması morfometrik çalışmalarda aranan standartlar haline gelmesine neden olmuştur.

**Anahtar kelimeler:** Stereoloji; Cavalieri yöntemi; Hacim analizleri; Deneysel çalışma

**ABSTRACT**

Stereology is a branch of science that allows for making inferences and interpretations about the three-dimensional properties of sections obtained from three-dimensional biological structures as a result of the data gained by analysing these sections in two-dimensional plane. In this way, stereology provides the opportunity to research the structural properties of biological elements that are quite complex and of different sizes. As a result of taking sections from the tissue, cross-sectional projections are obtained which provide information about the components of the related structures in two-dimensional plane in relation to their height, shape, volume and orientations. The change in the direction of the section causes the formation of different projections if the distribution of particles in the related tissue is not isotropic. This situation leads to highly misleading and biased results in quantitative studies on histological

sections. For this reason, histological sections obtained from tissues cannot provide a definite result about the volume or number of structures that make up the tissue. In this context, in morphometric studies, a large number of volumetric assessments, such as the ratio of a tissue or any part of a tissue to the overall tissue volume or the ratio between groups are often preferred to obtain quantitative data. Thus, the stereological method known as Cavalieri principle is one of the most preferred volumetric analysis methods to increase the reliability and accuracy of data. In order to apply the Cavalieri principle, the structure the volume of which is to be calculated is cut into slices from the beginning to the end according to systematic random sampling rules. Following this, the area of all slices facing the same direction is calculated by using an appropriate method. Surface areas obtained from all slices are added together, multiplied by the mean slice thickness and sampling coefficient and thus the volume of the structure is obtained with an unbiased calculation. Quantitative and objective data obtained from biological structures by using appropriate methods are very important in making definitive diagnosis in the clinic. In this context, one of the most important features of Cavalieri method is enabling to obtain unbiased and precise results within the framework of statistical accuracy by reducing work load. The fact that this method enables developing new approaches in line with its versatility, impartiality and simplicity has caused it to become demanded standard in morphological studies.

**Keywords:** Stereology; Cavalieri method; Volume analysis; Experimental study

**VAGINAL ERBIUM-DOPED YTTRIUM ALUMINUM GARNET(Er-yag) LASER APPLICATIONS (VELA); A NEW APPROACH FOR LONG- TERM TREATMENT OF SEXUAL DYSFUNCTION IN BREAST CANCER DURING AND AFTER TREATMENT**

**MEME KANSERİ TEDAVİSİ SIRASI VE SONRASINDA OLUŞAN SEKSUEL DİSFONKSİYONUN UZUN DÖNEM TEDAVİSİNE YENİ BİR YAKLAŞIM; VAGİNAL ERBİUM-DOPED YTTRIUM ALUMINUM GARNET(ER-YAG) LAZER UYGULAMALARI (VELA)**

*Seçil GÜNAY AVCI*

*Haliç Üniversitesi Sağlık Bilimleri Fakültesi, Ebelik Bölümü, İstanbul, Türkiye.*

*ORCID ID: 0000-00028545-0128*

## **INTRODUCTION**

Breast cancer (BC) is the most common cancer worldwide and in Türkiye(1). Female sexual dysfunctions (FSD) occur frequently in breast cancer patients. In Türkiye, FSD is 57.9 % in patients with BC (2). Hypoestrogenism related to BC therapies has a strong negative impact on vaginal dryness, burning, irritation. Results as discomfort or pain and as FSD(3).Mostly the breast surgeon does not approve estrogen for this problem.Lubricants will be the only option than.But lubricants are never long-term solutions. Vaginally applied erbium-doped yttrium aluminum garnet (Er-yag) laser (VELA) is a new treatment modality for the patients who does not approve estrogen and wants to live a healthy sexual life without pain during and after cancer treatment.VELA treatment in combination with a low-dose/short-term estriol mucosa preparation could be considered a preferred treatment with respect to effectiveness and safety. Improved vascularization and increased extracellular matrix component, while estriol-only treatment increases the glycogen level in the vaginal epithelium and its turnover, with less effect and only transient effect on vascularization and changes in the lamina propria, requiring maintenance treatment for the effects to be sustained. Laser therapy was known to have a different mechanism of action, resulting in induced vessel formation, reconstitution of the lamina propria, and consequent regeneration of the mucosa lasting for an extended period of time as much as 18 months, even after therapy has been ceased (4).

**AIM:** This paper aims to give a new perspective for the treatment of sexual dysfunction caused by vaginal dryness for breast cancer patients who need to feel sexual arousal without fear of pain and fear of cancer development. And to inform gynecologists about vaginal laser applications which are not for only vaginal laxity, pelvic prolapse or urinary incontinence.

**Key Words:** Vaginal Er-yag laser applications (VELA), breast cancer, sexual dysfunction,

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**ASTIMLI ÇOCUKLAR İÇİN AİLE YÖNETİMİ ÖLÇEĞİNİN TÜRKÇE GEÇERLİLİK VE GÜVENİRLİK ÇALIŞMASI**  
**TURKISH VALIDITY AND RELIABILITY STUDY OF FAMILY MANAGEMENT SCALE FOR CHILDREN WITH ASTHMA**

***Tubanur ÖZMEN<sup>1</sup>***

*<sup>1</sup>Ağrı İbrahim Çeçen Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu, Tıbbi Hizmetler ve Teknikler Bölümü, İlk ve Acil Yardım Programı, Ağrı, Türkiye.*

*<sup>1</sup>ORCID ID: 0000-0003-1171-241X*

***Türkan KADİROĞLU<sup>2</sup>***

*<sup>2</sup> Atatürk Üniversitesi, Hemşirelik Fakültesi, Çocuk Sağlığı ve Hastalıkları Hemşireliği, Erzurum, Türkiye.*

*<sup>2</sup>ORCID ID: 0000-0002-3703-7478*

**ÖZET**

**Amaç:** Araştırmanın amacı Astımlı Çocuklar İçin Aile Yönetimi Ölçeği'ni Türkçe'ye geçerlilik ve güvenilirlik çalışmasını yapmaktır.

**Materyal ve Metot:** Metodolojik tipte olan bu araştırma, 1 Aralık 2020- 1 Mayıs 2021 tarihleri arasında Atatürk Üniversitesi Sağlık Araştırma ve Uygulama Merkezi'nde yapıldı. Araştırma evrenini; 0-18 yaş aralığında olan astım tanılı çocukların ebeveynleri oluşturdu. Örneklemeye gidilmeden araştırmaya katılmayı kabul eden tüm gönüllü ebeveynler araştırmaya dahil edildi (N:293). Araştırmada verilerin toplanmasında, sosyodemografik özelliklerinin belirlenmesine yönelik Tanıtıcı Bilgi Formu ve Astımlı Çocuklar İçin Aile Yönetimi Ölçeği kullanıldı. Verilerin analizinde sayılar, yüzdeler, en az ve en çok değerler, ortalama, standart sapma, faktör analizi, Cronbach  $\alpha$  güvenilirlik katsayısı yöntemleri kullanıldı. Araştırma sürecinde etik ilkeler göz önüne alınarak, etik kurul izni ve gerekli kurum izni yazılı olarak alındı.

**Bulgular:** Ölçek maddelerinin KGİ 0.981'dir. Ölçeğin, KMO değeri 0.965, BTS  $x^2=18296.335$ ,  $p=0.000$ 'dır. Doğrulayıcı faktör analizi için uyum iyiliği indeks değerleri  $x^2/SD=1.61$ , GFI=0.95, AGFI=0.93, CFI=1.00, RMSEA=0.055 ve SRMR=0.081 olarak bulunmuştur ve tümü istenilen aralıktadır. Ebeveynler ölçekten ortalama  $203.53 \pm 39.68$  puan almışlardır. Araştırma sonucunda, orijinaline benzer şekilde Astımlı Çocuklar İçin Aile Yönetimi Ölçeği, 57 madde ve 'çocuk kimliği, durum görünümü, yönetim zihniyeti, ebeveyn karşılıklığı, ebeveynlik felsefesi, yönetim yaklaşımı, aile odaklılık, gelecek beklentisi' olmak üzere 8 alt boyuttan oluşmuştur. Ölçeğin toplam Cronbach  $\alpha$  katsayısı toplamda 0.981, alt boyutlarda ise 0.849-0.980 arasında değişmiştir.

**Sonuç:** Araştırmanın sonucunda Astımlı Çocuklar İçin Aile Yönetimi Ölçeği'nin Türkçe geçerli ve güvenilir bir ölçme aracı olduğu ve bundan sonraki yapılacak olan astımlı çocuklarda aile yönetiminin araştırıldığı farklı çalışmalarda güvenilir bir ölçme aracı olarak kullanılabileceği bulunmuştur.

**Anahtar Kelimeler:** Aile yönetimi, astım, çocuk, hemşire

**ABSTRACT**

**Aim:** The aim of the study is to perform the validity and reliability study of the Family Management Scale for Children with Asthma into Turkish.

**Materials and Methods:** This methodological study was conducted at Atatürk University Health Research and Application Center between December 1, 2020 and May 1, 2021. The research universe; Parents of children with asthma in the 0-18 age range. All voluntary parents who agreed to participate in the study without sampling method were included in the study (N:293). Introductory Information

Form and Family Management Scale for Children with Asthma were used to collect data in the study to determine sociodemographic characteristics. Numbers, percentages, minimum and maximum values, mean, standard deviation, factor analysis, Cronbach  $\alpha$  reliability coefficient methods were used in the analysis of the data. Ethics committee permission and the necessary institutional permission were obtained in writing, taking into account the ethical principles during the research process.

**Results:** The CVI of the scale items was 0.981. KMO value of the scale was 0.965,  $\chi^2=18296.335$ ,  $p=0.000$ . Goodness of fit index values for confirmatory factor analysis were found as  $\chi^2/SD =1.61$ , GFI=0.95, AGFI=0.93, CFI=1.00, RMSEA=0.055 and SRMR=0.08 and all values were within the desired range. Parents obtained an average of  $203.53\pm 39.68$  points from the scale. As a result of the study, the Family Management for Children Scale with Asthma, similar to the original, consisted of 57 items and 8 sub-dimensions which are 'children identity, view of condition, management mindset, parental mutuality, parenting philosophy, management approach, family focus, and future expectation'. The total Cronbach  $\alpha$  coefficient of the scale was found to be 0.981 in total and range between 0.849-0.980 in sub-dimensions.

**Conclusion:** As a result of the study, it was found that the Family Management Scale for Children with Asthma is a valid and reliable measurement tool in Turkish, and it can be used as a reliable measurement tool in different studies investigating family management in children with asthma.

**Keywords:** Family management, asthma, child, nurse

**HEMŞİRELERİN HASTA GÜVENLİĞİ KÜLTÜRÜ ALGILARI VE TIBBİ HATA TUTUMLARININ BELİRLENMESİ**

**DETERMINATION OF NURSES' PERCEPTIONS OF PATIENT SAFETY CULTURE AND ATTITUDES TO MEDICAL ERRORS**

*Sümeyye YOZGAT<sup>1</sup>*

*<sup>1</sup>Sultanbeyli Devlet Hastanesi, İstanbul, Türkiye.*

*<sup>1</sup>ORCID ID: 0000-0002-6917-0943*

*Alev YILDIRIM KESKİN<sup>2</sup>*

*<sup>2</sup>Selçuk Üniversitesi, Akşehir Kadir Yallagöz Sağlık Yüksekokulu, Hemşirelik, Konya, Türkiye.*

*<sup>2</sup>ORCID ID: 0000-0003-0981-5364*

**ÖZET**

Bu araştırma, çalışan hemşirelerin hasta güvenliği kültürü algıları ve tıbbi hata yapma tutumlarını belirlemek amacıyla kesitsel ve tanımlayıcı olarak yapılmıştır.

Araştırmanın evrenini İstanbul ilinde iki devlet hastanesinde çalışan toplam 627 hemşire oluşturmaktadır. Çalışmada yeterli örnek hacminin belirlenmesi aşamasında G-POWER 3.1 paket programı kullanılmıştır. Bu çalışmada ulaşılabilen maximum örneklem ile çalışılarak her iki hastaneden toplam 254 örneklem ile çalışılmıştır. Veriler, araştırmacı tarafından oluşturulan kişisel ve mesleki tanıtıcı bilgi formu , "Hasta Güvenliği Kültürü Ölçeği (HGKÖ) ve "Tıbbi Hatalarda Tutum Ölçeği " (THTÖ) kullanılarak toplanmıştır. Verilerin analizinde; sayı, yüzdelik, Min, Maks. değerleri, ortalama ( $\bar{X}$ ), standart sapma, Mann Whitney U testi, Kruskal-Wallis testi, Ki-kare ( $X^2$ ) testi ve Spearman Korelasyon testi kullanılmıştır. Anlamlılık düzeyleri  $p<0.05$  olarak kabul edilmiştir.

Çalışmaya katılan hemşirelerin yaş ortalamasının  $31,03\pm 6.73$  , %73,6'sının kadın, %55,5'inin evli, %82,3'ünün lisans mezunu, %50,8'inin yatan hasta servisinde çalıştığı, %59,4'ünün kurumda çalışma süresinin 1-4 yıl arasında olduğu ve % 42,5'inin meslekte çalışma süresinin 1-4 yıl arasında olduğu belirlenmiştir. Hemşirelerin HGKÖ toplam ölçek puanının  $2.91\pm 0.51$  olduğu ve THTÖ toplam ölçek puanının  $2.29\pm 0.43$  olduğu saptandı. Çalışmaya katılan hemşirelerin sosyodemografik ve mesleki özelliklerinden cinsiyet, eğitim durumu, çalıştığı kurum ve birim ile THTÖ toplam puanı ve alt boyutları arasında sırasıyla algı ve yaklaşım alt boyutları arasında anlamlı fark belirlendi ( $p<0.05$ ). Hemşirelerin cinsiyetleri, medeni durumları, çalıştığı kurum ve birim, çalışma süreleri ile HGKÖ toplam puanı, yönetim ve liderlik, çalışan eğitimi, beklenmedik olay, bakım ortamı ve çalışan davranışı alt boyutlarından aldıkları puanlar arasında anlamlı fark bulundu ( $p<0.05$ ). Hemşirelerin aldıkları THTÖ toplam puanı ile HGKÖ ve alt boyutlarından aldıkları puan arasında anlamlı ilişki bulunmadı ( $p>0.05$ ). Hemşirelerin THTÖ'ü hata algısı alt boyutu puanı ile HGKÖ toplam puan, yönetim ve liderlik, beklenmedik olay, bakım ortamı ve çalışan davranışı ve alt boyutlarından aldıkları puanlar arasında zayıf düzeyde pozitif ilişki tespit edildi ( $p<0.05$ ).

Bu sonuçlar doğrultusunda; yönetici hemşirelerin hasta güvenliği kültürünü daha fazla benimseyerek çalışan hemşireleri desteklemeleri, hataların bildirim konusunda daha teşvik edici bir tutum almaları ve tıbbi hata bildirim konusunda çalışanların endişelerini giderici bir yaklaşım sergilemeleri önerilmektedir. Hemşirelere tıbbi hata algısı, tıbbi hataya yaklaşım ve tıbbi hataların nedenleri konusunda etkili iletişim sağlanmalı ve ekip çalışması ruhu geliştirilmelidir.

**Anahtar Kelimeler:** Tıbbi hata, hasta güvenliği, hasta güvenliği kültürü, hemşire.

## **ABSTRACT**

The research was carried out as a cross-sectional and descriptive study in order to investigate the effects of nurses working in two state hospitals in Istanbul on their perceptions of patient safety culture and their attitudes towards making medical mistakes.

The population of the research consists of 627 nurses working in two state hospitals in İstanbul. In the study, the G-POWER 3.1 package program was used to determine the sufficient sample volume. In this study, we studied with the maximum sample that can be reached, with a total of 254 samples from both hospitals, with n=127 nurses from Tuzla state hospital and n=127 nurses from Sultanbeyli state hospital. The data were collected using the personal and professional descriptive information form created by the researcher, the "Patient Safety Culture Scale (HGKÖ) and the Attitude Scale in Medical Errors (THTÖ)". In the analysis of the data, number, percentage, Min, Max values, mean ( $\bar{X}$ ) and standard Deviation, Mann Whitney U test, Kruskal-Wallis test, Chi-square ( $X^2$ ), Spearman Correlation were used, and significance level were accepted as  $p<0.05$ .

The mean age of the nurses participating in the study was  $31.03\pm 6.73$ , 73.6% were female, 55.5% were married, 82.3% had a bachelor's degree, 50.8% worked in the inpatient service, 59.4% of them had a working period of 1-4 years in the institution and 42.5% was in the profession. It was determined that the working period was between 1-4 years. It was determined that the nurses' total scale score of HGKÖ was  $2.91\pm 0.51$  and the total scale score of THTÖ was  $2.29\pm 0.43$ . A significant difference was determined between the sociodemographic and professional characteristics of the nurses participating in the study, gender, educational status, institution and unit, and the total score and sub-dimensions of THTÖ, respectively, between perception and approach sub-dimensions ( $p<0.05$ ). A significant difference was found between the nurses' gender, marital status, institution and unit, working time, and the scores they got from the total score of HGKÖ, management and leadership, employee education, unexpected event, care environment and employee behavior sub-dimensions ( $p<0.05$ ). There was no significant relationship between the nurses' total THTÖ score and the scores they got from HGKÖ and its sub-dimensions ( $p>0.05$ ). A weak positive correlation was found between the nurses' error perception sub-dimension score of THTÖ and the total score of HGKÖ, management and leadership, unexpected event, care environment and employee behavior and sub-dimensions ( $p<0.05$ ).

In line with these results; It is recommended that manager nurses support nurses by adopting a patient safety culture more, take a more encouraging attitude in reporting errors, and show an approach that relieves employees' concerns about medical error reporting. Effective communication should be provided to nurses in the perception of medical error, approach to medical error and fear of the causes of medical errors, and team work spirit should be developed.

**Keywords:** Medical error, patient safety, patient safety culture, nurse.

**AÇIK KAMA YÜKSEK TİBİAL OSTEOTOMİ UYGULANAN HASTALARDA  
MEMNUNİYET VE YAŞAM KALİTESİ SKORLARI ÜZERİNDE POSTOPERATİF  
FOTOĞRAF VE BACAK UZUNLUK GRAFİSİ KULLANMANIN ETKİNLİĞİ**

*Uzm. Dr. Cem YILDIRIM<sup>1</sup>*

*<sup>1</sup> SBÜ Başakşehir Çam ve Sakura Şehir Hastanesi, Ortopedi ve Travmatoloji Kliniği, İstanbul,  
Türkiye*

*<sup>1</sup> ORCID ID: 0000-0003-4540-1927*

**ÖZET**

Açık kama yüksek tibial osteotomi yapılan küçük ama önemli bir hasta grubunda cerrahiden dolayı memnuniyetsizlik hala önemli bir sorundur. Çalışmamızın amacı medial açık kama yüksek tibial osteotomi sonrası hasta ve cerrahi kaynaklı memnuniyetsizliğe neden olan faktörleri ortaya koymak, hasta memnuniyeti ve cerrahi sonuçlarda pre-post operatif fotoğrafların etkinliğini değerlendirmektir.

Ameliyattan önce ve 6 ay sonra alt ekstremitte uzunluk grafipleri değerlendirildi. Yük taşıma çizgi oranı (WBL ratio), kalça-diz-ayak bilek (HKA) açısı, eklem çizgi konverjans açısı (JLCA) ve posterior tibial slope (PTS) preop ve post op 6. ayda ayakta çekilen anterior alt ekstremitte uzunluk grafiplerinde karşılaştırıldı. Fonksiyonel sonuçlar Short Form-36 (SF-36) sağlık durum anketi, Knee Injury and Osteoarthritis Outcome Score (KOOS), Oxford Knee Score (OKS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) skorları ile cerrahiden önce ve cerrahi sonrası 6. ay kıyaslandı. Çalışma grubundaki hastaların ameliyat sonrası 6. ay skorları, 1'er hafta ara ile radyografi ve fotoğrafları gösterilmeden ve gösterildikten sonra elde edildi. Kontrol grubu için 6. ay skorlar hastalara herhangi grafi ve fotoğraf göstermeden 1'er hafta ara ile elde edildi.

Çalışma ve kontrol gruplarına sırasıyla 20 ve 21 hasta dahil edildi. Hastaların yaş ortalamaları 54 idi. Tüm hastalarda postoperatif dönemde anlamlı oranda iyileşme gözlenen varus dizilim bozukluğu mevcut idi ( $p < 0.001$ ). Fonksiyonel ve hasta memnuniyetini bildiren tüm ölçütlerde ameliyattan sonra iyileşme gözlemlendi ( $p < 0.05$ ). Hastaların pre ve post operatif ayakta fotoğraflarını ve uzunluk grafiplerini gördükten sonra kendi kendilerine skorladıkları fonksiyonel ve memnuniyet puanları daha da iyileşti ( $p < 0.05$ ). Fotoğrafları gösterildikten sonra çalışma grubunda kontrol grubuna göre skorlamalarda önemli ölçüde iyileşme gözlemlendi ( $p < 0.05$ ).

Hastaların kendilerinin bildirdiği yaşam kalitesi ve hasta memnuniyetini arttırmak için ameliyattan önce ve sonrasındaki fotoğraf ve radyografilerindeki değişikliklerin kendilerine gösterilmesi uygulaması kolay bir yöntem olabilir. Ayrıca bu yöntem, klinisyenlerin hastaların dizilerindeki varus dizilim bozukluğunun düzeltilmesi için ameliyattan sonra hastaların benlik algısını olumlu yönde değiştirmesini sağlayabilir.

**Anahtar Kelimeler:** Yüksek tibial osteotomi, Varus dizilim bozukluğu, Bacak uzunluk grafisi, Hasta memnuniyeti.

**ABSTRACT**

Dissatisfaction with surgery remains a major problem in a small but significant group of patients who underwent open wedge high tibial osteotomy. The aim of our study is to reveal the factors that cause patient and surgical dissatisfaction after medial open wedge high tibial osteotomy, and to evaluate the effectiveness of pre-post operative photographs in patient satisfaction and surgical results.

Full-length lower extremity radiographs and standing photographs were evaluated before and 6 months after surgery. Weight bearing line ratio (WBL ratio), hip-knee-ankle (PCA) angle, joint line convergence angle (JLCA), and posterior tibial slope (PTS) were compared on anterior full-length lower extremity radiographs taken preop and post op sixth month standing. The changes in the following outcome measures were evaluated from baseline to 6 months after surgery: Short Form-36 Survey, Knee Injury



and Osteoarthritis Outcome Score, Oxford Knee Score and Western Ontario and McMaster Universities Osteoarthritis Index. The postoperative 6th month scores of the patients in the study group were obtained at 1-week intervals without and after showing the radiographs and photographs. For the control group, the 6th month scores were obtained at 1 week intervals without showing any radiographs and photographs to the patients.

20 and 21 patients were included in the study and control groups, respectively. The mean age of the patients was 54 years. All patients had varus malalignment, which showed significant improvement in the postoperative period ( $p < 0.001$ ). All self-reported outcome measures improved after surgery ( $p < 0.05$ ). After seeing the pre- and post-operative standing photographs and length radiographs of the patients, their self-scored functional and satisfaction scores improved further ( $p < 0.05$ ). After the photographs were shown, a significant improvement in scoring was observed in the study group compared to the control group ( $p < 0.05$ ).

In order to increase the self-reported quality of life and patient satisfaction, it can be an easy method to show the changes in the photographs and radiographs before and after the surgery. In addition, this method may enable clinicians to positively change the self-perception of patients after surgery to correct varus malalignment in the knees of patients.

**Keywords:** High tibial osteotomy, Varus malalignment, Full-length lower extremity radiographs, Patient satisfaction.

**THE USE OF ENDONASAL DEXAMETHASONE ELECTROPHORESIS IN THE COMPLEX TREATMENT OF POSTERIOR UVEITIS**

**ПРИМЕНЕНИЕ ЭНДОНАЗАЛЬНОГО ЭЛЕКТРОФОРЕЗА ДЕКСАМЕТАЗОНА В КОМПЛЕКСНОМ ЛЕЧЕНИИ ЗАДНИХ УВЕИТОВ**

*Rakhshanda Mirzazade*

*National Center of Ophthalmology named after acad. Z.Aliyeva, Baku, Azerbaijan*

**Keywords:** uveitis, endonasal electrophoresis, dexamethasone

One of the urgent tasks of ophthalmology is the diagnosis and treatment of inflammatory diseases of the choroid - uveitis. The incidence of uveitis is 15-38 per 100,000 population. Treatment includes the appointment of corticosteroids, immunosuppressants, as well as local administration of steroids in the form of instillations and injections. However, with periorbital injections, complications such as ptosis, scarring, periorbital retinal subatrophy, scleral perforation, and hemorrhage are possible. It is advisable to administer medicinal substances by the method of endonasal electrophoresis. Purpose: to evaluate the results of endonasal dexamethasone electrophoresis in the complex therapy of posterior uveitis. Materials and Methods: Under observation were 60 patients (68 eyes), divided into two groups of 30 patients each. Patients of both groups received systemic anti-inflammatory, immunosuppressive therapy. In addition, patients of the main group (35 eyes) received endonasal electrophoresis with dexamethasone. All patients underwent standard ophthalmological examinations: visometry, tonometry, perimetry, biomicroscopy of the anterior and posterior segments of the eye. Results. In patients of both groups, positive dynamics was observed with an increase in visual acuity and expansion of visual fields. Under the influence of the therapy, the subsidence of signs of inflammation was observed by 4-5 days from the start of treatment. Clinical improvement was noted in all patients, which was expressed by an increase in visual acuity, expansion of visual fields and a decrease in cystic and diffuse macular edema. According to OCT data, complete resorption of edema and normalization of the thickness of the foveolar zone of the retina were noted in the main group in the 28 eyes (80%), in the control group in the 22 eyes (67%). Conclusions. The inclusion of endonasal electrophoresis of dexamethasone in the complex treatment of posterior uveitis has a more pronounced clinical effect. There is a positive dynamic of clinical and functional, perimetric, electrophysiological parameters.

**Ключевые слова:** увеиты, эндоназальный электрофорез, дексаметазон

Одной из актуальных задач офтальмологии является диагностика и лечение воспалительных заболеваний сосудистой оболочки глаза - увеитов. Заболеваемость увеитами составляет 15-38 человек на 100 000 населения. Социальная и экономическая значимость увеитов определяется тем, что снижение зрения и слепота встречаются у лиц молодого, трудоспособного возраста. Лечение включает назначение кортикостероидов, иммуносупрессоров, а также местное введение стероидов в виде инстилляций и инъекций. Однако при периорбитальных инъекциях возможны осложнения в виде птоза, рубцевания, субатрофии периорбитальной сетчатки, перфорации склеры и кровоизлияния. Целесообразно вводить лекарственные вещества методом эндоназального электрофореза. Под действием тока лекарственные препараты проникают через слизистую оболочку носа в ткани и жидкости глазного яблока. Цель: оценить результаты применения эндоназального электрофореза дексаметазона в комплексной терапии задних увеитов. Материалы и методы: под наблюдением находились 60 пациентов (68 глаз), разделенные на две группы по 30 пациентов в каждой. Пациенты обеих групп получали системную противовоспалительную, иммуносупрессивную терапию. Помимо этого, пациенты основной группы (35 глаз) получали эндоназальный электрофорез с дексаметазоном. Всем пациентам были проведены стандартные офтальмологические исследования: визометрия, тонометрия, периметрия, биомикроскопия переднего и заднего отрезков глаза. Дополнительно проводились оптическая когерентная томография сетчатки, ультразвуковое исследование (B-scan), цветное

фотографирование глазного дна. Срок наблюдения составил 3 месяца. Результаты. У пациентов обеих групп наблюдалась положительная динамика с повышением остроты зрения и расширением полей зрения. Под воздействием проведенной терапии стихание признаков воспаления наблюдалось к 4-5 суткам от начала лечения. Клиническое улучшение отмечено у всех пациентов, что выразилось повышением остроты зрения, расширением полей зрения и уменьшением кистозного и диффузного макулярного отека. По данным ОКТ полная резорбция отека и нормализация толщины фовеолярной зоны сетчатки в основной группе отмечена в 28 глазах (80 %), в контрольной в 22 глазах (67 %). Выводы. Включение эндоназального электрофореза дексаметазона в комплексное лечение задних увеитов оказывает более выраженный клинический эффект. Отмечается положительная динамика клинико-функциональных, периметрических, электрофизиологических показателей. Процедура эндоназального электрофореза дексаметазона хорошо переносится пациентами и может широко применяться в амбулаторных и стационарных условиях в лечении задних увеитов.

**მორეციდივე აფთოზური სტომატიტი ბავშვებში  
RECURRENT APHTHOUS STOMATITIS IN CHILDREN**

*Veriko Gergauli*

*Tbilisi State Medical University, Faculty of Dentistry, Tbilisi, Georgia.*

*Nana Kipiani*

*Tbilisi State Medical University, Associate professor, Faculty of Dentistry, TSMU Department of Child and Adolescent Therapeutic Dentistry, Tbilisi, Georgia.*

**აბსტრაქტი**

ქრონიკული მორეციდივე აფთოზური სტომატიტი (stomatitis aphtosa chronica recidiva), მორეციდივე კეთილთვისებიანი აფთები აუტოიმუნური ინფექციურ-ალერგიული ფართოდ გავრცელებული დაავადებაა როგორც ბავშვთა, ისე მოზრდილთა სტომატოლოგიაში. მისთვის დამახასიათებელია არაკერატინიზირებული პირის ღრუს ლორწოვანზე (ლოყისა და ტუჩის ლორწოვანი გარსი, ენა, პირის ღრუს ფსკერი) მტკივნეული წყლულებისა და აფთების არსებობა. ბავშვს უჩნდება დისკომფორტის შეგრძნება, რაც უარყოფითად მოქმედებს მისი ცხოვრების ხარისხზე, საკვების მიღებასა და მეტყველებაზე.

ეს ელემენტები მრგვალი ან ოვალური ფორმის ეროზიებია, დაფარული მონაცრისფრო-თეთრი ფიბრინოზული ნადებით, რომლებიც შემოსაზღვრულია წვრილი ჰიპერემიული ყაეთნით. დამახასიათებელია რეციდიული გამონაყარი ხანგრძლივი მიმდინარეობით და გამწვავებით. ნაკლებად ხშირია სასის და ღრძილების ძლიერ კერატინიზებული ლორწოვანი გარსის ჩართვა. ძირითადად ვლინდება ბავშვებში და მოზარდებში, მოსახლეობის 25-50%-ში. დაავადების ეტიოლოგია და პათოგენეზი დღემდე არ არის ცნობილი, თუმცა ადგილობრივი, სისტემური, იმუნოლოგიური, გენეტიკური, ალერგიული, კვებითი და მიკრობული ფაქტორები განიხილება მის რისკ-ფაქტორებად. დიაგნოსტიკა ძირითადად ხორციელდება მხოლოდ კლინიკური მონაცემებისა და სრულყოფილი ანამნეზის საფუძველზე. როგორც ავღნიშნეთ ეტიოტროპული მკურნალობის არარსებობის გამო გამოიყენება სხვადასხვა მეთოდები, მაგრამ თერაპია არ არის საბოლოო. აქტუალურ მედიკამენტებს, როგორცაა ანტიმიკრობული, ანტისეპტიკური საშუალებები და ადგილობრივი კორტიკოსტეროიდები (დექსამეტაზონი, ტრამცინოლონი, ფლუოციონიდი ან კლობეტაზოლი), შეუძლიათ მიაღწიონ ძირითად მიზანს, შეამცირონ ტკივილი და გააუმჯობესონ შეხორცების დრო, მაგრამ არ აუმჯობესებენ რეციდივის ან რემისიის მაჩვენებელს.

განვიხილავთ ქრონიკული მორეციდივე აფთოზური სტომატიტის განვითარების რისკ-ფაქტორებს და მათ გავლენას დაავადების განვითარებაზე ბავშვთა ასაკში, კლინიკურ სურათსა და გამოკვლევის მეთოდებს. დიდი ყურადღება მიექცევა მისთვის დამახასიათებელ ძირითად ნიშნებს, რადგან ზუსტი დიფერენცირება მოვახდინოთ პირის ღრუს ლორწოვანზე სხვა მიზეზით გამოწვეული წყლულებისგან. ასევე ვისაუბრებთ მკურნალობის ძირითად პრინციპებზე, სამკურნალო ღონისძიებების კომპლექსურ შერჩევაზე, რომელიც დამყარებული იქნება კლინიკური სიმპტომების, თანხმლები დაავადებების მონაცემების, ლაბორატორიული გამოკვლევებისა და ასაკობრივი თავისებურებების, ასევე წინასწარგანწყობის იდენტიფიკაციისა და კონტროლის გათვალისწინებით.

გაგაცნობთ pubmed-ის სხვა სტატიებში მიღებულ კვლევების შესახებ, სადაც აღწერილია სხვადასხვა მაპროვოცირებელი ფაქტორის კორელაცია (მაგალითად გენეტიკური) ქრონიკულ მორეციდივე აფთოზურ სტომატიტთან.

**საკვანძო სიტყვები:** ქრონიკული მორეციდივე აფთოზური სტომატიტი, ბავშვთა ასაკი, ბავშვთა სტომატოლოგია, რისკ-ფაქტორები, დიფერენციალური დიაგნოზი.

## **ABSTRACT**

Chronic recurrent aphthous stomatitis (stomatitis aphtosa chronica recidiva), recurrent benign aphthae is an autoimmune infectious-allergic disease, widespread in both pediatric and adult dentistry. It is characterized by the presence of painful ulcers and aphthae on the non-keratinized oral mucosa (cheek and lip mucosa, tongue, floor of the mouth). The child feels discomfort, which negatively affects his quality of life, eating and speech.

Their clinical presentation is characterized by small, round or ovoid ulcers with erythematous haloes and yellow-gray floors. Recurrent rash with long course and exacerbation is characteristic. It is less common to involve the highly keratinized mucous membrane of the palate and gums. It mainly occurs in children and adolescents, in 25-50% of the population. The etiology of RAS is still unknown, but several local, systemic, immunologic, genetic, allergic, nutritional, and microbial factors, as well as immunosuppressive drugs, have been proposed as risk factors. Diagnosis is mainly carried out only on the basis of clinical data and complete anamnesis.

We will discuss the risk factors for the development of chronic recurrent aphthous stomatitis and their influence on the course of the disease in children, clinical data and research methods. Much attention will be paid to the main signs characteristic of it, in order to accurately differentiate it from ulcers caused by other causes on the oral mucosa. We will also talk about the basic principles of treatment, a comprehensive choice of treatment measures that will be based on clinical symptoms, data from concomitant diseases, laboratory results and age characteristics, as well as the identification and control of predispositions.

I will inform you of studies found in other PubMed articles describing the correlation of different predisposing factors (e.g., genetic) with chronic recurrent aphthous stomatitis.

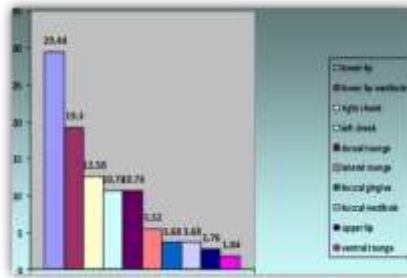
**Keywords:** children; pathogenesis; recurrent aphthous stomatitis; treatment; pediatric dentistry; risk factors.

## **ქრონიკული მორეციდივე აფთოზური სტომატიტი**

პირის ღრუს ლორწოვანის ფართოდ გავრცელებული დაავადებაა ბავშვთა ასაკში და ძირითადად პირველად ვლინდება 5-9 წლის ასაკში, ხოლო შემდეგ მისი გამოვლინებების სიხშირე იზრდება ასაკთან ერთდ. მისთვის დამახასიათებელია არაკერატინიზირებულ (გაურქოვანებელი) ლორწოვან გარსზე აფთებისა და წყლულების გაჩენა. სურათი 1-ზე ნაჩვენებია ლორწოვანი გარსის რომელ უბნებში გვხვდება ძირითადად.

## **ეპიდემიოლოგია**

როგორც ვთქვით საკმაოდ გავრცელებული დაავადებაა, მისი შეხვედრის სიხშირეა 25-50 %. ძირითადად გვხვდება 5-19 წლის ასაკის მოზარდებში. ვლინდება ორივე სქესში, თუმცა სტატისტიკური მონაცემების მიხედვით გოგონებში მეტად ვლინდება ვიდრე ვაჟებში, რასაც აკავშირებენ მდედრობით სქესის მეტად ლაბილურ ფსიქოემოციურ მდგომარეობაზე. ასევე თუ აღინიშნება ოჯახური ისტორია გამოვლინების შანსი იქნება 90%, ხოლო მისი არარსებობის დროს ვლინდა 20%-ში, რად დაკავშირებულია უკვე სხვა გარე ფაქტორებთან. [5,11]



სურათი 1.

### მორეციდივე ავთოზური სტომატიტის კლინიკა

ქრონიკული მორეციდივე ავთოზური წყლულების კლასიფიკაცია ხორციელდება სხვადასხვა მახასიათბლის მოხედვით. პირველ რიგში მისი გამოვლინებების მიხედვით, მეორე- ავთბის გაჩენის პერიოდულობის მიხედვით და მესამე- კლინიკური მიმდინარეობისა და მორფოლოგიური ტიპის მიხედვით.

კლინიკური გამოვლინების მიხედვით განარჩევენ სამ ტიპს: მცირე ზომის მორეციდივე ავთები, დიდი ზომის მორეციდივე ავთბი და ჰერპეტიფორმული ავთები (Cooke-ს ავთები).

მცირე ზომის მორეციდივე ავთები- ყველაზე ხშირად გვხვდება ეს ფორმა პაციენტებში. ძირითადად ლოკალიზდება გაურქოვანებულ ლორწოვან გარსზე (ლოყის, ტუჩის, ენის კიდის და ვენტრალური ნაწილის ლორწოვანზე). მისი ზომები 1 სმ-ს არ სცდება (2-10 მმ), მომრგვალო ფორმისაა. ძირითადად, ერთდროულად ჩნდება 5 ავთამდე. ეპითელიზაციას განიცდის 7-14 დღის განმავლობაში.[1] (სურათი 2.)



სურათი 2.

დიდი ზომის მორეციდივე ავთები- უფრო იშვიათდ გვხვდება ვიდრე მცირე ზომის ავთები. მისი ზომები აღმატება 1 სმ-ს (5-30 მმ). მისთვის დამახასიათბელია როგორც გარქოვანებულ, ისე გაურქოვანებულ ლორწოვანზე ავთების გაჩენა. წყლული მალევე იფარება სქელი, თეთრი-მონაცრისფრო ფიბრინოზული ნადებით. ეპითელიზაციას განიცდის რამდენიმე კვირიდან სამ თვემდე. იღვიათად შეიძლება ნაწიბური დარჩეს [1] (სურათი 3).

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სურათ 3.

ჰერპეტიფორმული აფთები- გვხვდება იშვიათად, მცირე ზომებით 1-2 მმ და დიდი რაოდენობით (100-მდე ელემენტი). მათთვის არ არის დამახასიათებელი გაერთიანება რითითაც განსხვავდება ჰერპესული სტომატიტისგან. ასევე არ არის დამახასიათებელი კლინიკური ნიშნების დაწყება ბუმტუკების წარმოქმნით [1].



სურათი 4.

აფთების გაჩენის პერიოდულობის მიხედვით განასხვავებენ მსუბუქ (წელიწადში ერთხელ ან უფრო იშვიათად), საშუალო (6 თვეში ერთხელ) და მძიმე ფორმებს (3 თვეში ერთხელ და უფრო ხშირად). [7] კლინიკური მიმდინარეობისა და მორფოლოგიური ტიპის მიხედვით განარჩევენ ფიბრინოზულ, ნეკროზულ, გლანდულურ, ნაწიბუროვან და ამდეფორმირებელ ფორმებს. [7]

აფთის განვითარების პროცესი საკმაოდ მნიშვნელოვანია, რომელიც მიმდინარეობს რამდენიმე ეტაპად: აფთის წარმოშობის პროცესი იწყება ლორწოვანზე ლაქის წარმოქმნით, რომელიც შემდეგ ამოიწვევს ლორწოვანიდან. ამის შემდეგ ყალიბდება ეროზია დაფარული ფიბრინოზული ნადებით, რომელსაც გარშემო შემოსაზღვრულია ჰიპერემიული ყეთონით-ყალიბდება აფთა. 2-4 დღის შემდეგ სცილდება ნეკროზული მასები, ხოლო 2-3 დღის შემდეგ განიცდის ეპითელიზაციას [7].

აქ ნაჩვენებია ზემოთ ხსენებული სამივე ფორმის დამახასიათებელი ნიშნები (ცხრილი 1).

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	Minor	Major	Herpetiform
Male to female ratio	M=F	M=F	F>M
Age at onset (years)	5-19	10-19	20-29
Number of ulcers	1-5	1-10	10-100
Size of ulcers (mm)	<10	>10	1-2 (although may coalesce to larger lesions)
Duration (days)	4-14	>30	<30
Rate of recurrence	1-4 months but may be wide individual variation	<Monthly but may be wide individual variation	>Monthly but may be wide individual variation
Site	Lips, cheeks, tongue, floor of mouth	Lips, cheeks, tongue, palate, pharynx	Lips, cheeks, tongue, pharynx, palate, gingivae, floor of mouth
Scarring	Uncommon	Common	Uncommon
Children affected	75-85%	10-15%	5-10%

ცხრილი 1. *Characteristics and presentation of recurrent aphthous stomatitis. Adapted from Porter, Scully and Pedersen, 1998.*

**ეტიოლოგია**

ავთოზური წყლულის ეტიოლოგია გაურკვეველია, მაგრამ არსებობს მტკიცებულება, რომ შეცვლილი იმუნური პასუხი პასუხისმგებელია ამ მდგომარეობის პათოგენეზზე. გენეტიკური ფაქტორები მნიშვნელოვანია და ზოგიერთ ბავშვში ავთოზურ წყლულს, როგორც ჩანს, ოჯახური საფუძველი აქვს. ასევე მიიჩნევენ რომ მისი განვითარების გზები შეიძლება იყოს დაკავშირებული ტრავმასთან, სტრესთან კუჭ-ნაწლავის ტრაქტის დაავადებებთან. მკვლევართა ერთი ჯგუფი ცდილობს დაადგინოს სტრეპტოკოკის როლი ავთოზური სტომატიტის განვითარებაში რამდენიმე მკვლევარი ცდილობდა დაედგინა პირის ღრუს სტრეპტოკოკის როლი ავთოზური წყლულის განვითარების პათოგენეზში. ანალოგიურად, ამჟამად არ არსებობს დამაჯერებელი მტკიცებულება ამ ტიპის წყლულების ვირუსული ეტიოლოგიის შესახებ. ქვემოთ განვიხილავთ სხვადასხვა ფაქტორებს, რომლებიც პირდაპირ თუ ირიბად იწვევენ მორეციდივე ავთოზური სტომატიტის განვითარებას.

*გენეტიკური ფაქტორი*

ქრონიკული მორეციდივე ავთოზური სტომატიტის მქონე პაციენტების ბავშვებს აქვთ ამ დაავადებისადმი გაზრდილი პრევალენტობა და ეს მტკიცედ ადასტურებს ჰიპოთეზას, რომ გენეტიკური ფაქტორი მონაწილეობს დაავადების განვითარებაში.[5] ბავშვებს, რომლებსაც აქვთ დაავადების დადებითი ოჯახური ანამნეზი, ასევე აქვთ ტენდენცია უფრო ადრეულ ასაკში განუვითარდეს ეს მდგომარეობა, ასევე კლინიკაც უფრო მძიმედ, ვიდრე ოჯახური ისტორიის გარეშე. დაახლოებით 90% ვითარდება დაავადება თუ ორივე მშობელს აღენიშნებოდა, შედარებით 20%-ს, ჯანმრთელი მშობლების შემთხვევაში. ასევე არსებობს RAU-ს მაღალი კორელაცია იდენტურ ტყუპებში არაიდენტურ ტყუპებთან შედარებით, მაგრამ გადაცემის გარკვეული მეთოდი ჯერ არ არის გამოვლენილი [5, 11]. მიუხედავად იმისა, რომ ოჯახის ისტორია მნიშვნელოვანია, ასევე ნაჩვენებია, რომ არსებობს ასევე გამობატული განსხვავება RAU-ს გავრცელებაში სკოლამდელ და სასკოლო პერიოდის ბავშვებში.

*იმუნოლოგიური ფაქტორი*

სამედიცინო ლიტერატურაში მოხსენებულია ადამიანის ლეიკოციტური ანტიგენის (HLA) და RAS ანტიგენის მრავალი ასოციაცია. კავშირი დაავადებასა და HLAB12-ს შორის აღწერილი იყო ზოგიერთი ავტორის მიერ Lehner et al. და Malmström et al., თუმცა ბოლომდე მაინც არ არის დამტკიცებული და დადასტურებული სხვა ავტორების მიერ. სხვადასხვა



ეთნიკური წარმოშობის პაციენტების ჯგუფებში, მნიშვნელოვანი კავშირი დაფიქსირდა HLA-DR2-სა და ქრონიკულ მორეციდივე ავთოზურ სტომატიტს შორის [13].

ავტორთა დიდი ნაწილი მიიჩნევს, რომ ავთოზური სტომატიტის პათოფიზიოლოგია დაკავშირებულია იმუნომოდულაციის დარღვევასთან. ლიმფოციტები ირკვევა, რომ უპირატესი უჯრედებია ავთოიდურ დაზიანებებში. აღმოაჩინეს CD4+/CD8+ თანაფარდობის ცვალებადობა მის სხვადასხვა სტადიაზე - პროდრომულზე, ავთების გაჩენის დროს და ეპითელიზაციის სტადიაზე. [9, 10]

#### *ტრავმული ფაქტორი*

ფიზიკური ტრავმა ერთ-ერთი მნიშვნელოვანია დაავადების განვითარებისთვის. ეს შეიძლება იყოს კარიესის შედეგად ბასრი კიდე, უხარისხო ორთოდონტიული ან/და ორთოპედიული კონსტრუქციები, „გულმოდგინედ“ ან არასწორი ჯაგრისით კბილების გახეხვა, თუმცა აუცილებლად უნდა განვასხვაოთ ტრავმულ წყლულთან [1]. პირველ რიგში მორფოლოგიური მახასიათებლებით და ასევე ტრავმული წყლულისთვის არ არის დამახასიათებელი მორეციდივე წყლულების ისტორია. როგორც წესი, მიზეზის მოხსნის შემდეგ უკუგანვითარებას განიცდის [14].

#### *სტრესული ფაქტორი*

კვლევებმა აჩვენა კავშირი დაავადებასა და ემოციურ ფაქტორს შორის. შესამჩნევი ზრდა არის დამახასიათებელი გამოცდების პერიოდში. მოსწავლეები აღნიშნავენ ავთებისა და წყლულების შემცირებას არდადეგების პერიოდში. შიფი და სხვა. [14] ფსიქოლოგიური სტრესი განიხილება ერთ-ერთ მნიშვნელოვან ფაქტორად, რომელმაც შეიძლება გამოიწვიოს ხშირი რეციდივები ავთებისადმი მგრძობიარე პაციენტში. ასევე სტრესული ფაქტორი არა მხოლოდ ზრდის გამოვლინების სიხშირეს არამედ მეტად მკვივნეულს ხდის ავთებისა და წყლულების გამოვლინებას [1].

#### *ვიტამინები*

ავტორთა ნაწილი მიიჩნევს, რომ გარკვეული ჯგუფის ვიტამინების დეფიციტი გავლენას ახდენს დაავადების განვითარებაში. Nalbantoğlu, B., & Nalbantoğlu, A. გამოიკვლიეს D ვიტამინის დონის კავშირი ავთოზური სტომატიტის დროს ბავშვთა ასაკში [2]. (ცხრილი 2) ერთ ჯგუფში შედიოდნენ დაავადებული პაციენტები (72 ადამიანი) დამეორე იყო საკონტროლო ჯგუფი (70 ადამიანი). (ცხრილი 3) კვლევების შედეგად დადგინდა D ვიტამინის საკმაოდ შესამჩნევი სხვაობა. ასევე აღსანიშნავია ისიც, რომ არ აღინიშნა კავშირი D ვიტამინის სტატუსსა და დაავადების სიმძიმეს შორის.

**December 09-11, 2022 / Tbilisi, Georgia**

Groups			
	Group I	Control	P Value
Age, years	8.7 (4.2)	7.6 (5.1)	.12
Sex, n (%)			
Male	33 (45.8)	36 (51.4)	.6
Female	39 (54.1)	34 (48.5)	
Place of residence, n (%)			
Rural	8 (11.1)	6 (8.5)	.69
Urban	64 (88.8)	64 (92.4)	

	Recurrent Aphthous Stomatitis Group, N 72	Control Group, N 70	P Value
25-Hydroxyvitamin D level, ng/mL	16.4 (8.6)	23.1 (11.5)	.002

ცხრილი 2.

ცხრილი 3.

*B12, ფოლიუმის, რკინის და ფერიტინის დეფიციტი*

არაერთმა კვლევამ აჩვენა, რომ RAU-ს მქონე პაციენტები უნდა გამოიკვლიონ სრული ჰემატოლოგიური სკრინინგით, რკინის, ფოლიუმის მჟავისა და ვიტამინის B12-ის შეფასების ჩათვლით, რომლებიც ყველა აუცილებელი ჰემატინია. ფილდი და სხვ. შეაფასა ჰემატოლოგიური სკრინინგის მნიშვნელობა 100 ბავშვში (7-16 წლის ასაკის), რომლებსაც აღენიშნებოდა ქრონიკული ავთოზური სტომატიტი. გამოიკვლიეს ვიტამინ B12-ის, ფოლიუმის მჟავას და რკინის დეფიციტზე. გამოკვლევის შედეგად 100 ბავშვიდან ოცდაერთმა აჩვენა ჰემატოლოგიური დარღვევები. მათგან 5-ს აღენიშნებოდა რკინადეფიციტური ანემია და კიდევ 13-ს ჰქონდა რკინის დეფიციტი ანემიის გარეშე. იმ ბავშვებს, რომლებსაც აღენიშნებოდათ ფოლიუმის დეფიციტი, ასევე ჰქონდათ შრატში რკინის დონის დაქვეითება. სკრინინგის არცერთ პაციენტს არ ჰქონდა B 12 ვიტამინის დაბალი დონე[12].

*ჰორმონალური ფაქტორი*

არ არსებობს დამაჯერებელი მტკიცებულება, რომ ბავშვებში ავთოზური წყლულის გაჩენა ემთხვევა პუბერტატულ პერიოდს [14]. თუმცა, ქალების მცირე ნაწილს აქვს წყლულის ნიმუში, რომელიც შეესაბამება მათი მენსტრუალური ციკლის ლუტეალურ ფაზას. თინეიჯერ გოგონებს, რომლებსაც უვითარდებათ ავთიები მენსტრუაციის დაწყების შემდეგ, შეიძლება ჰქონდეთ რკინის დეფიციტი, თუ მათი საკვებით რკინის მიღება არასაკმარისია მენსტრუალური სისხლის დაკარგვის ჩასანაცვლებლად და ასევე ამასთან ერთად სტრესული ფაქტორიც ერთვება. უკანასკნელი კიდევ უფრო მეტ ფაქტორებს რთავს, რაც მეტად ზრდის დაავადების განვითარების რისკს.

**დიაგნოსტიკა**

ქრონიკული მორეციდივე ავთოზური სტომატიტის დიაგნოსტიკა ხდება კლინიკური მონაცემებისა და სრულფასოვანი ანამნეზის საფუძველზე. უნდა მოხდეს ყველა შესაძლო რის-ფაქტორების გამოვლენა და მათი ლიკვიდაცია. ასევე ზუსტი დიაგნოზის დასადგენად

აუცილებელია დიფერენციალური დიაგნოზის გატარება სხვა დაავადებთან, რომელსაც ახასიათებს პირის ღრუს ლორწოვანზე წყლულების წარმოქმნა.

### **დიფერენციალური დიაგნოსტიკა**

პირველ რიგში დიფერენციალური დიაგნოზი ტარდება ტრავმულ წყლულთან, რადგან ტრავმის შედეგად შეიძლება განვითარდეს როგორც აფთოზური სტომატიტი, ისე ტრავმული წყლული. მისთვის დამახასიათებელია შესქელებული და მკვრივი ფსკერი და კედლები. ტრავმული ფაქტორის მოხსნის შემდეგ, როგორც წესი, წყლული განიცდის უკუგანვითარებას [7].

სიმსივნური წყლული ფუძე და კიდეები მკვრივია, მისთვის დამახასიათებელია ყვავილოვანი კომბოსტოს გარეგნობა და ხრტილისებრი კონსისტენცია. ციტოლოგიური გამოკვლევისას ვლინდება ატიპიური უჯრედები და დამახასიათებელია უჯრედული პოლიმორფიზმი[7].

ტუბერკულოზური წყლულს აქვს რბილი, უსწორმასწორო დაკბილული კიდეები. დამახასიათებელია კაზეოზური მასის არსებობა. პაციენტები უჩივიან საერთო სისუსტეს, ქრონიკულ ხველას. ციტოლოგიური გამოკვლევისას შეიმჩნევა პიროგოვ-ლანგჰარსის გიგანტური უჯრედები, ხოლო ბაქტერიოსკოპური კვლევისას- ამოითესება ტუბერკულოზის მიკობაქტერია[7].

სიფილისური წყლულისთვის დამახასიათებელია მოწითალო-ხორცისფერი ფსკერი. წყლულის გარშემო ლორწოვანი გარსი ფერშეუცვლელია. საბოლოოდ დიაგნოზი დგინდება მკრთლი ტრეპონემის აღმოჩენით[7].

ვენსანის წყლულოვან-ნეკროზული გინგივო-სტომატიტის დროს წარმოქმნილი წყლულისთვის დამახასიათებელია მომწვანო-მონაცრისფრო დაფარული ნადები, ლპობითი სუნი. ასევე მისთვის დამახასიათებელია ღრძილების დაზიანება, რაც აფთოზური სტომატიტის დროს თითქმის არ გვხვდება. ეტიოლოგიურ ფაქტორად გვევლინება სპიროქეტები და ფუზობაქტერიები[7].

ქრონიკული მორეციდივე ჰერპესული სტომატიტის დიფერენცირებას ვახდენთ ჰერპეტიფორმასთან. ჰერპესული სტომატიტისთვის დამახასიათებელი თვიდან ბუმტუკების წარმოქმნა და შემდეგ ჯგუფებად გაერთიანება[14].

### **მკურნალობა**

მკურნალობისა და პროფილაქტიკის მთავარ მიზნებს წარმოადგენს:

- ტკივილის შემცირება;
- აფთების პირის ღრუში არსებობის ვადის შემცირება
- რემისიის გახანგრძლივება.

დაავადების მკურნალობაში მეტად მნიშვნელოვანია ეტიოლოგიური ფაქტორის დადგენა და მისი აღმოფხვრა, რომლის დროსაც გარდა სტომატოლოგისა მკურნალობაში ერთვება სხვა დარგის სპეციალისტები (თერაპევტი, გასტროენტეროლოგი, ოტორინოლარინგოლოგი, ჰემატოლოგი და სხვა.).

მკურნალობის დროს ვიყენებთ როგორც ადგილობრივად მოქმედ ისე სისტემურ მედიკამენტებსაც. ადგილობრივი მკურნალობა მოიცავს ლორწოვანის გამაუტკივარებელ საშუალებებს (ვიყენებთ აპლიკაციურ ანესთეზიას მაგალით, ბენზოკაინის 4%-იანი ჟელე ან ლიდოკაინი 10%- იანი აეროზოლი); სუსტ ანტისეპტიკებს (0.06%-იანი ქლორჰექსიდინი, ჟანგბადოვანი მეთოდი); აფთების ზედაპირის ნეკროზული ნადებისაგან

გასასუფთავებლად პროტეოლიზური ფერმენტების გამოყენება (ქიმოტრიფსინი, ტრიფსინი); რეპარაციული რეგენერაციის მასტიმულირებელი თერაპია (სოლკოსერილის დენტალური ადჰეზიური პასტა, vea oris, Vea olio, ქაცვის ზეთი); ადგილობრივი იმუნომოდულატორები (ლიზობაქტი, იმუდონი). რაც შეეხება ზოგად მკურნალობას პაციენტს ენიშნება: ჰიპომასენსიბილიზირებელი საშუალებები (სუპრასტინი, ტავეგილი, ერიუსი); ვიტამინოთერაპია[7].

### **დასკვნა**

მორეციდივე აფთოზური სტომატიტი ჩება პირის ღრუს ლორწოვანის გავრცელებულ დაავადებად ბავშვთა სტომატოლოგიაში. ეტიოლოგიის საკითხი ისევ ღიად რჩება. განმაპირობებელი ფაქტორების აღმოფხვრა როგორც პაციენტს, ისე ექიმსაც ეხმარება დაავადების კონტროლში და ბოლის, სამწუხაროდ, არ არსებობს თერაპია მორეციდივე აფთოზური სტომატიტის რეციდივების აღმოსაფხვრელად.

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**CRISPR-Cas9 AND ITS APPLICATION AS A GENE-EDITING STRATEGY FOR  $\beta$ -HEMOGLOBINOPATHIES: A LITERATURE REVIEW**

*Sukhmani Ashok<sup>1</sup>*

*<sup>1</sup>Caucasus International University, School of Medicine, Tbilisi, Georgia.*

*Giorgi Dugashvili<sup>2</sup>*

*<sup>2</sup>Grigol Robakidze University, School of Medicine, Tbilisi, Georgia.*

**ABSTRACT**

The purpose of this literature review is to discuss the gene editing strategy of clustered regularly interspaced short palindromic repeats and CRISPR-associated protein 9 (CRISPR-Cas9) for  $\beta$ -hemoglobinopathies. With approximately 100,000 individuals affected by sickle cell anemia (SCA) in the United States and millions worldwide, the discovery of CRISPR-Cas9, has been one of the most prominent advances of the 21st century. It is a gene-editing tool, a technology that allows scientists to alter an organism's DNA, that was discovered as a part of the adaptive immune system of archaea and bacteria as they defend against plasmids and phages.

Clustered regularly interspaced short palindromic repeats and CRISPR-associated protein 9 is an advanced alternative to other gene-altering technologies resembling transcription activator-like effector nucleases (TALEN) and zinc-finger nucleases (ZFN). Attributed to its great efficiency and precision, CRISPR has been found to have many applications in the field ranging from the treatment of cancer to even  $\beta$ -hemoglobinopathies. Despite having a high prevalence rate and a chronic crippling nature,  $\beta$ -hemoglobinopathies are a group of monogenic diseases that have only a few therapeutic options available.

With the advancement in genome editing therapeutic strategies, a few clinical trials are in progress studying CRISPR-based treatments in Sickle cell anemia and  $\beta$ -thalassemia patients. Three patients who were treated with the therapy, two with transfusion-dependent  $\beta$ -thalassemia and one with SCA have discontinued RBC transfusions.

While CRISPR-Cas9 provides easy genome editing with several benefits, the ethical and biosafety issues cannot be ignored. Furthermore, any tool with such potential carries a risk of being unlawfully used for non-legal purposes. With the ever-growing developmental strides in the CRISPR-Cas9 technology, it may not only widen the scope of treatment options for  $\beta$ -hemoglobinopathies but to even envision a cure.

**Keywords:** CRISPR, gene editing, sickle cell anemia, hemoglobinopathy, genome engineering, thalassemia.

**Introduction**

Hemoglobin is a Heterotetramer meaning it comprises of four globin chains: adult hemoglobin (Hb A) has two  $\alpha$  and two  $\beta$  chains ( $\alpha_2\beta_2$ ) and fetal hemoglobin (Hb F) has two  $\alpha$  and two gamma chains ( $\alpha_2\gamma_2$ ). These chains transport oxygen throughout the body.  $\beta$ -hemoglobinopathies are a set of diseases that are distinguished by the qualitative or the quantitative defects in  $\beta$ -globin synthesis. Qualitative defects, such as in the case of Sickle Cell Anemia, emerge from the mutations in the HBB gene (which encodes  $\beta$ -globin) giving rise to an altered  $\beta$ -globin molecule. Sickle Hb (HbS) is a structural variant of the adult Hb (HbA) that is caused by a single nucleotide change from A-to-T transversion in the 6th codon of the HBB gene, substituting hydrophilic glutamic acid with a hydrophobic valine, i.e, a p.Glu6Val substitution. Any  $\beta$ -hemoglobinopathy which contains the HbS allele falls under the term Sickle cell disease (SCD) (Modell, 2008). Sickle Cell Anemia (SCA) is the most severe type of SCD that results from the homozygosity of the HbS allele. There are two more common structural variants of the  $\beta$ -globin chains, HbC (Nagel, Fabry, & Steinberg, 2003) and HbE (Orkin et al., 1982). Homozygosity of

the HbC mutation causes a condition known as hemoglobin C disease presenting with mild hemolytic anemia (Nagel, Fabry, & Steinberg, 2003) (Hannemann et al., 2011) whereas HbE results in diminished levels of the  $\beta$ -globin and is characterized by a mild  $\beta$ -thalassemia phenotype. Deletion or point mutations, the quantitative defects, of HBB or its regulatory elements results in diminished productions of the  $\alpha$ - and  $\beta$ -globin chains. When the intricate balance in the production of  $\alpha$ - and  $\beta$ -globin chains is disrupted, the resulting accumulation and thereafter the precipitation of the surplus  $\alpha$ -globin molecules in the erythroid precursors cause their premature death. In many cases there are severe phenotypes that emerge as the qualitative and quantitative defects are inherited simultaneously. The HbVar database hosts a detailed catalog of the mutations and the variants that cause thalassemias.

In SCA, the hemoglobin S (HbS) rapidly polymerizes under the hypoxic or acidic conditions, reducing the deformity of the red blood cells (RBCs) turning them into rigid sickle shape and a shortened lifespan. Sickled RBCs either lyse or occlude capillaries causing catastrophic clinical complications (Paulukonis et al., 2016). SCA Patients suffer from vasculopathy and various comorbidities that occur in all the body organs due to this chronic hemolysis and occlusion. Hemolytic anemia, acute chest syndrome, liver disease, crippling recurrent pain crisis (Powars, Chan, Hiti, Ramicone, & Johnson, 2005). Kidney failure, pulmonary hypertension, thromboses, avascular necrosis and stroke are responsible for not only a poor quality of life but early morbidity as well (Powars, Chan, Hiti, Ramicone, & Johnson, 2005; Platt et al., 1994; Hulbert et al., 2011).

There are approximately 100,000 individuals in the United States and millions worldwide affected by Sickle Cell Disease (SCD) which is one of the most common monogenic blood disorder (Hassell, 2010). More than 95% of SCD patients in high income countries survive through childhood due to ample newborn screening programs and medical services. However, in countries like Africa and South Asia most patients go undiagnosed and die before reaching 5 years of age (Grosse et al., 2011). Aside from impacting the lives of the afflicted individuals, SCD puts a lot of financial burden on the health care systems worldwide as well. The cost of direct medical care for SCD patients surpasses \$1 billion annually in just the United states alone (Kauf, Coates, Huazhi, Mody-Patel, & Hartzema, 2009).

Despite being discovered more than a century ago and being the first molecular disease whose genetic basis has been known for more than 60 years, the treatment options for SCD remain very limited with little to no improvement to the average lifespan of the patients over the last few decades. So far there are four FDA approved drugs that can reduce acute complications; hydroxyurea (1998), L-glutamine (2018), crizanlizumab-tmca (2019) and voxelotor (2020) (Leibovitch et al., 2022). Hematopoietic stem cell transplant (HSCT) is the only curative therapy, usually taken from an available matched donor. It's accessible to only approximately 15% of the patients (Walters et al., 2001; Mentzer, Heller, Pearle, Hackney, & Vichinsky, 1994). If matched but unrelated or even haploidentical donors are used in HSCT (Walters et al., 2001; Mentzer, Heller, Pearle, Hackney, & Vichinsky, 1994), the morbidity and mortality increase remarkably. This curative therapy comes with its treatment related risks as well as complications, Hence, it is not safe for widespread adoption (Shenoy et al., 2016).

Hereditary persistence of fetal hemoglobin (HPFH) is a benign condition in which the mutations within the  $\beta$ -globin gene cluster cause elevated Hb F levels well into adulthood (Km et al., 2012). Multiple studies have shown a correlation between the elevated Hb F levels in patients and milder consequences of SCD. SCD patients with inherited HPFH mutations experience significantly milder clinical severity of SCD (Km et al., 2012). Hence, it is deduced that higher HbF levels are an important modifier for the mortality and morbidity of patients with SCD (Km et al., 2012). Moreover, it is recognized that if the levels of HbF are low, patients with  $\beta$ -thalassemia are more likely to have thalassemia major. These findings have motivated research in the understanding of the globin locus regulation such that approaches can be developed in therapeutically manipulating the induction of Hb F expression. There are several ways that can achieve Hb F induction such as silencing of the transcription factors like B-cell lymphoma/leukemia 11A (BCL11A) (Masuda et al., 2016) or imitation of beneficial HPFH mutations (Traxler et al., 2016). Furthermore, research is underway to identify other novel HbF regulators (Grevet et al., 2018).

Gene editing technology uses programmable nucleases, meganucleases and their derivatives, such as transcription activator like effector nucleases (TALENs), zinc finger nucleases (ZFNs) and CRISPR-

associated nuclease Cas9 systems to precisely edit the genome at user defined locations in the loci by introducing double stranded breaks (DSB) (Cox, Platt, & Zhang, 2015). This technology provides the possibility to delete, correct, add and even disrupt specific sequences in the disease causing mutations of the genome, eradicating them completely. The DSBs subsequently induct either non-homologous end-joining (NHEJ) or homology directed repair (HDR) mediating the genome editing (Cox, Platt, & Zhang, 2015).

The purpose of this study was to focus on various approaches that use CRISPR/Cas9 gene editing technology for the treatment of SCD and emphasize the achievement and challenges on the potential of gene editing technologies for curing SCD.

### **Materials and Methods**

“Preferred Reporting Items for Systematic Reviews and MetaAnalyses” (PRISMA) guidelines were followed to conduct this literature review. An electronic search was conducted via PubMed, Elsevier, Scopus, PubMed Central on November 2nd 2022. The following search strategies were used:”(crisprcas OR crispr cas9 OR crispr OR crisp\* OR cas9 OR cas9 proteins OR CRISPR-Cas nucleases) AND (gene-editing OR genome editing OR gene editing\* OR editing OR gene editing technologies OR editing technologies\*) AND (thalassemia OR  $\beta$ -thalassemia OR thalasse\* OR sickle cell disease OR sickle cell diseas\* OR sickle cell anemia OR sickle cell anemi\* OR  $\beta$ hemoglobinopathies OR  $\beta$ hemoglobinopath\* OR hemoglobinopathy OR hemoglobinopath\*) AND (human hematopoietic cells OR stem cells OR stemcell\* OR hemoglobin OR hemoglobin\* OR fetal hemoglobin OR HBB gene OR BCL11A gene OR BCL11A\*)”. For full-text review, a manual search of the reference lists of the retrieved articles was carried out. No time or language restrictions were imposed. The duplicate articles were identified and eliminated before the evaluation was conducted. Reviewing of the titles and the abstracts was followed by a full-text review of the selected relevant articles for inclusion. The screening of the abstracts as well as the full text review was manually performed by the author.

The data collection process included in the review was performed by the author and reviewed by the scientific supervisor. The Initial selection of the titles and abstracts was done by the author and an exclusion process of the tiles and abstracts was carried out that did not meet the criteria of inclusion or were irrelevant for the purpose of this review. In the circumstance where the titles or the abstract had insufficient information to make a decision regarding its exclusion or inclusion, the full article was read and then a decision was made. Each relevant article’s reference list was manually searched and reviewed in order to obtain more articles relevant to the search. The final list was made and to reduce selection bias and possible double counting, only the latest published articles were selected.

Data extraction was performed through flow charts and spreadsheets that were routinely updated. The information collected was organized into a chronological order in order to understand the treatments already in use as well as the new changes with gene technologies and current clinical trials.

### **Discussion**

As mentioned in the above, the key modifier for the clinical severity of SCD is the level of HbF. The reactivation of HbF by the targeting of genes which are involved in the Hb F regulation is an approach that is currently being researched. Numerous causative genome loci have been identified through genome-wide association studies (GWAS) through the analysis of individuals with HPFH. These studies have indirectly linked multiple transcription factors to HbF silencing. One such chief regulator of HbF is BCL11A gene which associates with DNA bound factors at various locations within the  $\beta$ -globin locus and directly inhibits the HBG promotor to limit the fetal hemoglobin expression (Liu et al., 2018). Further studies have emphasized single nucleotide polymorphisms (SNPs) that were discovered in extended  $\beta$ -globin locus BCL11A and HBSIL-MYB linked to HPFH (Uda et al., 2008; Lettre et al., 2008). Additional molecular studies validate BCL11A as a direct repressor of fetal hemoglobin (Vg et al., 2008; Esteghamat et al., 2013). As a result, HbF reactivation caused by the loss of BCL11A or BCL11A binding motifs suggests an appealing and distinct target for therapeutic gene editing to treat SCD.

HbF levels and BCL11A expression have an inverse relationship (Vg et al., 2008). BCL11A has proven to be an authentic  $\gamma$ -globin repressor as demonstrated by the knockout and knockdown methods in both

mouse and human models (Xu et al., 2010; Esteghamat et al., 2013). Although HbF suppression appears to be BCL11A's primary function in erythroid precursors, this multiple transcription factor is also known to have functions outside the erythroid lineage.

Multiple lineages, including B-lymphocytes, hematopoietic stem cells (HSCs), dendritic, breast, and pancreatic cells, as well as cells in the central nervous system, have been linked to BCL11A's development, maturation, or self-renewal (Luc et al., 2016; Greig, Woodworth, Greppi, & Macklis, 2016). In addition to this, complete loss of BCL11A results in perinatal lethality in mice, and humans with rare mutations that give rise to BCL11A haploinsufficiency (Liu et al., 2003), exhibit high levels of HbF and autism-like neurological disorders (Basak et al., 2015; Funnell et al., 2015). However, erythroid-specific deletion of BCL11A in mice de-represses  $\gamma$ -globin as well as restores the signs and symptoms of SCD without interfering with erythropoiesis (Xu et al., 2011). Therefore, the best treatment for SCD would be to disable BCL11A's erythroid-specific activity while preserving its non-erythroid functions.

As described above, gene editing technologies can create a genomic modification in a targeted manner. For the purposes of this review, our focus will be on the CRISPR-Cas9 system of streptococcus pyogenes. CRISPR-Cas9 is a two component system that, in its most basic form, consists of Cas9 nuclease and a guide RNA (gRNA). In a nutshell, the Cas9 protein needs the protospacer adjacent motif (PAM) of 5'-NGG-3' to bind DNA effectively. The sequence specificity is further solidified through the gRNA, a short RNA molecule with roughly 20 base pair (bp) sequence that combines with Cas9 and "guides" it to a user-defined location in the genome by complementary base pairing to the DNA region of interest next to the PAM, enabling Cas9 to incise the correct location in the genome.

A DSB that is unrepaired can not only be harmful but fatal as well, making mammalian cells highly effective at healing such breaks. The endogenous cellular repair mechanism will restore the DNA lesion once the nuclease-induced DSB is produced by one of several methods, including but not limited to non-homologous end joining (NHEJ), microhomology mediated end joining (MMEJ), or homology direct repair (HDR). NHEJ has the potential to be error-prone, and erroneous repair by this process results in aleatory insertions and/or deletions (indels) at the location of the break and is beneficial for gene disruption, binding sites, and particular DNA motifs. In addition to disrupting genes, binding sites, and DNA patterns, MMEJ relies on brief microhomologies at or near the cut site, which frequently lead to the deletion of the intervening sequences.

In the case of NHEJ and MMEJ, only the targeted DSB is required for an automatic repair to occur. HDR, on the other hand, requires the usage of a donor template with homology to incise and to be introduced into the targeted cell nucleus. Hence it is labeled as "user-defined" as the donor template can be integrated with the desired genomic alteration.

Normal adult RBCs are terminally differentiated with an average life span of 120 days while Sickled RBCs live for about 20 days (Eadie, Brown, & Curtis, 1955). These RBCs are enucleated, i.e, there is no DNA for any mutation to be corrected. With the SCA being caused by a single point mutation in the HBB gene, the hematopoietic stem cells (HSCs) need to be modified for any therapy to be curative in SCA.

In the case of  $\beta$ -hemoglobinopathies, there are two ways that gene editing therapy can be employed: 1. Gene correction, a way to modify the underlying genetic mutation; 2. Elevation of HbF levels. The first approach, the causative mutation in HBB gene is targeted through the CRISPR gRNA/Cas9 RNP complex together with the donor template. This complex and the template is delivered into HSPCs isolated from SCD patients through electroporation. Numerous viral-based vector approaches, including as integrase-deficient lentiviral systems (IDLVs), adenovirus 5/35 serotype (Ad5/35), and adeno-associated viruses (AAVs), have been studied in HSPCs for donor template distribution (Romero et al., 2019). AAV has two key advantages over the other vectors; the low frequency of vector integration into the genome DNA of the host and the low risk of associated insertional mutagenesis and genotoxicity. In several investigations, RNP in conjunction with single-stranded oligodeoxynucleotides (ssODNs) exhibited effective targeted integration at the HBB locus in CD34+ HSPCs (Hoban et al., 2016; Dever et al., 2016). A low ratio of HDR to NHEJ in long-term reconstituting HSCs currently prevents clinical translation of SCD mutation correction utilizing the correcting donor template. The potential for Cas9



cutting of HBB to cause  $\beta$ -thalassemia major, intermediate, or minor has not been thoroughly examined. Additionally, a clinical trial will need to evaluate the in vivo consequences of Cas9 cleaving HBB and the decrease in functional  $\beta$ -globin levels in a patient with SCD.

In regards to targeting the BCL11A gene locus and elevating the fetal hemoglobin, there are a few clinical trials underway studying the CRISPR based treatments in  $\beta$ -thalassemia and SCD patients. Vertex pharmaceuticals and CRISPR Therapeutics have developed Exa-cel, formerly known as CTX001 which is an investigational, autologous, *ex vivo* CRISPR/Cas9 gene-edited therapy based on the discovery of the BCL11A erythroid-specific enhancer. Exa-cel creates indels at the GATA/TAL1 (transcription factors) binding sites in the BCL11A erythroid enhancer (Bauer et al., 2013). This specifically curtails the expression of BCL11A expression exclusively in the erythroid lineage, elevating the fetal hemoglobin levels. The expression of BCL11A is suppressed more than 50% with the Cas9: gRNA RNP complex targeting CD34+ HSPC as it achieves up to 90% indels (Wu et al., 2019). At the moment, there are five ongoing clinical trials, CLIMB-111, CLIMB-121, CLIMB-131, CLIMB-141 and CLIMB-151. CLIMB-111 and CLIMB-121 are ongoing Phase 1/2/3 open-label trials which are designed to evaluate the efficacy and safety of a single dose of exa-cel in patients with transfusion-dependent thalassemia (TDT) and SCD, respectively, between the ages of 12 and 35 years. On the other hand, CLIMB-141 and CLIMB-151 are ongoing phase 3 open-label trials evaluating patients between the ages 2 and 11 years. Patients from the above mentioned trials are going to be followed up for up to 15 years in the open-labeled, long term trial of CLIMB-131.

Corbacioglu et al., 2020 showed results of three patients, two with transfusion-dependent  $\beta$ -thalassemia ([NCT03655678](#)) and one with SCA ([NCT03745287](#)) who were treated with exa-cel discontinued RBC transfusions. The patients showcased high levels of HbF even until 6 months after exa-cel infusion (Corbacioglu et al., 2020). The patient's HSPCs are extracted using apheresis, CD34+ cells isolated and CRISPR/Cas9 is delivered through electroporation. Exa-cel is reinfused in the patients after busulfan myeloablative conditioning. This method is widely applicable since it targets a consensus motif rather than patient-specific variations, enabling the synthesis of a single gRNA for all patients.

New data with positive findings from CLIMB-111 and CLIMB-121 were presented at the 2022 European Hematology Association (EHA) Congress held on 9-12 June. Out of 75 patients 44 patients were with TDT and 31 patients were with SCD. They were followed for 12.3 and 9.6 months for patients with TDT and SCD respectively. Findings demonstrated that 95% of the patients with TDT had eliminated need for RBC transfusions after the exa-cel infusion. The requirements of RBC transfusions for two patients were reduced by 75% and 89%. Analogously, 100% of the 31 DCS patients did not experience vaso-occlusive crisis (VOCs) any more after the exa-cel infusion. Even the fetal hemoglobin showed clinically meaningful increase for both the groups. At the same time, there were stable proportions of the edited BCL11A alleles in HSPCs of the bone marrow and the peripheral mononuclear cells. With a report of no malignancies, discontinuations or deaths, it is evident that a single exa-cel infusion showed remarkable ability to eliminate the need of RBC transfusions in TDT and VOCs in SCD patients (Corbacioglu et al., 2020).

All gene editing techniques run the risk of operating at unexpected regions and causing unintended genomic modifications. Similarity to the target sequence, with or without mismatches, bulges, or non-canonical PAMs, may lead to off-target modifications to the genome. Each genomic tool will have different off-target sites. Additionally, every Cas9 and gRNA combination has a distinct off-target profile. Hence different gRNA and variant Cas9 fusions will have distinct off-target potential. It has been demonstrated that administration of CRISPR reagents via RNPs reduces off-target editing (Kim, Kim, Cho, Kim, & Kim, 2014). Moreover, there is a possibility of off-target integration if a donor is needed for a particular strategy. One of the more distressing outcomes of off-target mutagenesis with a CRISPR-Cas9 treatment applied to HSPCs is the probability of leukemogenesis and clonal expansion.

The identification of the off-target sites with the expansive genome is a repetitive process. First step is discovery, done either through in-silico prediction of analogous sequences, in-vitro methods or the nuclease on genomic-context or naked DNA, or even a combination of both the methods. They are used to predict and make a list of alleged off-target sites that are then further interrogated by targeted PCR amplifications of the interested sites or a multiplexed targeted amplification approach called RNAse H-

dependent (rhAmp) PCR (Dobosy et al., 2011). This is followed by next generation sequencing (NGS). Indel containing sites are considered as verified off-target sites. With several tools and protocols that can be used for the identification and validation of potential off-target sites, there are in-depth reviews elsewhere (Porter, Levine, & Pruett-Miller, 2019; Li, Hong, Chen, Zuo, & Yang, 2019).

### **Conclusion**

Autologous transplant of gene-edited hematopoietic stem cells could potentially provide a cure for most patients with SCD and TDT as CRISPR/Cas9 technology makes its advancements. With the deepening of knowledge of gene-editing technologies comes the challenges of translating this treatment strategy to clinics, including the necessity for low off-target effects as well as high editing efficiency. The production cost of gene-editing based therapies will be high as the cost of development, manufacturing, the distribution along with the personalized cell product approval is taken into account. Additionally, ex-vivo editing of the HSPCs and reimplantation of the modified cell product requires a proficient group of trained physicians as well as highly specialized equipment and facilities. This eventually would lead to restricted and limited access to a population most likely belonging to low-income and developing areas that lack sufficient equipment and facilities in order to isolate, edit, culture and deliver the cellular product to humans. Hence it is imperative to simultaneously think and evaluate strategies that would make accessibility of the treatment in resource-constrained regions easier especially in areas where  $\beta$ -hemoglobinopathies are prevalent.

The development of editing strategies that would provide with a high yield of long term repopulating HSCs that would have polyclonal high proportion of gene-edited cells even after engraftment, remains a challenge that needs to be overcome. Adding further to this is the fact that the source of HSPCs and the SCD pathology of the individuals could have a notable effect on both the engraftment potential as well as gene-editing outcomes. This includes the differences in the conditions of the patients. Other factors likely to be an influence in the viability and the functionality of the HSPCs in SCD are genetics and environmental factors.

Current ex-vivo editing technologies have their own set of shortcomings. Harvesting of the HSCs from the bone marrow is an invasive procedure and only a small percentage of the CD34+ from SCD patients are typically HSCs. Since the patients go through busulfan myeloablative therapy, they experience the side effects of chemotherapy such as infections and delayed neutrophil engraftment and thrombocytopenia. Furthermore, any tool with such potential carries a risk of being unlawfully used for non-legal purposes.

The development of treatment options for SCD has been sluggish and restricted despite SCD being known for over a century and its genetic composition having been determined over 60 years ago. With the ever-growing developmental strides in the CRISPR-Cas9 technology, it may not only widen the scope of treatment options for  $\beta$ -hemoglobinopathies but to even envision a cure.

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**THE CONNECTION BETWEEN ORAL DISEASES SUCH AS PERIODONTITIS AND CARDIOVASCULAR DISEASES**

*Sopo Goglidze<sup>1,2</sup>, Mariam Jincharadze<sup>1</sup>*

*1. Faculty of Dentistry of Tbilisi State Medical University, Tbilisi, Georgia*

*2. Student Scientific-Research Organization "ENDEAVOR" of TSMU, Tbilisi, Georgia*

**ABSTRACT**

Periodontitis is a chronic inflammatory disease of the tooth-supporting connective tissue and alveolar bone that is initiated by a bacterial biofilm in periodontal pockets. It is associated with a range of systemic diseases such as cardiovascular disease (CVD).

After a detailed systematic review of the evidence, the experts produced a consensus report outlining our current understanding of the relationship between periodontitis and atherosclerotic cardiovascular disease.

An international panel of leading clinicians and research scientists convened at a landmark meeting in Spain, to review the latest scientific research into periodontitis and ACVD.

Periodontitis has been shown to increase the risk of a first ACVD event, (such as heart attack or stroke), independent of other known cardiovascular risk factors.

There is gathering evidence that periodontitis is a risk factor for future cardiovascular disease and that periodontal therapy can reduce systemic inflammation. It follows that effective prevention and early treatment of periodontitis may have an important role in reducing an individual's susceptibility to ACVD events and also in contributing to improved cardiovascular health at a population level.

Current results seem to confirm the thesis that periodontitis is associated with the biochemical features of heart failure in the course of myocardial infarction.

There is evidence of significantly higher levels of fibrinogen in periodontitis patients versus healthy controls, and in CVD and periodontitis patients compared with either condition alone. Periodontal therapy appears to result in a significant decrease in fibrinogen levels

There is scientific evidence of pleiotropy between periodontitis and cardiovascular diseases. The highly pleiotropic genetic locus CDKN2B-AS1 (chromosome 9, p21.3) associated with coronary artery disease, type 2 diabetes, ischemic stroke and Alzheimer's disease is also consistently associated with periodontitis.

Cardiovascular diseases are considered social diseases. They are also among the most common causes of death worldwide. Periodontal diseases, in turn, belong to the most common illnesses of the oral cavity and, along dental caries, constitute the main cause of teeth loss. Periodontal infections are also linked to the risk pattern of several systemic diseases such as cardiovascular diseases. Scientific evidence also indicates the presence of genetic factors in periodontitis and cardiovascular diseases.

It has been known for a while that periodontitis alone is an independent risk factor contributing to the development of atherosclerotic vascular disease and the underlying mechanism is systemic inflammation. As a progressive, chronic inflammatory disease, untreated periodontitis has the potential to undermine overall health and even exacerbate other inflammatory conditions, such as atherosclerotic cardiovascular disease (ACVD).

An international panel of leading clinicians and research scientists convened at a landmark meeting in Spain, to review the latest scientific research into periodontitis and ACVD. After a detailed systematic review of the evidence, the experts produced a consensus report outlining our current understanding of the relationship between periodontitis and atherosclerotic cardiovascular disease. They also formulated new evidence-based guidelines for general dental practice.

### **Effects of periodontitis on the incidence of cardiovascular events**

Periodontitis has been shown to increase the risk of a first ACVD event, (such as heart attack or stroke), independent of other known cardiovascular risk factors. The size of the increase in risk varies according to the type of ACVD event, and also depends upon age and gender. For example, the extra risk posed by periodontitis is greater for cerebrovascular disease than for coronary heart disease and also greater in males and in younger people

### **The link between periodontitis and ACVD**

The most likely explanation for how periodontitis affects ACVD is that periodontal bacteria and their products (e.g. endotoxin) from periodontal pockets enter the circulation and provoke an acute-phase and subsequent inflammatory response. Mediators produced as part of this host response then promote the development, maturation and instability of fatty lesions (atheroma) in the arteries, increasing the risk of an ACVD adverse event.

### **The effects of periodontal treatment on cardiovascular outcomes**

Studies have demonstrated that periodontal treatment reduces the overall level of inflammation within the circulation. Specifically, periodontal therapy had favorable effects on two key factors known to be important in ACVD risk: levels of a pro-inflammatory acute-phase protein agent called C-reactive protein (CRP); and measures of endothelial cell function. Cholesterol levels, however, were not affected by treatment. More limited evidence suggests that periodontal therapy improves other known markers of inflammation, coagulation and endothelial cell activation, and also arterial blood pressure and subclinical ACVD.

### **ACVD treatments influence treatment outcomes for periodontitis**

There is some new evidence that various anti-inflammatory agents prescribed to patients with ACVD – such as aspirin, statins, fish oil and vitamin D – may also help reduce periodontal inflammation.

### **Implications for general dental practice**

There is gathering evidence that periodontitis is a risk factor for future cardiovascular disease and that periodontal therapy can reduce systemic inflammation. Effective prevention and early treatment of periodontitis may have an important role in reducing an individual's susceptibility to ACVD events and also in contributing to improved cardiovascular health at a population level.

The main assumption of the thesis that periodontitis affects the initiation and progression of atherosclerosis is the fact that the periodontal disease causes subtle systemic inflammation. The study of Bokhari et al. has revealed elevated levels of inflammation markers in the study group. Leukocytes count was  $10.82 (\pm 3.87) 10^9/L$ , ESR  $28.69 (\pm 17.62) \text{ mm/h}$ , the levels of hsCRP  $8.34 (\pm 18.72) \text{ mg/L}$ , and fibrinogen  $4.62 (\pm 1.09) \text{ g/L}$ . In the conducted analysis, a correlation was revealed between the values of periodontal parameters attesting to the presence and the severity of a periodontal disease and the blood level of inflammation parameters. Moreover, there was an inverse correlation between the number of teeth and ESR ( $R = -0.31; p = 0.01$ ). This may be due to the fact that periodontal inflammation is the main reason for tooth loss.

Another extremely important result of the present study is the relationship between periodontal disease and fibrinogen. Namely, a positive correlation between the values of the BOP marker, indicating active inflammation of periodontium, with the level of fibrinogen ( $R = 0.36; p = 0.006$ ). Fibrinogen is a protein synthesized by hepatocytes and fibroblasts in response to inflammation. The level of fibrinogen in the blood correlates with the severity of atherosclerotic lesions, the risk of an acute coronary syndrome, and mortality among patients with myocardial infarction. Fibrinogen participates in the thrombotic process; it is also pro-inflammatory, as it increases the expression of adhesion molecules and stimulates production of inflammatory mediators by endothelial cells. This has an additional significance in the studied group of patients with acute myocardial infarction, where prothrombotic hyperactivity is a key pathogenic factor. The study by Bokhari et al. in which 317 patients with coronary artery disease and periodontitis were examined, indicated correlation between BOP and the level of fibrinogen. Also Górski et al. documented positive correlation between the concentration of fibrinogen and the values of BOP ( $p = 0.0587$ ), as well as between the number of lost teeth and the level of fibrinogen ( $p = 0.0003$ ).

Seringec et al. in turn, demonstrated considerably higher levels of HSCRP, fibrinogen, and globulins among patients with chronic periodontitis, as well as a higher tendency of erythrocytes to aggregate than in people with healthy periodontium.

Current results seem to confirm the thesis that periodontitis is associated with the biochemical features of heart failure in the course of myocardial infarction. It probably depends on the size of heart injury, as it was asserted by Marfil-Alvarez. This author indicated the correlation between periodontitis and the size of myocardial infarction. This observation is reflected by the higher level of troponin and myoglobin depending on the extent of the myocardial injury. This observation in patients with myocardial infarction is extremely important from a prognostic point of view.

An interesting observation is the relationship between the severity of periodontitis and TNL levels. Linear regression analysis showed that significant predictors of the level of TNL are API and BOP. With 1% increase in API, TNL levels decrease by 0.3 units, while with 1% BOP increase, TNL levels increase by 0.26 units. The present research is consistent with the results obtained by Marfil-Alvarez et al., who found a significant correlation between BOP and TNL level ( $R=0.21, p<0.025$ ). Moreover, hierarchical linear regression has shown that the TNL concentration was positively associated with indicators of the extent and severity of chronic periodontitis. Interestingly, the relationship between chronic periodontitis severity and TNL was mediated by the total leukocytes count. On the contrary, current results for patients with acute myocardial infarction are quite different from the data presented by Vedin et al. Indeed, they found no relationship between periodontal disease, which a simple index was the loss of teeth, and the level of troponin. It should be noticed, however, that this study focused on patients with stable coronary heart disease. In earlier studies these authors showed no relationship between tooth loss and myocardial infarction in this population.

An equally important and original result of the study is the significant association of periodontitis with risk of myocardial infarction. The logistic regression analysis showed that API and BOP are significant predictors of myocardial infarction. With the increase in API by 1%, the probability of myocardial infarction increases by 8% ( $OR=1.08$ ), while with a 1% increase in BOP, the probability of myocardial infarction decrease by 7% ( $OR=0.93$ ). The current findings are consistent with the results of the PAROKRANK study of 805 people. A relationship has been demonstrated between moderate to severe periodontitis, objectively confirmed by radiological bone loss, and the first myocardial infarction. Stability Study dedicated to similar topics. In contrast to the PAROKRANK study, this showed no association with periodontal disease and the onset of the first myocardial infarction. However, while various aspects of cardiovascular risk were assessed in this study, including myocardial infarction, all analyzes were based on a single but very simple indicator of periodontitis which is the number of teeth preserved.

The thing we need to acknowledge from this research is the fact that the increase in the BOP ratio by 1% is accompanied by a reduction in the risk of heart attack by 7% also requires comment. Of course, higher BOP indicates a greater severity of periodontitis. It should be remembered, however, that during the dental examination, patients in accordance with acute coronary syndromes treatment standards were already on dual antiplatelet therapy, which undoubtedly increases the risk of bleeding. Moreover, the severity of bleeding may be clear evidence of the effectiveness of antiplatelet therapy, while it might be a problem in dental treatment in the period after acute coronary syndromes. The explanation for this apparently unexpected relationship can therefore be seen in that—it is a net effect of the severity of periodontitis and the increased bleeding tendency associated with dual antiplatelet therapy (DAPT). Metabolic syndrome is another important aspect to consider. It is well known that the syndrome constitutes a risk factor for the occurrence of a heart attack and is closely associated with high mortality. The latter may be additionally connected with the frequent occurrence of the coronary atherosclerosis in patients with the pro-inflammatory and prothrombotic state characteristic of the metabolic syndrome. On the other hand, metabolic syndrome is also associated with periodontitis and tooth loss. The basic exponents for the metabolic syndrome include: visceral obesity, triglyceride, HDL cholesterol, blood pressure, and fasting blood glucose. All markers related to the metabolic syndrome indicated increased values in the present study group. Considering the metabolic syndrome related markers and adjusted analysis were performed. This analysis confirmed that API and BOP are still important indicators of myocardial infarction, although with a slightly lower statistical significance, when compared to the



analysis not taking into account the metabolic syndrome markers (for API respectively:  $p = 0.001$  and  $p > 0.001$ ; for BOP respectively:  $p = 0.006$  and  $p = 0.001$ ). Patients with acute myocardial infarction have worse periodontal status compared to people without coronary heart disease. Higher severity of periodontal disease, poorer oral hygiene and increased activity of the periodontitis lead to greater manifestation of systemic inflammation in patients with acute myocardial infarction. Periodontitis is a risk factor for myocardial infarction and also affects the degree of post-infarction left ventricular damage, which means that there is an inflammatory link between these two pathogenetically inflammatory diseases.

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**HIV GENOME ERADICATION IN HOST CELLS EMPLOYING CRISPR Cas9 TECHNOLOGY**

*Debleena Chand*

*International School of Medicine, Alte University*

*Second Year, MD Program*

*Dr. Ana Sukhiashvili*

*MD, Gynecologist-Obstetrician*

**ABSTRACT**

In this evolving era of 21st century where scientific advancements via research and experiments are being developed every hour especially the ones that facilitate the editing of human genome it is necessary to conduct a detailed study on these tools and acquire an understanding about their functioning for efficient incorporation in therapeutic practices. Understanding of targeted nucleases have enabled researchers to theoretically manipulate and modify any part of human DNA promoting fascinating possibilities for human gene therapy.

One of the highly useful gene editing tools that we will be discussing here is CRISPR-Cas9 complex namely clustered regularly interspaced short palindromic repeats. The development of CRISPR-Cas9 gene editing tool is for the purpose of altering any DNA composition in cell primarily employed editing mutations resulting in hereditary disorders especially recessive (autosomal and sex-linked) and chronic viral infestations. The physiological functioning of pathogenic viruses is dependent on their ability to integrate viral genome with human DNA. Talking about infestation of host genome by viruses, statistically HIV-AIDS is one of the globally rising infections. The dormant period of HIV virus persists as long as 29 days to 20 years after exposure resulting in varied insidious outcomes in the host organism.

According to the researchers at Northwestern Medicine, US 86 genes have been estimated that may play a role in the way HIV replicates, including over 40 which have never been looked at in the context of HIV infection. Eradication of the correlated genes using CRISPR/Cas9 complex can aid in the revolutionizing treatment of this life-threatening immunodeficiency disorder among millions.

**Introduction**

CRISPR has the potential to enter into a cell's DNA and excise any damaged DNA that may lead to disease or a chronic illness such as HIV which has further potential to develop further into AIDS. Potential applications of CRISPR include genetic screening to identify genes, especially those involved in cancer immunotherapy and the therapeutic management of AIDs, and many more. Other than cancer and AIDs CRISPR has also found immense application in developing assays to detect Sars-Cov2 infection.

This site specific gene editing technology can one day also be administered in the field of genome editing on human embryos aiming to prevent various diseases and prevent the inheritance of gene linked disorders.

**Why HIV?**

HIV is a retrovirus, meaning it can write its genetic code into the genome of infected cells, co-opting them into making more copies of itself. When the virus enters the body, it infests the immune cells. It particularly targets helper T cells (CD4+), which help defend the body against bacterial and fungal infections.

During a period from a few months to several years the patient might be perceived as completely healthy, however the virus continues to replicate and destroy T cells which indicates the dormancy of the virus.

About 6 weeks after HIV infestation, a clinical “latency” period is noted where the patient presents no symptoms and during this stage there is a slow reduction in the number of CD4 T cells with time, and a gradual increase in the amount of HIV particles in the body. When T cell count decreases, patients are in serious danger of contracting deadly infections which a healthy immune system can normally handle. This stage of HIV infection is known as AIDs.

The most commonly prescribed drugs prevent the viral genome from being copied and incorporated into a host cell's DNA. There are other drugs that prevent the virus from maturing, causing HIV to be unable to infect new cells in the body. Along with presenting with several severe side effects like appetite loss, diarrhoea, fatigue, nausea, vomiting, anxiety, higher than normal levels of cholesterol, etc the reason why antiretroviral drugs can't cure the virus is because of the tendency of the virus to integrate into the genome and in some cases become transcriptionally silent or latent.

HIV can subsequently be reactivated on withdrawal/ cessation of the anti-retroviral drug administration. Therefore, complete removal of the viral genome by gene editing tools like CRISPR, zinc-finger nucleases, etc prove to be more efficient mode of therapy.

### **History of CRISPR**

The existence of this revolutionary gene editing tool CRISPR was first realised by a group of Japanese scientists, Atsuo Nakata group in 1987 who then discovered an odd DNA sequence in E.Coli bacterium .The repeated palindromic sequences (eg-ATCTA) in the genome of E.coli that read identically forward and backward for approximately 30 bases with an interval of about 36 non palindromic bases was observed. The purpose of these repeated sequences was further elucidated by Francisco Mojica in 1992, a 28 year old student in the university of Alicante, Spain who discovered that sequences of DNA had repeats in them, with regularly-spaced intervals while working with Archaea and named it as CRISPR, short for “Clustered-Regularly-Interspaced-Short-Palindromic-Repeats”. The presence of palindromic sequence along with E.coli were also outlined in gram positive and negative bacteria along with Archae questioning the relevance of CRISPR in these organisms. When evaluated using a bioinformatics analysis tool (BLAST) the sequences resembled that of a virus. The last component of CRISPR i.e., trans activating CRISPR RNA/ tracer RNA was accidentally discovered by Emmanuelle Charpentier . Jennifer Doudna and Emmanuelle Marie Charpentier, were awarded the 2020 Nobel prize in chemistry for their ground breaking work with the model of CRISPR-Cas9 gene editing tool.

### **Basis of CRISPR Technology**

CRISPR is an innovative mechanism that has been adapted from normal bacteria, the defence system they use to protect themselves from viral invasion; it is a programmable nuclease system that can prevent/ relieve viral infection of bacterial cells. This potential of bacterial immune response in gene editing was recognised by the scientific community. It was perceived that bacteria were able to copy parts of viral gene following an attack and insert these genes into their own genome as spaces .

After viral infection, the unique sequence present in between the palindromic repeats, which are called spacers, are sections of DNA that are peculiar, and do not belong to the bacterium, but instead originate from mobile genetic elements, or MGEs, such as bacteriophages, transposons, or plasmids that have previously infected the prokaryote. When attacked again by the same virus bacteria simply copy their spacer sequences which can then bind to the matching region on the viral genome initiating their destruction of the viral DNA .

Therefore, CRISPR-Cas system is considered as a unit of adaptive immune system in bacteria , which provides specific and acquired immunization against exogenic mobile genetic elements like bacteriophages and this discovery was first made in *S. thermophilus* in 2007.[1]

The CRISPR or guide RNA component is basically a stretch of about 20 or so nucleotides of RNA homologous to DNA sequence of interest and this guide RNA then brings in the Cas9 protein which has endonuclease activity and hence this complex will launch a site-specific DNA break and act as very precise molecular scissors.

CRISPR array can undergo transcription, to form CRISPR RNA, abbreviated as crRNA, although this longer strand is called pre-crRNA. In particular, Cas9 is one of the nucleases found in *Streptococcus*

pyogenes, which is one of the most extensively researched and characterized CRISPR-associated nuclease proteins. There are also molecules of tracrRNA that have sections that are complementary to and therefore can anneal to the palindromic repeats. So for each spacer and palindromic repeat, we end up with a complex consisting of that segment of pre-crRNA, a tracrRNA, and a Cas9 protein.

RNase III, will cleave the strand in between these complexes, leaving behind individual crRNA complexes called effector complexes. With these effector complexes formed, the cell is now ready to defend against the invader whose genome produced that crRNA. If this complex encounters a section of viral DNA that has a sequence that is complementary to this crRNA, the nuclease enzyme will coordinate, and if it recognizes a short sequence unique to the viral genome called a protospacer adjacent motif, or PAM, then it will snip both stands of the DNA, just a few base pairs upstream from the PAM. Cas9 has two domains, and each one will snip one of the DNA strands.

After the incision is made, the natural DNA repair mechanism is enacted for the target DNA. The cleaved dsDNA can undergo repair via two routes. Either by homology-directed repair, abbreviated HDR, or by non-homologous end joining, abbreviated NHEJ. The NHEJ pathway repairs double-strand breaks in DNA by directly ligating without the need for a homologous template, which means a DNA strand with a similar sequence that can act as a template. The NHEJ mechanism can also introduce insertion or deletion of specific sequences at the joining ends, thus creating what is referred to as indels. Indels are DNA strands with either an insertion or deletion of nucleotide sequences.

### **TRIALS ON ERADICATING HIV EMPLOYING CRISPR Cas9**

Such trials have already been conducted in rhesus monkeys who are affected with the simian Immuno virus which is the equivalent to HIV and as a result, these trials have indicated complete eradication or the potential to completely disrupt HIV or SIV's ability to replicate which essentially provides for a functional cure.[4] So, as discussed in human cells even in mammalian cells the simplest DNA repair pathway is called non-homologous end-joining and behaves like an emergency DNA repair system where the ends of the DNA break are put back together and this leads to small insertions or deletions of the sequence at the site of the break that leaves behind a scar or an InDel.

And in addition, if targeted nucleases are recognized as HIV sequence this could also lead to disruption of the HIV virus. Restriction factors are intracellular anti-HIV defenses for example Tetherin, SERINC3, etc act naturally in one's cell against the virus and the reason why HIV can still infect despite the activity of restriction factors is that HIV has developed antagonists of these various factors. So for example, the VPU protein degrades the tetherin restriction factor.[5]

It has been observed that for primate rhesus macaques HIV hasn't evolved to be able to infect rhesus macaques, so, therefore, the sequences of the human and primate forms can be compared, for example, the difference between amino acid sequences between the two and which might therefore be candidates to insert into human genes. Based on this trial the strategies undertaken are based on firstly introducing a couple of mutations that exist in the rhesus macaque form which can convert the human form into the form that can now recognize HIV resulting in having a combination of both the normal gene and a mutated gene. An edited gene might prove something that the virus can't mutate around.

### **Conclusion**

Genome editing has garnered great interest in the prevention and treatment of various human diseases. But currently, this tool is used primarily in cells and animal models in research labs.

The majority of the trials have been conducted on primates such as rhesus monkeys. Since these trials have predominantly produced positive results, more research pathways and avenues have opened up for the same.

With further research, these tools might be able to eliminate the HIV virus completely in humans which will alleviate the lifelong usage of antiretroviral drugs.

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**ROLE OF WATER-SOLUBLE VITAMINS IN REDUCING THE RISK OF  
CARDIOVASCULAR HEART DISEASE IN PREMATURE OVARIAN INSUFFICIENCY  
PATIENTS**

*Rushikesh Rajesh Patil*

*Alte University, International School of Medicine, MD program, Tbilisi, Georgia.*

*ORCID NO: 0000-0002-6196-946X*

**ABSTRACT**

The main objective of the study is to analyze the effect of vitamin B and vitamin C i.e., water-soluble vitamins on Premature Ovarian Insufficiency (POI) patients who are at higher risk for cardiovascular disease. Menopause is a naturally occurring event, its early occurrence causes a condition known as POI. For its treatment, water-soluble vitamins were considered because as we know they are less toxic and can pass out of the body if overdosed. Also, to cause harm, these vitamins should be taken in much higher units i.e., 10 times the recommended dose. There are 15% increased risk of CVD in early menopause out of which Women who experienced premature menopause had a 33% higher risk of heart failure and a 9% higher risk of atrial fibrillation compared to those who did not. I tried to connect this problem and to find solution with vitamins. Vitamins chosen were B2, B6, B12, C. Their correlations are mentioned in the main body of paper. My Primary concern was to develop a cost effective and safe treatment options.

**INTRODUCTION**

In patients with Premature Ovarian Insufficiency Syndrome (also known as early menopause), the estrogen level in the body drops critically low. Estrogen is a hormone that plays important role in the female reproductive system. It is in sync with other hormones and plays an important function in the menstrual cycle. Estrogen also helps maintain some of the important cardiovascular functions. Menopause is an event that takes place in the female body after 51 years [3] in which the ovarian function ceases, as a result, estrogen level drops low. If this event takes place between the age group of 35 to 50 years it is known as Premature Ovarian Insufficiency or early menopause. There is a 15% increased risk of all-cause mortality among patients of early menopause out of which Women who entered menopause before age 45 were also about 20 percent more likely than women with later menopause to die from cardiovascular disease (including heart attacks and strokes) [4]. It is essential to increase the blood estrogen level in these patients to avoid cardiovascular disease and other conditions. Studies have highlighted that low estrogen can increase homocysteine levels in the blood. With the help of some water-soluble vitamins and proper diet and exercise, it is possible to achieve a desirable estrogen level in early menopause. I aimed to treat the cardiovascular disorder which results from Premature Ovarian Insufficiency Syndrome patients with the help of water-soluble vitamins i.e., Vitamin B2 (Riboflavin), Vitamin B6 (Pyridoxine), Vitamin B12 (Cobalamin), Vitamin C (Ascorbic Acid).

**MATERIAL & METHODS**

A Systematic Review and meta-analysis were conducted on the articles about early menopause and cardiovascular disease of the latest 7 years i.e., from 2015 from PubMed and Science Direct databases, and were interlinked to find a solution. To find a risk for cardiovascular disease related to early menopause, data from 5 hospitals in India were analyzed. Patients with a confirmed diagnosis of early menopause or exhibiting symptoms related to early menopause were screened for cardiovascular health. Cholesterol profile tests were carried out on 20 patients to check for their heart function. For a Statical representation of the graph, data from the European Society of Cardiology (ESC) [5] was collected and combined with the above hospital data for better outcomes.

## **FINDINGS AND DISCUSSION**

Vitamins of our interest have various effects on the cardiovascular system as well as the reproductive system. As in Premature Ovarian Insufficiency patients, estrogen level drops critically low, so as a treatment we need to increase the estrogen level. It can be achieved in multiple ways, some of which are Hormone Replacement Therapy (HRT), and maintaining a proper lifestyle i.e., reducing body weight, reducing stress, enough sleep, and proper exercise. It can be also achieved by proper vitamin supplementation and diet regulation together, which is the most harmless, easy, and cheap way. Some of these vitamins are involved in increasing blood estrogen levels naturally whereas other vitamins boost cardiac function. Water soluble vitamins are chosen because they have fewer toxic effects because any excess amount gets excreted out of the body via urine. Vitamin B2 and Vitamin B6 increase estrogen levels naturally. Specific vitamins with their functions are mentioned below:

### **Vitamin B2 (Riboflavin)**

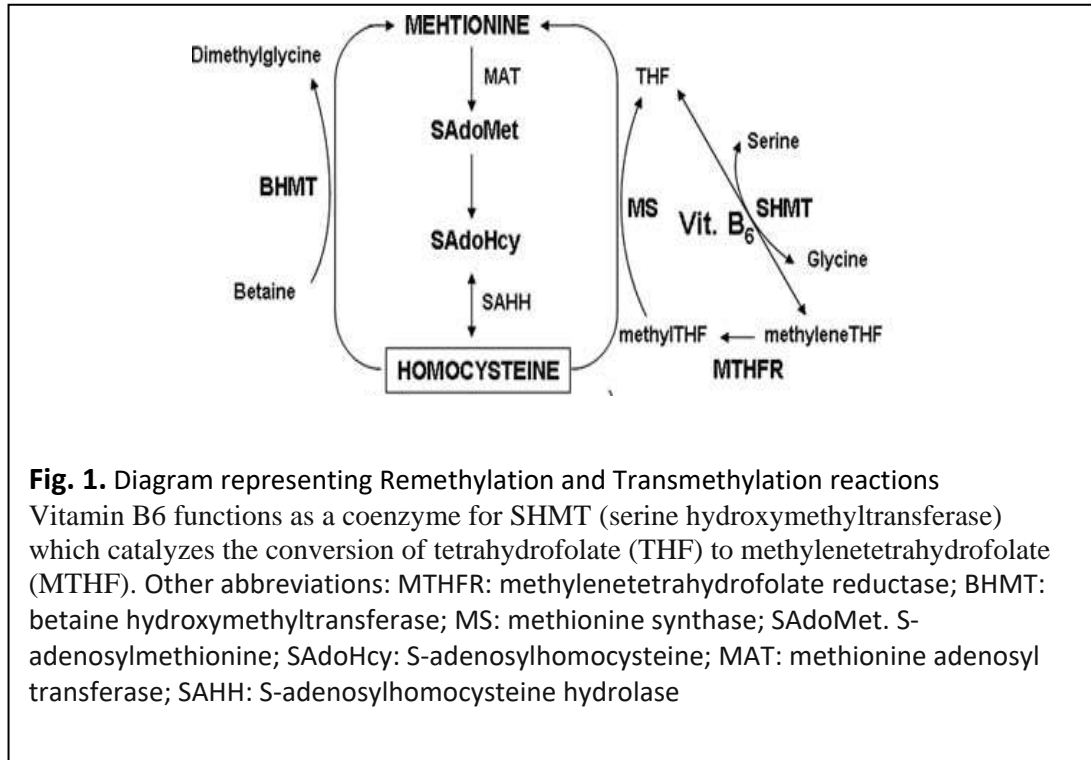
It is known for increasing estrogen levels, which is our primary concern in POI patients. Some studies have shown that brain and heart disorders and some cancers can be developed from long-term B2 deficiency. Riboflavin regulates the circulating level of homocysteine, an amino acid that enters the body from animal protein like meat. High levels in the blood are the risk factor for CVD. It works with other vitamins for homocysteine breakdown. American heart association does not advocate for the use of vitamin B supplements in reducing CVD. But studies have shown that if these vitamins are taken in the proper dosage followed by proper diet and body dynamics, can help reduce CVD. Riboflavin helps in preventing oxidative stress, In the failing heart, oxidative stress occurs in the myocardium and correlates with left ventricular dysfunction. Reactive oxygen species (ROS) negatively affect myocardial calcium handling, cause arrhythmia, and contribute to cardiac remodeling by inducing hypertrophic signaling, apoptosis, and necrosis [6]. It acts as a potent antioxidant. It also lowers blood pressure.

### **Vitamin B6 (Pyridoxine)**

Studies have shown that it too has an estrogen-increasing property. Several studies report an association between low plasma vitamin B6 and a higher risk of cardiovascular disease (CVD) as well as its major thrombotic complication, myocardial infarction. Additional prospective evidence on the role of vitamin B6 in the increased incidence of cardiovascular disease (CVD) was then provided from findings of a nested case-cohort design within the ARIC (The Atherosclerosis Risk in Communities) study. High homocysteine levels in the blood can damage the lining of the arteries. High levels may also make the blood clot more easily than it should. This can increase the risk of blood vessel blockages. A clot inside your blood vessel is called a thrombus. A thrombus can travel in the bloodstream. In an analysis primarily intended to determine whether homocysteine-related

factors including the B6 vitamin are associated with the incidence of CVD, studies show quite strongly an independent role of vitamin B6 as a protective factor in case of adequate levels of the vitamin i.e., B6 helps in reducing homocysteine levels in blood as it acts as co-factor in the transsulfuration pathway. Mentioned below are the two figures that represent the event in homocysteine metabolism homocysteine is an amino acid that is not involved in protein formation. It acts as an intermediate in methionine metabolism. Homocysteine is either converted to cysteine or again back to methionine. It is followed by 3 different pathways named: Transmethylation, Remethylation, and Transsulfuration. A schematic representation of one-carbon metabolism in which vitamin B6 acts as a major player for its functions as a coenzyme in a number of enzymatic reactions. Homocysteine remethylation to methionine is catalyzed by the methionine synthase (MTR) enzyme and links the folate cycle with homocysteine metabolism (Fig. 1).

MTR requires cobalamin (Cbl) as a cofactor, and the resulting complex, Cbl(I)MTR, binds the methyl group of 5-methylTHF to form methylcbl(III)MTR. (Fig. 2). Upon transfer of the methyl group to homocysteine, Cbl(I)MTR is reformed, which can accept another methyl group from 5-methyltetrahydrofolate (5-methylTHF). Cob(I)alamin can also be oxidized to cob(II)alamin, which results in an inactive Cbl(II)MTR complex. [7].



Transsulfuration is an irreversible reaction that converts homocysteine to a less toxic substance called cysteine. Transsulfuration is facilitated by the action of two vitamin B6-dependent enzymes: cystathionine  $\beta$ -synthase (CBS) and cystathionine  $\gamma$ -lyase (CTH). From the above statement, we can say that Vitamin B6 deficiency induces hyperhomocysteinemia through the inhibition of cystathionine- $\beta$ -synthase.

The mechanisms for vitamin B6-related atherogenesis are still poorly understood. Nevertheless, considering the epidemiologic evidence and understanding some of the potentially implicated mechanisms for the relationship between low vitamin B6 and atherosclerotic disease may facilitate, by correcting the vitamin status, the design of potentially easy-to-perform preventive and therapeutic measures.

Other important functions of vitamin B6-related atherogenesis

- Coagulation pathway: Vitamin B6 affects platelet aggregation by inhibiting ADP receptors and prolonging bleeding time, occupancy of glycoprotein IIb/IIIa receptor, or down-regulation of the glycoprotein IIb gene.
- Arterial wall degeneration: Impairment of lysyl oxidase activity by vitamin B6 deficiency induces arterial wall degeneration. Vitamin B6 also inhibits endothelial cell proliferation and induces endothelial dysfunction.
- Cholesterol metabolism: Inhibition of advanced glycation and lipoxidation end-products by Vitamin B6 deficiency induces hypercholesterolemia.
- Fatty acids composition: Vitamin B6 deficiency impairs conversion of linoleic acid to arachidonic acid and the metabolism of n-3 PUFA from alpha-linoleic acid to eicosapentaenoic and docosahexaenoic acid
- Inflammation: Low plasma levels of PLP are inversely related to inflammatory biomarkers such as high-sensitivity C-reactive protein and fibrinogen.

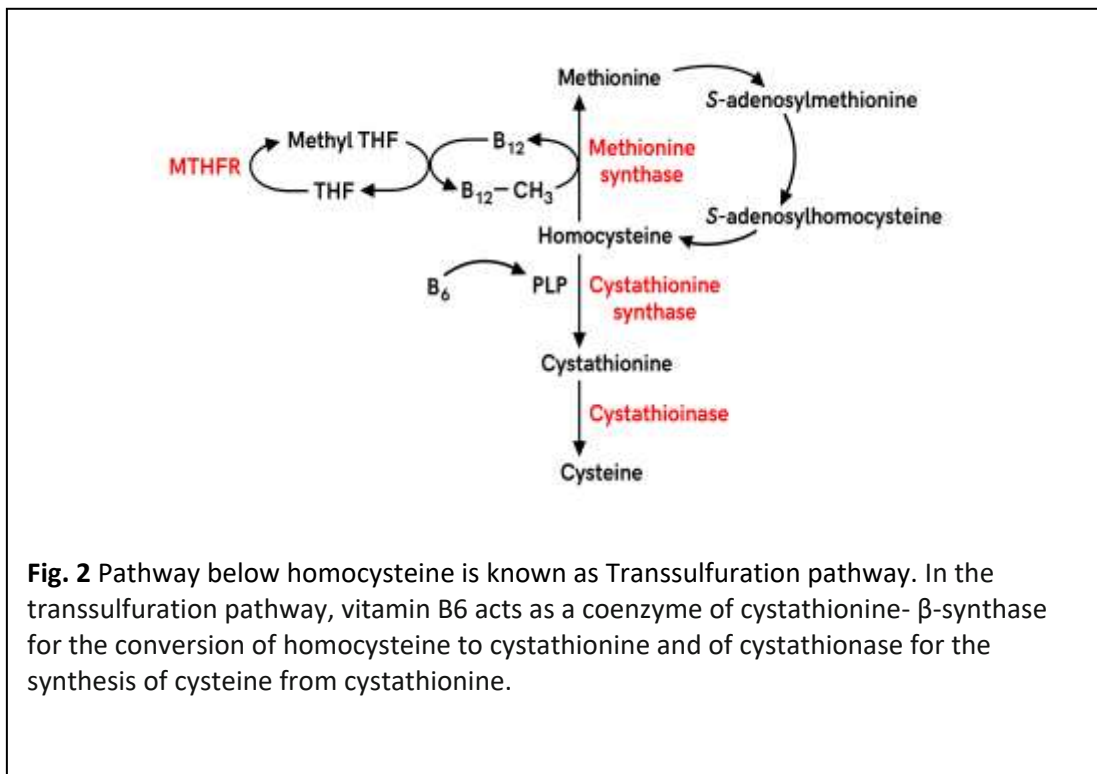


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➤ Immunological function: Vitamin B6 deficiency impairs T lymphocyte and macrophage differentiation and interleukins production.

#### Vitamin B12 (Cobalamin)

Cobalamin is the most important vitamin mostly involved in cardiology and neurological functions. Its deficiency leads to the most common condition known as macrocytic anemia. Vitamin B-12 (cobalamin) plays an essential role in red blood cell formation, cell metabolism, nerve function, and the production of DNA. As mentioned in the above section, vitamin B12 is used in transmethylation reaction in homocysteine metabolism. It is involved with folic acid which is vitamin B9. Studies have shown that B12 reduces heart palpitations. The common side effect of Vitamin B2 is that it causes heart palpitations, the main reason for the inclusion of cobalamin is that it counteracts the side effect of B2. It also shows its activity in Dementia Vitamin B-12 deficiency is associated with dementia and low cognitive function, but it's not clear whether vitamin B-12 supplements might help prevent or treat dementia



**Fig. 2** Pathway below homocysteine is known as Transsulfuration pathway. In the transsulfuration pathway, vitamin B6 acts as a coenzyme of cystathionine-β-synthase for the conversion of homocysteine to cystathionine and of cystathionase for the synthesis of cysteine from cystathionine.

#### Vitamin C (Ascorbic acid)

It naturally increases the blood estrogen level. Vitamin c is known for its powerful antioxidant properties. vitamin C has been shown to improve nitric oxide production of the endothelium, which, in turn, increases vasodilation, reducing blood pressure, hence it is involved in endometrial thickening. Vitamin C supplementation reduces systolic and diastolic pressure. It is well established that vitamin C inhibits the oxidation of LDL-protein, thereby reducing atherosclerosis. High levels of the same result in atherosclerosis, keeping this in mind vitamin B6 has been used to its full potential to counteract the side effects of vitamin C. The requirement for dietary vitamin C is based on its role as an antioxidant and was determined by estimating the quantity of dietary vitamin C needed to maximize its concentration in neutrophils, where it reduces reactive oxygen species produced during phagocytosis [10].

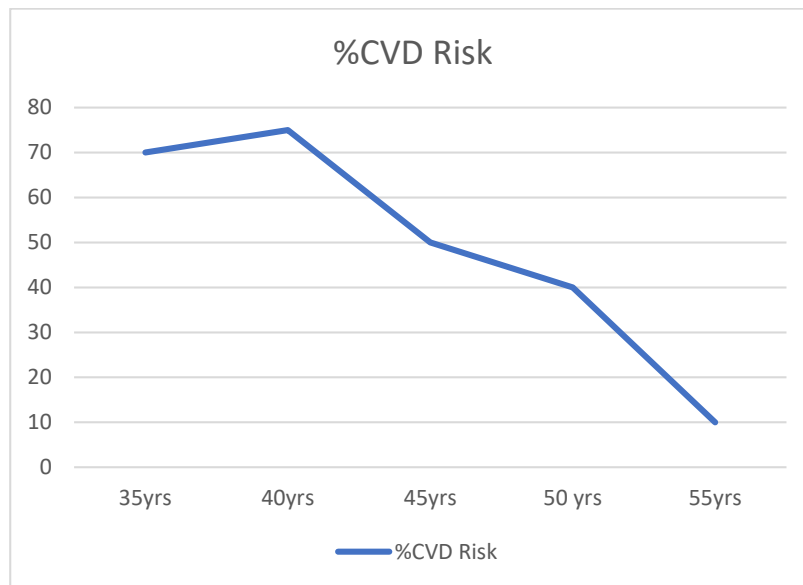
Taking vitamin B-12 with vitamin C might reduce the available amount of vitamin B-12 in your body. To avoid this interaction, take vitamin C two or more hours after taking a vitamin B-12 supplement.

#### CONCLUSION

Women approaching their menopause at age of 38 to 45 years are at higher risk of developing cardiovascular disease. Out of which women at age of 40 are at their peak. These vitamins if taken in

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the proper dosage, can reduce the risk of CVD. Also, increase the estrogen level which is the main concern for patients with premature ovarian insufficiency.



Considering the Side effects of vitamins, some precautionary vitamins were added to avoid further complications. If this vitamin dose is supported by proper physical exercise and a balanced diet it could help reduce CVD risk. This vitamin dose should be considered for 3 to 6 months for better results.

Vitamins B and C should be taken after a few hours to get better results.

### **RECOMMENDATIONS.**

The author's best daily recommended dosage in form of capsules is as follows B2 (400mg), B6 (250mg), B12 (500mcg), and vitamin C (500mg). Also, a high fiber diet is recommended during the vitamin course to avoid constipation. Walking or jogging is also suggested to reduce CVD.

### **ACKNOWLEDGEMENTS**

Extreme gratitude to Alte University for supporting and financing my work. Special thanks to Dr. Yogesh Talekar, Dr. Nino Lochoshvili & Dr. Ketevan Chakhnashvili. Also, I would like to thank my father Dr. Rajesh Patil and mother Vaishali Patil for their constant support and motivation. Finally, I would like to thank my friends who supported me.

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**THROMBOTIC MICROANGIOPATHY SECONDARY TO SOLITARY LYMPHOMA OF THE SPLEEN- A CASE REPORT AND LITERATURE REVIEW**

*Nithesh Hariharan*

*Medical student of Tbilisi State Medical University, Tbilisi, Georgia, US MD program*

**Dr. Irma Tchokhonelidze**

*Professor, Head of Nephrology Department at the Tbilisi State Medical University and Ingorokva High Medical Technology University Clinic, Tbilisi, 0144, Georgia;*

*ORCID NO: 0000-0003-2303-6631*

**ABSTRACT**

Thrombotic microangiopathy is a cluster of clinical syndromes including the formation of microvascular thrombus, microangiopathic haemolytic anemia and end organ damage, usually the kidneys, heart, brain or GI system. Classical causes are TTP, Shiga toxin induced HUS or complement over activation in atypical HUS. However, metastatic cancers, especially to the bone marrow can also result in thrombotic microangiopathy. This is because of abnormal angiogenesis in the marrow with aggressive growth of tumours and secondary myelofibrosis may injure the endothelial cell lining of the marrow vasculature by direct invasion. Damage on endothelium results in release of vWF which causes platelet clumping and formation of clots in small vessels. As RBC goes through clots, it results in haemolysis and formation of schistocytes. This is the case of a 58-year-old man who had splenomegaly due to solitary lymphoma in his spleen and was admitted to the hospital for splenectomy. His total and direct bilirubin were high, thrombocytopenic and had normocytic anemia (Hb- 8). However, splenectomy couldn't be done cause his platelet count was even after 5 days after admission and there was a risk of increased bleeding. He was discharged and 3 days later, re admitted to the hospital cause of diffuse abdominal pain, fever (38.9), chills. Lab reports showed high creatinine (206), anion gap metabolic acidosis, increased lactate, elevated LFT, normocytic anemia with severe thrombocytopenia, increased procalcitonin. CT scan showed massive splenomegaly and colon ischemia. The patient had thrombus formation in renal arteries and mesenteric vessels, resulting in splenic flexure necrosis and sepsis.

**Keywords:** Thrombotic microangiopathy, Lymphoma of the spleen, TTP, atypical HUS, chemo induced thrombotic microangiopathy.

**INTRODUCTION**

Thrombotic microangiopathy (TMA) is cluster of clinical syndromes including the formation of microvascular thrombus, microangiopathic haemolytic anemia, thrombocytopenia, and end organ damage, usually the brain, kidneys, heart, colon or the liver. Thrombotic microangiopathy has some specific findings-

- Coombs negative MAHA, elevated LDH level, undetectable or markedly decrease serum haptoglobin and the presence of schistocytes on a peripheral blood.
- Thrombocytopenia
- Organ injury: kidney disease, neurologic symptoms and gastrointestinal manifestations, amongst others; kidney involvement may include acute kidney injury (AKI), proteinuria or hypertension (HTN).
- Normal coagulation.

The most common causes are Thrombotic Thrombocytopenic Purpura (TTP) and Haemolytic Uremic Syndrome (HUS). TTP is more commonly seen in woman and pathophysiology is due to deficiency of ADAMTS13, a Von Willebrand Factor (vWF) cleaving protease. vWF is secreted by Weibel Palade

Bodies in the endothelium and is responsible for providing glycoprotein Ib receptor site for platelet adhesion and thrombus formation. Classical symptoms include thrombocytopenia, microangiopathic haemolytic anaemia (MAHA), neurologic deficits, such as seizures, hemiplegia and visual disturbances, acute kidney injury, and fever. HUS is commonly seen in children and is caused predominately by Shiga toxin-producing *Escherichia coli* (STEC) infection (serotype O157:H7), which causes profound endothelial dysfunction. People with HUS usually present with thrombocytopenia, MAHA, acute kidney injury and bloody diarrhea. The differentiation of what is the cause of thrombotic microangiopathy is important as management and prognosis is different for different causes. TTP is usually treated with plasma exchange and HUS is usually given palliative and symptomatic care.

The above-mentioned causes are primary causes, where TMA has a definitive cause, either hereditary or acquired. However, in some cases, TMA is secondary manifestation of underlying diseases such as systemic infections, pre-eclampsia, cancer or autoimmune conditions. There has been increasing incidence of TMA as a secondary manifestation in cancer patients. The pathophysiology is multicomplex and more research is being conducted about it. Currently, TMA in cancer patients can be the manifestation of cancer itself or due to chemotherapy. In this case report, we try to find how cancer induced TMA can present and discuss about the different investigations and management in the setting of TMA due to hematologic malignancy.

### **CASE PRESENTATION**

In the end of September (29/09/22), 58-year-old man with solitary lymphoma of the spleen was brought to ER due to diffuse abdominal pain, fever, chills, palpitations, cough, weakness. The patient was hypotensive, nauseous and had dysuria. In the beginning of August, he noticed that he suddenly became dizzy, fatigued and started shaking. He denied any fever. After a couple of days, he started developing severe chills, sweating, productive cough with yellow sputum and shortness of breath. He was diagnosed with pneumonia. However, even after his cough was treated, he had dizziness, fatigue and shortness of breath. He went to his family doctor in the village for an ultrasound and noticed that there was splenomegaly which couldn't be treated there and was advised to visit HTMC.

In the beginning of September, he came to HTMC and was admitted because of severe anemia and shortness of breath on rest. Bone marrow biopsy was done for any malignancy. He was supposed to be admitted only for 3 days, but seeing that his haemoglobin was still low, he was at the hospital until middle of September and was discharged with medications and was asked to come for follow-up. On the day of follow up, his spleen size had not changed and was admitted for splenectomy (on 19/09/22). 1 week later, the patient was discharged as splenectomy could not be done as his platelet count was low (check Table-1 for lab values) and anaemic and there was risk of increased bleeding.

He noticed easy bruising, and pinching sensation on left upper quadrant of the abdomen. He has had a loss of appetite for the past 1 year and has lost 25kg. He has constipation and says it is because of his diet (bread and curd), but denied any change in the colour of his stool and has not noticed any blood, red streaks or clots in his stool. Before the recent hospitalization, he has vomited twice (no food content, yellow, no blood). He finds difficulty in urinating and feels like he did not completely void his bladder. No prostate tests were done. He describes his urine as 'tea coloured' and this started after hospitalization.

He did not have any chronic illness and described himself healthy before this incident. The only medications he used to take were Heptral (Ademetionine) (800mg daily), prednisolone- (3-4 times daily), omeprazole (40mg daily), folic Acid (400mcg). Family history is unremarkable. Social history is relevant for smoking 2 packs of cigarettes every day since school age.

On physical examination, the patient was thin and fatigued, but was oriented and mentating clearly. There was no sign of scleral icterus, but there was conjunctival pallor. Cardiovascular examination was normal. On lung auscultation, mild crackles were heard on right lower lobe and increased work of breathing. Bowel sounds and percussion were normal. The abdomen was tender on palpation, but no signs of rebound tenderness. Liver was palpable below the rib cage. There was marked splenomegaly and it was painful on palpation. There were no rashes on the skin or signs of bruises. There was mild posterior cervical lymphadenopathy (around 1 and half cm).

**Investigations**

**Lab test**

Lab tests were conducted on the patient on the day of admission (29/10/22) and on 19/10/22 (Check Table 1). On analysis of the lab reports of 29/09/22, it is found that the patient has acute inflammation, compensated metabolic acidosis with increased anion gap (lactic acidosis), hyponatremia, hyperkalaemia and increased creatinine. CBC results show acute infection, normocytic anemia and thrombocytopenia. Coagulation studies are normal and liver function test showed signs of acute liver injury. On urinalysis, it is seen that there is increased urobilinogen, proving that there is indirect hyperbilirubinemia and nitrite positive. Procalcitonin level was high.

<i>Lab Test</i>		<b>29/09/22</b>	<b>19/09/22</b>	<b>Normal Range</b>
<i>Inflammatory</i>	CRP (mg/L)	209	150	10
	ESR (mm/hr)	35	22	0-22
	LDH (IU/L)	1850	1450	105-333
<i>ABG</i>	pH	7.42	7.37	7.35-7.45
	pCO <sub>2</sub> (mmHg)	20.8	40	35-45
	pO <sub>2</sub> (mmHg)	105.5	83	80-100
	HCO <sub>3</sub> (mmol/L)	13.2	20	22-26
	Anion Gap (mmol/L)	24.3	15	10-18
	Lactate (mmol/L)	8.22	1.2	1-1.8
	Na <sup>+</sup> (mmol/L)	130.9	137	135-145
	K <sup>+</sup> (mmol/L)	6.59	4.2	3.5-5
	Ca <sup>++</sup> (mmol/L)	1.12	1.23	1.15-1.35
<i>CBC</i>	RBC (x10 <sup>12</sup> /L)	2.56	2.48	3.92 - 5.08
	Haemoglobin g/dL	8.3	9	11.90 - 14.60
	MCV (fl)	87	102	82.90 - 98.00
	WBC(x10 <sup>12</sup> /L)	13.7	10.1	4.49 - 12.69
	Neutrophil differential (10 <sup>9</sup> /L)	9.1	3.38	2.10 - 8.89
	Platelet(10 <sup>9</sup> /L)	50	83	173.00 - 390.00
<i>LFT</i>	Urea (mmol/L)	23.6	(Not done)	2.1-8.5
	Total bilirubin (µmol/L)	81.9	32	2-17
	Direct bilirubin (µmol/L)	65.9	13.5	0-5
	AST (U/L)	283	(Not done)	12-38
	GGT (U/L)	82	(Not done)	5- 40
	Albumin (g/L)	21	(Not done)	35-52
<i>Coagulation study</i>	PT (sec)	14.2	(Not done)	11.00 - 15.00
	a PTT (sec)	27.9	(Not done)	26.00 - 40.00
	Fibrinogen(g/L)	2.16	(Not done)	2.00 - 4.00
<i>Creatinine</i>	(g/L)	206	85	35.00 - 52.00
<i>Urinalysis</i>	Colour	Dark yellow	Dark yellow	yellow
	Nitrite	positive	negative	negative
	Urobilinogen	200+	negative	negative
	Bilirubin	17	negative	negative
	Erythrocyte	300	negative	negative
<i>Procalcitonin</i>		positive	(Not tested)	negative

TABLE 1- Comparison of lab tests that were conducted on 29<sup>th</sup> September 2022 and 19<sup>th</sup> September 2022. Source-High Technology Medical Centre. Abbreviations- CRP- C reactive protein, ESR erythrocyte sedimentation rate, LDH- lactate dehydrogenase, pCO<sub>2</sub>- partial pressure of CO<sub>2</sub>, pO<sub>2</sub>- partial pressure of O<sub>2</sub>, ABG- Arterial Blood Gas, CBC- complete blood count, MCV- mean corpuscular volume, LFT- liver function test, AST- aspartate amino transferase, GGT- Gamma Glutamyl Transferase, PT- prothrombin time, a PTT- activated partial thromboplastin time

**CT scan of the abdomen (Figure 1)**

Spleen was enlarged, 22x8 cm. It was compressing the tail of pancreas, left kidney dislocated medially and compressed due to mass effect. A small amount of liquid in the more lateral grooves in the abdominal cavity was present. The para-aortic is oedematous. The walls of the oblique and sigmoid colon thickened and swollen. The walls of the duodenum are also slightly swollen. Several lymph nodes from small to maximum 13 mm in size are seen periportally. Paraaortically, in the intramesenteric spaces- excess of lymph nodes from small to maximum 12 mm in size is seen. The portal vein is 13 mm. Varicose veins of the spleen. The diameter of the main branch is 21 mm. Visible thrombotic masses passing through the lumen are not show Liver, pancreas, gallbladder, both kidneys and adrenal glands without noteworthy focal-infiltrating changes.



Figure 1- Transverse section of the abdomen showing enlarged spleen and liver. Source- High Technology Medical Centre

**Bone Marrow Biopsy Result**

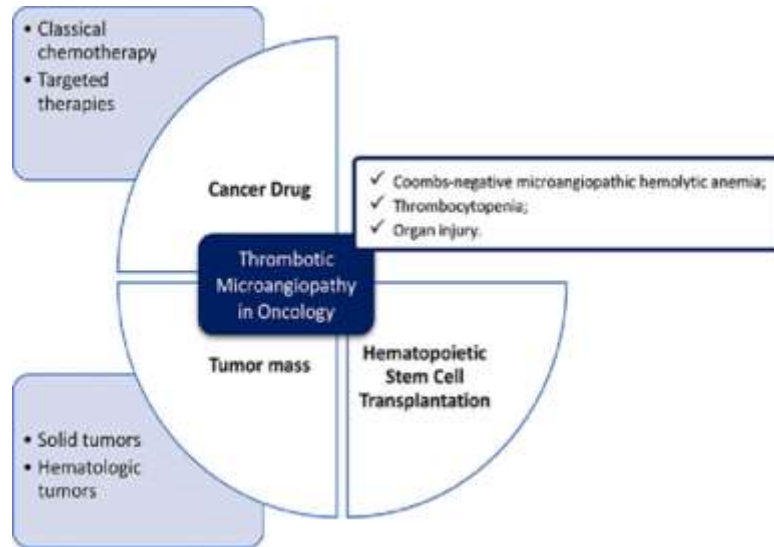
Bone Marrow biopsy was done on his first hospitalization. This is a trephine bone marrow biopsy sample from the iliac bone/crest, without a clinical diagnosis. The bony tissue is represented by trabeculae and bony fragments. Hemopoietic bone marrow with all the 3 blood cell lines is seen in intertrabecular spaces - There are granulocytes (mostly mature forms), megakaryocytes (with normal amounts), and red blood cell lines. On this background lymphocytes (as clusters and individual cells), plasma cells, and a few monocytes, mitotic figures, and small calibre vessels with connective tissue components are visualized.



## DISCUSSION

One of the secondary manifestations of cancer can be TMA. There are 3 possible aetiologies in this situation- due to cancer itself, drug induced or bone marrow transplantation.

**Figure 2-** Causes of TMA in oncology. Source- Microangiopathic Haemolytic Anemia and Thrombocytopenia in Patients with Cancer- Jordan M. Morton, MD, and James N. George, MD



Most commonly, cancer associated TMA is by mucin producing adenocarcinomas with disseminated malignancy or carcinomas with metastasis to lymph nodes and bone marrow. Common incidence is between 0.25 to 0.45 persons per million. There have been multiple postulations on pathophysiology of cancer induced TMA. One of them is that as the tumour metastasize to the bone marrow, abnormal angiogenesis can occur resulting in endothelial damage and myelofibrosis. These can result in destruction of endothelial lining, resulting vast release of vWF and causing diffuse platelet adhesion and thrombus formation. In some studies, it has been shown that patients with cancer have autoantibodies formed against ADAMST13, which decreases the availability of free ADATS13 and increased levels of vWF, mimicking TTP. Also, tumour emboli can cause obstruction of blood vessels and fragmentation of red blood cells as well. Another possible hypothesis is bone marrow necrosis resulting in TMA. This is more commonly seen in hematologic malignancy with Acute lymphoblastic leukaemia (ALL) being the most common cause. Another hypothesis is that cancer cells may also promote the activation of host platelet, leukocyte and endothelial cell coagulation through direct cell-cell contact by specific surface adhesion receptors, by the release of inflammatory cytokines and proangiogenic and growth-stimulating factors, which results in diffuse complement activation. This can result in activation of platelets, leukocytes and endothelial cells which can favours the release of blood-cell procoagulant microparticles and neutrophil extracellular traps.

In this patient who has solitary lymphoma of the spleen, laboratory results have concluded that the patient has MAHA and thrombocytopenia suggesting TMA. Also, the patient has signs of acute kidney and liver injury. From the CT scan, it is seen that there is increased thickening of the walls of splenic flexure. This can possibly be due to ischemia of the bowel due to thrombus formation in the superior mesenteric artery. Another possible reason can be due to the mass effect of the enlarged spleen. Splenomegaly can compress and push the splenic flexure resulting in thickening of the mucosal layer. However, the fact that patient has diffuse abdominal tenderness and fever points towards bowel ischemia than mass effect. Multiple paraaortic and periportal lymph nodes were enlarged, showing signs of disseminated lymphoma. His coagulation panel was normal which indicates that DIC can be ruled out. His procalcitonin level being high indicates sign of sepsis. In this situation, there are 2 possible causes of his sepsis- UTI and bowel necrosis. For this, urine and blood culture are helpful to find the underlying cause. Even though bone marrow biopsy showed no metastasis, other causes such as tumour emboli, damage of endothelium by the tumour, direct activation of platelets by tumour cells are possible.

### **Work Up Plan and Differentials**

Diagnosing cancer induced TMA can be only done based on laboratory and radiologic finding. However, it is essential to differentiate cancer induced TMA and TTP as management varies in both cases. Bone marrow biopsy is essential to look for the evidence of malignancy. Marrow infiltration by metastatic carcinoma or lymphoma may lead to thrombocytopenia and MAHA

It is important to rule out other causes which can mimic TMA. In patients who has thrombocytopenia and is critically ill, disseminated intravascular coagulation (DIC) has to be ruled out. Initial sign of DIC is thrombocytopenia. This is due to dysregulation of coagulation patterns leading to the formation of fibrin clots that causes organ failure with concomitant consumption of platelets and coagulation factors that may result in excessive bleeding. However, in this case, coagulation studies (PT, aPTT) would be increased (in contrast to TMA where coagulation panel is normal). Differentiating cancer induced TMA and primary causes of TMA such as TTP is important as they both have similar presentation, but their management plans are different. Rapid evaluation is needed in order to rule out TTP in acutely ill patients with TMA as prompt initiation of adequate treatment has a critical impact on the outcome. Some ways of differentiating them are –

- Cancer induced MAHA seen at older age (mean age: 56 years) versus those with TTP associated with severe ADAMTS13 deficiency (mean age: 40 years).
- Evidence of active malignancy in those with a history of cancer with systemic symptoms like weight loss, pain, progressive weakness
- Pulmonary involvement is a feature of cancer-associated MAHA.
- Leucoerythroblastic reaction and extreme and extreme elevation of LDH are seen in those with cancer-associated MAHA.
- Cancer induced TMA fails to respond to plasma exchange
- Level of ADAMTS13 is lower in TTP

Chemo drugs can also cause TMA, mainly through acute immune-mediated reaction or dose-dependent toxicity. Common chemo drugs that cause this are oxaliplatin, gemcitabine, 5-fluorouracil, bleomycin, cisplatin, cytosine arabinoside, daunomycin, deoxycoformycin, estramustine, and methyl-CCNU. Also, atypical HUS (a HUS) have to be taken into consideration as well. This is due to overactivation of complement resulting in endothelial damage and release of vWF. Complement-mediated TMA causes microangiopathic haemolytic anemia and thrombocytopenia as well. These clinical features do not help in distinguishing complement-mediated TMA from either cancer-induced TMA or drug-induced TMA. Complement-mediated TMA can only be diagnosed when all other aetiologies of TMA, including cancer and drugs, are excluded. Kidney biopsy is useful to diagnose atypical TMA. Biopsy results show glomerular endothelial cell swelling, and tubular injury with interstitial fibrosis.

### **Management**

It is important to identify the cause of TMA as different causes have different management plans. Some studies have shown that it is recommended to start plasmapheresis or plasma exchange (PEX) until ADAMTS13 activity is known unless an alternative diagnosis is clear. PEX replaces patient plasma with donor plasma, allowing the removal of potential endothelial damaging agents or autoantibodies, and the replacement of certain molecules essential for endothelial function, such as ADAMTS13. This is important when the diagnosis is TTP. However, some studies have shown that if the diagnosis is not TTP, then plasmapheresis should be contraindicated. According to some documentations of the patients from Oklahoma Registry, since 1996, it is seen that in 342 patients, there have been seven deaths (2%) four caused by complications of central venous catheter insertion and three caused by sepsis related to the central venous catheter. Nonfatal complications have included 31 patients with bacteraemia, seven with catheter-related venous thrombosis requiring systemic anticoagulation, and one with pericardial tamponade caused by the catheter guide wire perforating the right ventricle

However, plasmapheresis or PEX is not beneficial in cancer induced TMA. The prognosis of patients with cancer TMA is usually extremely poor due to disseminated cancer but specific anticancer therapies

should be indicated whenever possible. Platelet infusion can be given to treat thrombocytopenia, but this is debatable since some cases have shown increased platelet aggregation after platelet transfusion. In drug induced TMA, withdrawal of the drug is the first step, followed by plasmapheresis.

## **CONCLUSION**

Cancer induced TMA is still one of the topics where more research has to be done to find exact mechanism. When a patient with history of cancer comes with thrombocytopenia, cancer induced TMA as well as drug induced TMA has to be evaluated. This can be proven with bone marrow biopsy result. Other causes of TMA (TTP, HUS, a HUS) has to be ruled out. Early chemotherapy for systemic malignancy has to be initiated to prevent TMA.

## **HUMAN ETHICS**

As the name, surname, or any other personal information has not been presented, consent was not necessary.

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**კორტიკოსტეროიდული თერაპიის როლი მწვავე პანკრეატიტის მკურნალობასა და გართულებების პრევენციაში**

**გიორგი ასათიანი (Giorgi Asatiani)**

თსუ მედიცინის ფაკულტეტის ქირურგიის დეპარტამენტის პროფესორი

**მამუკა გურგენიძე (Mamuka Gurgენidze)**

თსუ მედიცინის და სტომატოლოგიის საერთაშორისო ფაკულტეტის ქირურგიის დეპარტამენტის ასისტენტ-პროფესორი  
მეცნიერების დარგი - მედიცინა

**რობერტი ავალიშვილი (Robert Avalishvili)**

თსუ მედიცინის ფაკულტეტის ქირურგიის დეპარტამენტის რეზიდენტი

### **პროგრამაში წარმოდგენილი საკითხის თანამედროვე მდგომარეობა**

მწვავე პანკრეატიტის სიხშირისა და დაავადებასთან დაკავშირებული გართულებების სიმრავლის გამო, აღნიშნული დაავადების მკურნალობაში ახალი გზების ძიება კვლავ მნიშვნელოვან საკითხს წარმოადგენს თანამედროვე სამედიცინო საზოგადოებაში. წლების განმავლობაში, მწვავე პანკრეატიტის მკურნალობაში, მეცნიერების მიერ შესწავლილი და გამოყენებული იქნა მრავალი მედიკამენტი, მათ შორის ციმეტიდინი, ატროპინი, გლუკაგონი, სომატოსტატინის ანალოგები, აპროტინინი, ფოსფოლიპაზას ინჰიბიტორები [30, 8, 12, 31, 18, 47], თუმცა ვერცერთმა მათგანმა ვერ მიაღწია სასურველ შედეგს. უკანასკნელ წლებში, აქტიურად მიმდინარეობს საუბარი კორტიკოსტეროიდული თერაპიის როლზე და მის ეფექტურობაზე პანკრეასის ანთებითი დაავადების წინააღმდეგ ბრძოლაში. ლიტერატურაში არსებული ცნობების თანახმად, აღნიშნული თერაპია მნიშვნელოვნად აუმჯობესებს დაავადების მიმდინარეობასა და გამოსავალს ცხოველებში [44, 54], თუმცა ადამიანებზე ჩატარებული კვლევები მეტად მწირია, წარმოადგენს მხოლოდ ვარაუდებს და აუცილებლად საჭიროებს ღრმა მეცნიერულ მტკიცებულებებს [39].

### **კვლევის აქტუალობა და სამეცნიერო სიახლის არგუმენტაცია**

მწვავე პანკრეატიტი და მისი დიაგნოსტიკის, მკურნალობისა და გართულებათა პრევენციის სხვადასხვა დეტალი კვლავ რჩება მიმდინარე კამათის საგნად მსოფლიოს თანამედროვე ლიტერატურაში. აღნიშნული დაავადება, მიუხედავად მრავალწლიანი ცოდნისა და გამოცდილებისა, არ კარგავს აქტუალობას. მთელს მსოფლიოში, უკანასკნელი ორი ათწლეულის განმავლობაში, მწვავე პანკრეატიტის შემთხვევათა რაოდენობამ მკვეთრად მოიმატა, მეტიც, ეს ტენდენცია დღესაც მზარდია [3]. მწვავე პანკრეატიტი გაერთიანებულ სამეფოში ყოველი 100,000 მოსახლიდან დაახლოებით 56 ადამიანს უდასტურდება [35], ხოლო ამერიკის შეერთებულ შტატებში, აღნიშნული დაავადებით ყოველი წლიურად 220.000 მეტი ადამიანი ხვდება ჰოსპიტალში [49]. ეპიდემიოლოგიური კვლევით დადგინდა, რომ ინგლისსა და ევროპის მასშტაბით მზარდია ყველა ეტიოლოგიური ფაქტორით განვითარებული მწვავე პანკრეატიტი. აღნიშნული ადასტურებს, რომ მწვავე პანკრეატიტი არის საჭმლის მომნელებელი ტრაქტის დაავადებათა შორის ერთ-ერთი ყველაზე გავრცელებული ნოზოლოგია. აღსანიშნავია, რომ დაავადების სიხშირის ზრდა დაკავშირებულია ასაკთან და სქესთან [50]. მდებარეობით

სქესთან შედარებით, მამრობითი სქესის პოპულაციაში დაავადების სიხშირე 10-30%-ით მაღალია [45]. პაციენტთა უმრავლესობაში დაავადება მიმდინარეობს მსუბუქად, თუმცა დაახლოებით 10-20%-ში, ანთების საპასუხო რეაქციის განვითარება განაპირობებს მის სწრაფად პროგრესირებას, რაც თავის მხრივ იწვევს საწოლ-დღეების ზრდას, მეტ გართულებებსა და სიკვდილობას. სიკვდილიანობისა და გართულებების მაჩვენებელი ნაკლებად მძიმე პანკრეატიტების დროს არ აღემატება 1%-ს [3], თუმცა მძიმე შემთხვევებში ის შესაძლოა მერყეობდეს 10%-50%-მდე [3]. მწვავე პანკრეატიტების დროს სიკვდილიანობა გამოწვეულია სხვადასხვა მიზეზით. პირველი კვირის განმავლობაში (ადრეული ფაზა) პანკრეასის ანთება განაპირობებს ანთებითი კასკადის ჩართვას, შემდგომი პოლიორგანული უკმარისობის განვითარებით. სიკვდილიანობა ორი კვირის შემდეგ (მოგვიანებითი ფაზა), უმეტესად გამოწვეულია სეფსისის განვითარებით [3]. მიუხედავად მრავალწლიანი გამოცდილებით შემუშავებული სტანდარტული თერაპიული მიდგომებისა, როგორცაა ანტიბიოტიკოთერაპია, ადრეული ენტერალური კვება, ადექვატური ქსოვილოვანი პერფუზია, ელექტროლიტების დისბალანსის კორექცია და სხვა, მწვავე პანკრეატიტი 20%-ში პროგრესირებს და ვითარდება ზემოხსენებული სისტემური ანთების საპასუხო რეაქცია შემდგომი შოკითა და პოლიორგანული უკმარისობის განვითარებით [40, 42].

მწვავე პანკრეატიტის მკურნალობის ტაქტიკის გასამჯობესებლად ახალი გზების ძიება კვლავ წარმოადგენს რთულ ამოცანას. აღნიშნული დაავადების სამკურნალოდ და გართულებების პრევენციისათვის, სხვადასხვა ტაქტიკური ვარიანტების გამოყენების შესახებ მსოფლიო ლიტერატურაში აზრთა სხვადასხვაობაა. მკურნალობის სქემები ხშირად ცვალებადია, რაც განპირობებულია დაავადების მრავალფეროვანი ეტიოლოგიით, სხვადასხვა კლასიფიკაციის არსებობითა და დაავადების სიმძიმის შესაფასებელი ერთიანი კრიტერიუმის არარსებობით. შედეგად წარმოქმნება დაგვიანებული დიაგნოსტიკების, არაადექვატური ქირურგიული ჩარევის და/ან ჩარევისაგან გაუმართლებელი თავის შეკავების პრობლემა, რასაც ხშირად მივყავართ არაკეთილსაიმედო გამოსავლამდე. გამომდინარე აქედან, მწვავე პანკრეატიტის მკურნალობის ხარისხის გაუმჯობესების გზები უნდა ვეძებოთ ორგანიზმში მიმდინარე პათომორფოლოგიური თუ ფუნქციური ცვლილებების დეტალიზაციაში და დაავადების სხვადასხვა ეტაპზე ეტიო-პათოგენეზური მკურნალობის არგუმენტირებული ტაქტიკის შერჩევაში. მწვავე პანკრეატიტს, როგორც პრობლემას, კლინიკური და ექსპერიმენტული კვლევისთვის მიმზიდველობასა და აქტუალობას მატებს გამომწვევ ფაქტორთა მრავალფეროვნება, დაავადების არამკაფიო პათოგენეზი, პოლიორგანული დაზიანებათა ფართო სპექტრი. აღნიშნული ნათლად მიუთითებს ახალი მეთოდების დანერგვის საჭიროებაზე. სწორედ ამ მიზეზებმა განაპირობა მოცემული თემით ჩვენი დაინტერესება. შრომაში პირველად, სხვადასხვა ინსტრუმენტულ და ლაბორატორიულ კვლევათა კრიტერიუმების საფუძველზე შეფასებული იქნება გლუკოკორტიკოიდული თერაპიის ეფექტურობა მწვავე პანკრეატიტის მკურნალობასა და გართულებების პრევენციაში.

პაციენტთა დაახლოებით 20%-ში მწვავე პანკრეატიტი პროგრესირებს და მისი დაწყებიდან 72 სთ-ის განმავლობაში, ვითარდება სისტემური ანთებითი პასუხის სინდრომი შემდგომი შოკითა და პოლიორგანული უკმარისობით [5, 22, 40]. სისტემური ანთებითი პასუხის სინდრომი არის ორგანიზმის დაცვითი რეაქცია სხვადასხვა პროანთებითი მედიატორების, თრომბოციტების აქტივაციის ფაქტორის, ნიტრიტის ოქსიდის აქტივაციის საპასუხოდ. მოციკულირე ციტოკინები, როგორებიცაა სიმსივნის ნეკროზული ფაქტორი- $\alpha$  (TNF-  $\alpha$ ), ინტერლეიკინი (IL), ფოსფოლიპაზა A2 (PLA-2), თამაშობენ უმთავრეს როლს ანთებითი პროცესის პროგრესირებასა და სისტემატიზაციაში. აქტიურდება ვასკულარული ენდოთელიუმი, იზრდება კაპილარული განვალადობა, რაც ახდენს ლეიკოციტების ქსოვილიდან სისტემურ მიმოქცევაში მიგრაციის პროვოცირებას [32, 26].

გლუკოკორტიკოიდები წარმოადგენს ანთების დამთრგუნველ მედიკამენტთა ჯგუფს, რომელთაც გააჩნიათ ფართო სპექტრის ანთების საწინააღმდეგო ეფექტი. დღესდღეობით, კარგადაა შესწავლილი გლუკოკორტიკოსტეროიდების ეფექტურობა იმ დაავადებებთან მიმართებაში, როგორებიცაა ასთმა, ფილტვების ქრონიკული ობსტრუქციული დაავადება, სისტემური ვასკულიტები და სხვა. აღნიშნული თერაპია წარმატებით გამოიყენება სხვადასხვა ტიპის ანთებითი პროცესების დროს, როგორებიცაა სეფსისი, პნევმონია, დამწვრობა, მწვავე რესპირატორული დისტრეს სიდრომი [1, 9, 16, 11, 29, 54]. ბოლო ათწლეულების განმავლობაში შესწავლის საგანს წარმოადგენს, გლუკოკორტიკოსტერიოიდული თერაპიის როლი მწვავე პანკრეატიტების მკურნალობაში [43]. ცხოველებში, მწვავე პანკრეატიტების მკურნალობაში სტეროიდებმა გამოავლინეს განსაკუთრებულად მაღალი ეფექტურობა [44, 54].

ციკლოოქსიგენაზა-2 (COX-2) არის მაღალადაპტაციური ფერმენტი, რომელიც ხელს უწყობს ანთებითი პროცესის გაღრმავებას. ის დაუყოვნებლივ, დიდი რაოდენობით აკუმულირდება ანთებითი პროცესის ადგილას [48]. რამდენიმე კვლევამ ცხადყო, რომ COX-2-ის ინჰიბიტორებმა შესაძლოა ხელი შეუშალოს მწვავე პანკრეატიტის განვითარებას [17]. COX-2-ის ინჰიბიტორები აბლოკირებენ პროსტაგლანდინების სინთეზას არაქიდონის მჟავასაგან შემდგომი ანთების საწინააღმდეგო ეფექტის განვითარებით [6]. თავისი ანტიანთებითი ეფექტის გამო, გლუკოკორტიკოსტეროიდები მნიშვნელოვნად თრგუნავენ COX-2 ის პროდუქციას [51]. აღნიშნული თეორია ნათლად მიუთითებს მწვავე პანკრეატიტის მკურნალობაში გლუკოკორტიკოსტეროიდების შესაძლო, პოტენციურად დადებით ეფექტზე.

პანკრეატიტთან ასოცირებული პროტეინი (PAP) არის ცილა, რომელიც არ გვხვდება ნორმალური პანკრეასის პარენქიმაში, თუმცა მისი რაოდენობა მკვეთრად იმატებს საშუალოდ მძიმე და მძიმე პანკრეატიტების დროს [20, 24, 36]. სხვა მრავალ ფუნქციასთან ერთად, PAP - ს გააჩნია ანტიბაქტერიული, ანტიაპოპტოზური და მიტოგენური ეფექტი. კვლევების თანახმად, PAP თრგუნავს მწვავე ფაზის ციტოკინების გენის ექსპრესიას, რითაც დაავადების მიმდინარეობისას ასრულებს დამცველობით როლს [23]. ერთ-ერთმა კვლევამ ცხადყო, რომ დექსამეტაზონით მკურნალობამ მნიშვნელოვნად შეამცირა როგორც ლოკალური, ასევე სისტემური ანთებითი პარამეტრები, რაც დაკავშირებულია PAP ექსპრესიის up-რეგულაციასთან [38]. შესაბამისად, მიზანშეწონილად მიგვაჩნია, რომ კორტიკოსტეროიდული თერაპიის როლის შესწავლა, ფრიად პრესპექტიულ მიმართულებას წარმოადგენს და მნიშვნელოვნად დადებით გავლენას იქონიებს მწვავე პანკრეატიტების მკურნალობასა და გართულებების პრევენციაში.

### **საკითხის ირგვლივ არსებული სამეცნიერო ლიტერატურის მიმოხილვა**

თემის ირგვლივ არსებული მაღალი ინტერესისა და ჩატარებული კვლევების მიუხედავად, მწვავე პანკრეატიტების მკურნალობასა და გართულებების პრევენციაში კორტიკოსტეროიდული თერაპიის ეფექტურობა ჯერ კიდევ მსჯელობის საგანს წარმოადგენს. აღნიშნულ საკითხზე საბოლოო კონსენსუსი არ არსებობს. 2006 წლის ნოემბერში ამერიკის ჯანმრთელობის ნაციონალური ინსტიტუტის მიერ ჟურნალში „World Journal of Gastroenterology“ გამოქვეყნდა სტატია [13], სადაც გამოითქვა ვარაუდი, რომ დექსამეტაზონით თერაპია მნიშვნელოვან დამცველობით როლს ასრულებს მწვავე პანკრეატიტების მკურნალობაში. აღნიშნული თერაპია იწვევს PAP ცილის ექსპრესიის გაზრდას, რის შედეგადაც მნიშვნელოვნად მცირდება მწვავე პანკრეატიტის სიმძიმის ხარისხი [23].

PAP არის სტრეს ცილა, რომელიც ნორმალური პანკრეასის ქსოვილში არ გვხვდება. მისი რაოდენობა მკვეთრად იმატებს ანთებითი პროცესის დაწყებიდან 6 საათის განმავლობაში

და პიკს აღწევს 48 საათში [52, 20]. ადამიანებსა და ვირთაგვებში აღმოჩენილია PAP გენის სამი იზოფორმა (PAP1, PAP2, PAP3) [19, 20, 27, 21]. PAP-1 იზოფორმას გააჩნია ბაქტერიების შებოჭვის უნარი. შესაბამისად, აღნიშნული ანტიბაქტერიული ეფექტის გამო იგი მნიშვნელოვან დამცველობით როლს თამაშობს მწვავე პანკრეატიტის ინფექციური გართულებების წინააღმდეგ მიმართულ პროცესში [21]. აღსანიშნავია, PAP-ის ანტიაპოპტოზური ეფექტი. ანთებითი პროცესის დროს, თავისუფალი რადიკალებისა და ანთებითი ციტოკინების გამომუშავება იწვევს PAP-ის up-რეგულაციას, აღნიშნული პროტეინის ექსპრესიის მატება, მნიშვნელოვნად ზრდის პანკრეასის უჯრედულ რეზისტენტობას აპოპტოზის წინააღმდეგ [37]. გარდა ამისა, PAP-ს გააჩნია მიტოგენური ეფექტი პანკრეასული წარმოშობის უჯრედების მიმართ. ანთებითი პროცესის საპასუხოდ იზრდება აღნიშნული პროტეინის ექსპრესია. შედეგად, მატულობს პანკრეასის უჯრედების პროლიფერაცია [52]. კვლევის შედეგად ასევე ირკვევა, რომ PAP - ის down-რეგულაცია და ცილის რაოდენობის შემცირება, მკვეთრად აუარესებს მწვავე პანკრეატიტის მიმდინარეობას [53].

ერთ-ერთ კვლევაში ცხოველების დაყოფა მოხდა 2 ჯგუფად. პირველ ჯგუფში მკურნალობა ჩატარდა დექსამეტაზონით, ხოლო მეორე ჯგუფში ფიზიოლოგიური ხსნარით. შედეგების მიხედვით დადგინდა, რომ მეორე ჯგუფთან შედარებით, პირველ ჯგუფში მკვეთრად გაიზარდა PAP - ის სამივე იზოფორმის ექსპრესია [14] და მკვეთრად დაბალი აღმოჩნდა შრატის ამილაზას დონე [25]. ჰისტომორფოლოგიური კვლევის საფუძველზე დადგინდა, რომ ცხოველებში, რომელთაც დექსამეტაზონით ჩაუტარდათ მკურნალობა, პანკრეასის ანთებითი და ნეკროზული ცვლილებები ნაკლებად აღინიშნებოდა [52].

ბოლონიაში, Orsola-Malpighi-ს უნივერსიტეტის მიერ ჟურნალ „Journal of the Pancreas-ში“ გამოქვეყნდა სტატია [39], სადაც შესწავლილ იქნა ენდოგენური გლუკოკორტიკოიდების მეტაბოლიზმისა და მასში შემავალი თითოეული კომპონენტის (საერთო და თავისუფალი კორტიზოლი, კორტიკოსტეროიდებთან დაკავშირებული გლობულინი, ადრენოკორტიკოტროპული ჰორმონი) ცვლილება და მათი მოქმედების გავლენა პანკრეასის ანთებითი პროცესის მიმდინარეობაში. კვლევაში ყურადღება გამახვილდა მწვავე პანკრეატიტის დროს მიმდინარე ისეთ ცვლილებებზე, როგორებიცაა სისტემური ანთებითი პასუხის სინდრომი, პოლიორგანული უკმარისობა, ანთებითი მარკერების მნიშვნელოვანი მატება (C-რეაქტიული ცილა, პროკალციტონინი, ალფა-1 ანტიტრიფსინი, TNF-  $\alpha$ , PLA-2) [7, 46, 33]. დაისვა კითხვა, თუ არსებობს კავშირი აღნიშნულ ცვლილებებსა და პანკრეასის ნეკროზის განვითარებას შორის [34]. კვლევით დადგინდა, რომ ანთებითი პროცესის საწყის ეტაპზე, ადრენოკორტიკოტროპული ჰორმონისა და კორტიკოსტეროიდებთან დაკავშირებული გლობულინის დაკლებული დონეებისაგან განსხვავებით, მნიშვნელოვნად მოიმატა საერთო და თავისუფალი კორტიზოლის მაჩვენებლებმა. რუტინული შეფასებით გაირკვა, რომ ყოველდღიურად მატულობდა ადრენოკორტიკოტროპული ჰორმონის დონე. აღნიშნულის საპასუხოდ აგრეთვე მზარდი იყო კორტიზოლის მაჩვენებელი. კორტიზოლის კლების ტენდენცია შეინიშნა პანკრეასის ნეკროზული ცვლილებების დროს. ჰიპოთეზის თანახმად, კორტიზოლთან დაკავშირებული გლობულინის დონის კლება განაპირობებელია თირკმელზედა ჯირკვლის შედარებითი უკმარისობით, რაც ხელსაყრელ გარემოს ქმნის აცინური უჯრედების აპოპტოზისა და ნეკროზული ცვლილებების განვითარებისათვის [24]. ავტორების მიერ, აღნიშნულ კვლევაზე დაყრდნობით, გამოითქვა ვარაუდი, რომ ჰიდროკორტიზონით ადრეული მოკლევადიანი თერაპია ახდენს სისტემური ანთებითი პასუხის სინდრომისა და პანკრეასის ნეკროზული ცვლილებების განვითარების პრევენციას. კორტიკოსტეროიდების ზემოქმედებით მნიშვნელოვნად ითრგუნება ანთებითი მარკერების წარმოქმნა [43].



1997 წელს Lazar and colleagues მიერ, ვირთაგეგმზე ჩატარებული ცდებით დადასტურდა, რომ კორტიკოსტეროიდული თერაპიის შემდეგ მნიშვნელოვნად შემცირდა IL-6 – ის დონე. კორტიკოსტეროიდები ზრდიან სელექტიური პროტეაზების ინჰიბიტორების აქტივობას, რის შედეგადაც, ირიბად იწვევენ PLA-2 - ის ინჰიბირებას [28, 4]. მწვავე პანკრეატიტების დროს იზრდება ლეიკოციტების მიგრაცია პანკრეასის პარენქიმაში [10]. ცხოველთა მოდელებზე ჩატარებულ ექსპერიმენტულ კვლევებში დადასტურდა, რომ სტეროიდებით თერაპიამ, ლეიკოციტების აქტივაციის დათრგუნვის ხარჯზე შეამსუბუქა აღნიშნული პროცესი [28].

განვითარება. ჰიპოვოლემიური მდგომარეობის დროს მნიშვნელოვნად მცირდება პანკრეასის წვენის, ბიკარბონატებისა და ენზიმების სეკრეცია. გახანგძლივებული ჰიპოვოლემიური სტატუსის დროს, პანკრეასის წვენისა და ბიკარბონატების მაჩვენებელი კიდევ უფრო იკლებს, რაც თავის მხრივ იწვევს პანკრეასის აცინური და სადინრის უჯრედების დაზიანებას [2], ხოლო შრატის ამილაზას დონე მატულობს, რადგან ამილაზა, პანკრეასის დაზიანებული უჯრედული მემბრანიდან, პირდაპირ გადადის სისხლში. ცხოველებზე ჩატარებული ექსპერიმენტული კვლევით დადგინდა, რომ ჰიპოვოლემიური სტატუსის პირობებში საკონტროლო ჯგუფთან შედარებით, ექსპერიმენტულ ჯგუფში გლუკოკორტიკოიდული თერაპიის შემდეგ, ამილაზას დონე იყო მკვეთრად დაბალი [15]. შედეგად, გამოთქმულ იქნა ვარაუდი, რომ ჰიპოვოლემიური სტატუსის დროს, კორტიკოსტეროიდული თერაპია მნიშვნელოვნად ამცირებს ამილაზას პროდუქციას და იცავს აცინურ და პანკრეასის სადინრის უჯრედებს დაზიანებისაგან [41].

ლიტერატურაში იშვიათად თუ მოიპოვება ცნობები მწვავე პანკრეატიტის მქონე ადამიანებში კორტიკოსტეროიდული თერაპიის ეფექტურობის შესახებ. 2004 წლის მაისში „Journal of the Pancreas“-ში გამოქვეყნდა სტატია, სადაც ნათლადაა ასახული, რომ ადამიანებში დექსამეტაზონით ჩატარებული თერაპია მნიშვნელოვნად ამცირებს სხვადასხვა ანთებითი მედიატორის წარმოქმნას და აუმჯობესებს მწვავე პანკრეატიტის პროგნოზულ მაჩვენებელს [48]. კვლევაში ჩართული იყო 32 პაციენტი, რომელთა საშუალო ასაკი მერყეობდა 26-63 წლის ფარგლებში. თითოეული მათგანის მკურნალობა დაიწყო სიმპტომების დაწყებიდან 8 სთ-დან 4 დღემდე პერიოდის განმავლობაში. რუტინული მკურნალობის გარდა, პაციენტებს ყოველდღიურად, 3-5 დღის განმავლობაში უტარდებოდათ დექსამეტაზონით მკურნალობა საშუალოდ 0,5-1,0მგ /კგ დოზით. შედეგად, პაციენტთა ნაწილს (27 პაციენტი) მკურნალობის დაწყებიდან 4-8 სთ-ის შემდეგ შეუმსუბუქდა ტკივილი და მნიშვნელოვნად გაუმჯობესდა მათი ზოგადი მდგომარეობა. მიუხედავად იმისა, რომ 5 პაციენტის მდგომარეობა გაუარესდა და საჭირო გახდა ქირურგიული ჩარევა (ნეკრექტომია), დექსამეტაზონით მკურნალობის ფონზე მნიშვნელოვნად შემცირდა ანთებითი მედიატორების პროდუქცია (TNF- $\alpha$ , IL-1, IL-6, IL-8, პროსტაგლანდინები). შედეგად, მნიშვნელოვნად გაუმჯობესდა მწვავე პანკრეატიტის მიმდინარეობა და გამოსავალი [49].

### **კვლევის მიზანი და ამოცანები**

სხვადასხვა ფორმის, სიმძიმის მქონე მწვავე პანკრეატიტების მკურნალობასა და გართულებების პრევენციაში კორტიკოსტეროიდული თერაპიის როლისა და ეფექტურობის შესწავლა.

აღნიშნული მიზნის მისაღწევად დასახულ იქნა შემდეგი ამოცანები:

1. კორტიკოსტეროიდული თერაპიის ფონზე PAP– ის რაოდენობრივი შეფასება;
2. მწვავე პანკრეატიტის საშუალოდ მძიმე და მძიმე ფორმის მქონე პაციენტებისგან კორტიკოსტეროიდული და რუტინული თერაპიის ორი, ექსპერიმენტული და

საკონტროლო ჯგუფის შექმნა და მათი რადიოლოგიური მონაცემების შედარება;

3. ლაბორატორიული მაჩვენებლების - შრატის ლიპაზის, IL-6 - ის, სისხლის საერთო ანალიზის (ლეიკოციტოზი, ლეიკოციტური ფორმულის მარცხნივ გადახრის ხარისხი), CRP-ს, პროკალციტონინის, მჟავა-ტუტოვანი წონასწორობის ხარისხის ცვლილებების შედარება ექსპერიმენტულ და საკონტროლო ჯგუფში;

4. ჰოსპიტალიზაციის დროისა და ფინანსური ეფექტის შედარება ექსპერიმენტულ და საკონტროლო ჯგუფებს შორის;

5. რენიმაციაში გატარებული საწოლ-დღეების, საერთო საწოლ-დღეების, დაავადების რეციდივების (1 წლის განმავლობაში) რაოდენობის შედარება ექსპერიმენტულ და საკონტროლო ჯგუფში.

**გამოკვლევის მოსალოდნელი შედეგების თეორიული და პრაქტიკული ღირებულება**

1) შეფასდება გლუკოკორტიკოსტეროიდული თერაპიის როლი საშუალოდ მძიმე და მძიმე მწვავე პანკრეატიტის მკურნალობასა და გართულებების პრევენციაში;

2) შეფასდება გლუკოკორტიკოიდული თერაპიის ფონზე განვითარებული PAP-ის რაოდენობრივი მახასიათებლის ცვლილება. დასაშვებია, რომ აღნიშნულმა კორელაციამ მნიშვნელოვნად დადებითი ცვლილებები შეიტანოს მწვავე პანკრეატიტის მკურნალობაში;

3) განისაზღვრება ანთებითი მარკერების (IL-6, შრატის ლიპაზა, ლეიკოციტოზი, ლეიკოციტური ფორმულის მარცხნივ გადახრის ხარისხი, CRP, პროკალციტონინი, მჟავა-ტუტოვანი წონასწორობა), ცვლილებები გლუკოკორტიკოიდული თერაპიის შემთხვევაში და მის გარეშე, რაც ასევე დაადასტურებს ჰორმონთერაპიის დადებით როლს მწვავე პანკრეატიტის მკურნალობაში.

ყოველივე აღნიშნულის დადასტურების შემთხვევაში, შესაძლებელი იქნება გლუკოკორტიკოიდული თერაპიის რუტინული დანერგვა მწვავე პანკრეატიტების მკურნალობაში, რაც რეალურად იქნება ღირებული სიახლე და ექნება მაღალი პრაქტიკული ღირებულება.

**კვლევის მასალა და მეთოდები**

ჩატარდება პროსპექტული, რანდომიზებული კვლევა მულტიცენტრული კლინიკების ბაზაზე. შეირჩევა ნებისმიერი ეტიოლოგიით გამოწვეული საშუალო და მძიმე პანკრეატიტის მქონე პაციენტები, რომელთა ასაკი იქნება 18 წლიდან. დაავადების კლასიფიკაციისა და სიმძიმის შესაფასებლად გამოყენებულ იქნება, ატლანტას რევიზირებული კლასიფიკაცია, რომელიც წარმოადგენს ატლანტაში 1992 წელს გასტროენტეროლოგთა საერთაშორისო კონგრესსზე მიღებული ვარიანტის მოდიფიკაციას.

კვლევაში მონაწილეობას არ მიიღებენ ორსულები და ლაქტაციის პერიოდში მყოფი პაციენტები, აგრეთვე პაციენტები, რომლებსაც აქვთ შემდეგი დაავადებები:

1. არტერიული ჰიპერტენზია III ხარისხის;
2. კუჭისა და თორმეტგოჯა ნაწლავის წყლულოვანი დაავადება;
3. ნაწლავის ანთებითი დაავადებები (დადგენილი წყლულოვანი კოლიტი ან კრონის დაავადება);
4. მეოთხე სტადიის ოსტეოპოროზი;

5. ღვიძლის ციროზი (Child-Pugh C);
6. გულის მწვავე და ქრონიკული უკმარისობა (NYHA III-IV);
7. კუშინგის დაავადება;
9. გლაუკომა;
10. ფსიქოზური აშლილობა;
11. ეპილეფსია;

პაციენტები დაიყოფიან ორ ჯგუფად. პირველი ჯგუფს შეადგენს მწვავე პანკრეატიტის მქონე 60 პაციენტი. მათ მკურნალობა ჩატარდება სტანდარტული მკურნალობის კურსით (საკონტროლო ჯგუფი). მეორე ჯგუფს შეადგენს იგივე დიაგნოზის მქონე ასევე 60 პაციენტი. მათ, გარდა სტანდარტული მკურნალობისა, ჩატარდება კორტიკოსტეროიდული თერაპიის კურსი (ექსპერიმენტული ჯგუფი). კვლევისათვის გამოყენებული იქნება შემდეგი მეთოდები:

1. PAP შეფასდება (მინიმუმ) მკურნალობის დაწყებიდან 24 სთ-ში და მე-4-5 დღეს (კვლევა ჩატარდება „მედიკალ ვორლდ დიაგნოსტიკის“ ლაბორატორიაში ELISA მეთოდით, DIAREader ანალიზატორზე).
2. IL-6 შეფასდება (მინიმუმ) პაციენტის ჰოსპიტალიზაციიდან არაუმეტეს 24-სთ-სა და მე-4-5 დღეს (კვლევა ჩატარდება „მედიკალ ვორლდ დიაგნოსტიკი“ ლაბორატორიაში ELISA მეთოდით, DIAREader ანალიზატორზე).
3. ლიპაზის კონცენტრაციის შეფასდება (მინიმუმ) პაციენტის ჰოსპიტალიზაციიდან რამდენიმე საათში და მე-4-5 დღეს (კვლევა ჩატარდება კლინიკის ბაზაზე არსებულ ლაბორატორიაში).
4. სისხლის საერთო ანალიზი, CRP, პროკალციტონინი, მჟავა-ტუტოვანი წონასწორობა შეფასდება (მინიმუმ) პაციენტის ჰოსპიტალიზაციიდან რამდენიმე საათში და გაწერამდე ერთი დღით ადრე (კვლევები, ჩატარდება კლინიკის ბაზაზე არსებულ ლაბორატორიაში).
5. განისაზღვრება გლუკოზის კონცენტრაცია სისხლში, კორტიკოსტეროიდის გადასხმამდე და მის შემდეგ.
6. ინსტრუმენტული - კომპიუტერული ტომოგრაფიული ან მაგნიტურ რეზონანსული ქოლანგიოპანკრეატოგრაფიული კვლევა, რომელიც ჩატარდება (მინიმუმ) პაციენტის ჰოსპიტალიზაციიდან 48-72 სთ-ში და შემდგომ, დაავადების დინამიკიდან და საჭიროებიდან გამომდინარე პერიოდში.
7. კვლევის ჩატარებიდან 1 წლის განმავლობაში, მოხდება პაციენტების პერიოდული მონიტორინგი.

#### **გამოყენებული ლიტერატურა**

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**MITOCHONDRIAL DISEASES AND MODERN APPROACHES TO THEIR DIAGNOSTICS AND MANAGEMENT**

*Elene Makaridze*

*Supervisor: Manana Pruidze*

*Associate professor, Department of Biology and Parasitology*

*Tbilisi State Medical University, Faculty of Medicine-Semester 1, Tbilisi, Georgia*

**ABSTRACT**

It is widely known that Mitochondria are membrane-bound cell organelles which generate most of the chemical energy needed to power the cell's biochemical reactions. Chemical energy produced by the mitochondria is stored in a small molecule called adenosine triphosphate (ATP), which is why these organelles are frequently referred to as the “powerhouse” or “battery” of the cell. Mitochondrion is the only organelle that contains its own genome-its own circular DNA called mitochondrial DNA (mtDNA), which is particularly interesting to scientists due to its distinct properties, such as a high rate of polymorphisms and mutations. mtDNA is 100 000 times smaller than Nuclear DNA and produces 2 ribosomal RNA-s, 22 transfer RNA-s and 13 proteins.

Mitochondrial diseases are genetic disorders that are extremely rare with the spread statistics of approximately one in every 5000 individuals in the US having a genetic mitochondrial disease. Mentioned diseases are caused by point and non-point mutations that take place inside the mitochondrial genes. Mitochondrial diseases can be congenital, but can also arise at any age. Physicians have been working hard to study the methods of diagnosis of this disease, since there is no single laboratory or diagnostic test that can identify the diagnosis of a mitochondrial disease. One of the recently developed methods of diagnosis is biochemical testing in tissue. Functional in vitro assays in tissue (typically muscle) have been the mainstay of diagnosis of mitochondrial disorders, especially prior to the recent advances in genomics. Nowadays there are no cures for mentioned diseases, but symptomatic treatment is used, which can help reduce patient's condition and make their lives a bit easier.

Examples of mitochondrial diseases include Leigh Syndrome, Leber's hereditary optic neuropathy (LHON), Diabetes mellitus and deafness (DAD), MELAS syndrome and more.

The study of mitochondrial diseases and their diagnosis is a highly relevant topic in the modern molecular Biology of the cell.

**Keywords:** Mitochondria, Disease, Mitochondrial DNA, Diagnosis.

**December 09-11, 2022 / Tbilisi, Georgia**

**THE COMPOSITE MASSES ADHESION PECULIARITIES ON THE TOOTH ENAMEL-CEMENT CONNECTION (CEJ) STRIP**

*Professor Marina Mamaladze*

*Tbilisi State Medical University, Department of Odontology, Tbilisi, Georgia*

*Dr., PhD candidate Ekaterine Zarkua*

*Tbilisi State Medical University, Tbilisi, Georgia*

*Assoc. Professor Lia Sanodze*

*Tbilisi State Medical University, Department of Odontology, Tbilisi, Georgia*

**ABSTRACT**

The success of tooth restoration with composite materials depends on many factors. The widespread introduction of new generation composites and adhesive systems significantly increased the long-term operation time of teeth, raised the aesthetic parameters of the restoration and ensured the restoration of not only the anatomical indicators of the tooth, but also its function.

Despite the above, with composites, which belong to the group of plastics, the dentist faces a constant challenge in the process of filling/restoring teeth. This is primarily determined by the eclecticism of the tooth structure and the "content" of the composite. In the later, dentin's water content and especially in cementum is high.

That is why, in the case of diseases and injuries in the area of the tooth neck (cervical), where the cement covering the root is exposed and the dentin uncovered by enamel is visible, the selection of adhesive systems is of crucial importance in the tooth restoration process.

During the research, the condition of 35 human teeth was evaluated. All teeth belonged to the group of lower premolars. In the area of 15 teeth neck, class V - medium caries was diagnosed, in 10 cases of recession and 10 of wedge defects.

In the restoration process, V generation adhesive system Ena bond (Micerium) (for 18 teeth) and VII generation adhesive Peak Universal (Ultradent.corp) (for 17 teeth) were used. The tooth restoration was performed using the composite Enamel+ to ensure the maximum visual identity of the restored tooth. After one year, the quality of the restorations and the areas of depressurization were evaluated using the caries detector Sable Seek (Ultradent). During the implementation of the mentioned method, the perimeter of the marginal connection remained colored, the intensity of which was further adjusted by a specially designed algorithm. During the dental treatment, the restoration protocol was followed: adequate anesthesia, sparing, minimally invasive preparation, isolation of the operative field, restoration and post-restoration treatment of the tooth.

The results of our study revealed the following: it was found that cases of dental feelings depressurization (discoloration, deformation, increased sensitivity, etc.) when using of the VII generation adhesive system were 1.25 times more frequent, than when restoring teeth with the V generation adhesive.

**Keywords:** Composites, adhesive systems, cervical lesion, restoration.



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**TRIMETAZIDINE AS A MODIFIER OF AC-MODE OF CHEMOTHERAPY-DRIVEN HYPERDYSLIPIDEMIA**

*Avagimyan A. A.<sup>1,2</sup>*

*<sup>1</sup>MD, Pathological Anatomy and Clinical Morphology Department,  
Yerevan State Medical University after M. Heratsi, Yerevan, Armenia*

*<sup>2</sup>PhD student, A. P. Avtsyn Research Institute of Human  
Morphology of FSBI "NRCS Petrovsky", Moscow, Russia*

*ORCID ID: 0000-0002-5383-8355*

*Kakturskiy L.V.<sup>3</sup>*

*<sup>3</sup>MD, PhD, MsD, Acad., Scientific Director, A. P. Avtsyn Research Institute of Human  
Morphology of FSBI "NRCS Petrovsky", Moscow, Russia*

*ORCID ID: 0000-0001-7896-2080*

## **Introduction**

Cardio-oncology confers is a multidisciplinary crisis of contemporary medicine [1]. Doxorubicin+cyclophosphamide (AC) mode of chemotherapy serves as an effective strategy for breast cancer treatment. However, the development of widely variable cardiovascular complications, from sinus arrhythmia to decompensated heart failure, have been noted [2,3]. The latter is aggravated by the fact that, despite the time map of various multidisciplinary studies conducted within the recent 60 years, the scientific world hasn't reached a consensus on the question - How to protect the heart and vessels from chemotherapy-related failure without reducing the effectiveness of chemotherapy?

## **Purpose of the study**

The present research is aimed to assess the proatherogenic potential of the AC chemotherapy mode, with substantiation of trimetazidine (TMZ) intake.

## **Material and methods**

The fundamental, randomized, controlled, experimental *in vivo* study was conducted on 80 inbred, male Wistar rats who were randomly divided into four equal groups (1 - saline, 2 - AC, 3 - AC + TMZ, 4 - TMZ). The course dosages of doxorubicin, cyclophosphamide, and TMZ were administered at 15, 150, and 42 mg/kg, respectively. The experiment duration last was 14 days (chronic cardiotoxicity). TMZ was chosen as a probable stabilizer of cholesterol metabolism. The deviations of the following parameters were evaluated in the framework of this study: total cholesterol (TC), triglycerides (Tg), high-density lipoproteins (HDL), low-density lipoproteins (LDL), coronary risk index (CRI), and atherogenic coefficient (CA). The markers of cholesterol metabolism mentioned above were measured via certified test systems produced by Elabscience Biotechnology (China) using SpectraMax 250 rider (Molecular Devices, USA).

## **Results**

In group № 2, the concentration of TC is higher by 80.3 and 80.7%, Tg is higher by 80.5 and 88.0%, LDL is higher by 149.3 and 158.6%, HDL is lower by 46.8 and 43.5%, CA is higher by 187.4 and 172.8%, CRI is higher by 115.8 and 113.9% than in groups № 1 and 4, respectively. While the comparative groups № 3 and 2, it was noted that TMZ induces a decrease in the TC level by 26.6%, Tg by 46.4%, LDL by 38.2%, an increase in HDL by 18.2%, as well as a decrease in CA by 55.5% and CRI by 44.2% (Tukey's post-hoc test,  $p < 0.05$ , one-way ANOVA,  $p < 0.0001$ ).

**Conclusions**

AC mode of chemotherapy is an inducer of atherogenic hyperlipidemia. TMZ provides a slight but pathogenically important tendency to cholesterol-metabolism stabilization.

**Keywords:** cardiotoxicity, cardio-oncology, trimetazidine.

**RHEOLOGICAL PROPERTIES DURING THE ATRIAL FIBRILLATION**

*Maia Gotsadze*<sup>1</sup>

<sup>1</sup>*Tbilisi State Medical University, Internal Medicine Department, Tbilisi, Georgia.*

*Tamar Khandashvili*<sup>2</sup>

<sup>2</sup>*Tbilisi State Medical University; Internal Medicine Department, Tbilisi, Georgia*

*Nugzar Narsia*<sup>3</sup>

<sup>3</sup>*Tbilisi State Medical University; Internal Medicine Department, Tbilisi, Georgia*

*Nana Momtselidze*<sup>4</sup>

*Ivane Beritashvili Experimental Center of Biomedicine; Tbilisi, Georgia*

*Maia Mantskava*<sup>5\*</sup>

<sup>5</sup>*European University/Tbilisi State Medical University/Ivane Beritashvili Experimental Center of Biomedicine; Tbilisi, Georgia*

**ABSTRACT**

Atrial fibrillation affects approximately 1% of the global population, according to current data. Its prevalence is expected to increase 2.5 times over the next 50 years as the average age rises. The disease's unfavorable epidemiological picture determined the reality of our project. The study's goal was to study rheological parameters during various types of atrial fibrillation. There were 58 patients examined (average age 65±10). Three patient groups have been identified based on the progression of rhythm disorders to the permanent, persistent, and paroxysmal states. There were nearly healthy people in the study-the control group. The erythrocyte aggregability index, erythrocyte deformability, and plasma viscosity were all investigated. We used a new innovative method known as the "Georgian Technique" to evaluate the index of erythrocyte aggregability, which was developed by Georgian scientists and is well-known around the world for being direct, numerical, and precise. The filtration method was used to calculate the index of erythrocyte deformation. In 370 C, plasma viscosity was measured using a capillary viscosimeter. As a result, the average values of EAI-RBC in arrhythmia patients were 34.23±10.83, EDI-RBC: 2.29 ±0.321, VP: 1.20 ±0.674; in the control group, EAI-RBC was 25.6±11.28, EDI-RBC: 2.088± 0.24, VP: 1.09± 0.353; Rheological properties were disturbed in all three types of arrhythmia when compared to the control group. When the mean values of erythrocyte aggregation index, erythrocyte deformability, and plasma viscosity of each group were compared, we discovered that the difference between patients with atrial fibrillation and the control group was reliable, with a confidence index of -1%. As a result, regardless of their types, patients with atrial fibrillation have all rheological characteristics impaired. Since atrial fibrillation is a predictor of death [A.J. Camm, P. Kirchhof, and G.Y. Lip., 2010], expanding research in this area is especially important.

**Keywords:** Erythrocyte aggregability, arrhythmia, blood rheology;

**ROLE OF CORTICOSTEROID THERAPY IN ACUTE PANCREATITIS TREATMENT AND PREVENTION OF DISEASE COMPLICATIONS**

***Roberti Avalishvili***

*Tbilisi State Medical University, Faculty of Medicine, General Surgery, Tbilisi, Georgia*

***Mamuka Gurgenidze***

*Tbilisi State Medical University, International Faculty Of Medicine and Stomatology, Department of surgery, Tbilisi, Georgia*

***Giorgi Asatiani***

*Tbilisi State Medical University, Faculty of Medicine, General Surgery, Tbilisi, Georgia*

Acute pancreatitis (AP) is a commonly occurring acute abdominal disease with multiple causes. Severe acute pancreatitis (SAP) may be life-threatening and result in serious economic and health burdens. AP is associated with a high mortality rate, and its incidence has been increasing in recent years. Due to the frequent rise of acute pancreatitis and the number of complications associated with the disease it has been identified that the research for new approaches to treat the disease is still an important issue in the modern medicine.

AP is an acute inflammatory response to pancreatic injury and induces important changes. Among these, the most profound change is that of the pancreatitis-associated protein (PAP) family, the expression of which is very low in the normal pancreas and becomes strongly overexpressed after even mild pancreatic inflammation. Multiple functions have been ascribed to PAP. It has been shown to be anti-bacterial, anti-apoptotic and mitogenic. PAP expression is upregulated by free radicals or cytokines, and such upregulation confers cellular resistance to apoptosis. PAP has mitogenic affect for pancreatic-derived cells, thus implicating PAP in the proliferative response of pancreas to injury. Dexamethasone demonstrates protective function in acute pancreatitis, which may be via UP-regulation of PAP gene expression during injury.

The goal of our research is layered differently, the main aspect is to study how affective corticosteroid therapy can be for acute pancreatitis and for prevention forms. The research will be conducted follows:

1. To structure two different research group, with and without corticosteroid therapy.
2. To measure level of PAP during corticosteroid therapy
3. To compare and analyze the change in research group. Monitor serum lipase level, IL-6, whole blood count (leukocytosis, shift to the left), CRP, procalcitonin, Acid- base balance and imaging studies (CT, MRSP) in experimental and control group in the research.
4. Compare time of hospitalization and financial affect in between research group.

Therefore, we believe studying the role of Corticosteroid therapy could be very beneficial aspect, also it would have very important role on treating and preventing complications of acute pancreatitis.

**FORMULATION AND CHARACTERIZATION OF ETHOSOMAL GEL FROM PAPAIN**

***Tamar Korinteli***<sup>1</sup>

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Doctoral student of Tbilisi State Medical University, Tbilisi, Georgia.*

***Aliosha Bakuridze***<sup>2</sup>

*TSMU, Faculty of Pharmacy, Department of Pharmaceutical Technology, Tbilisi, Georgia.*

***Nana Gorgaslidze***<sup>3</sup>

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

*ORCID ID: 0000-0002-4563-5224*

**ABSTRACT**

Musculoskeletal disorders (MSDs) are one of the most important medical issues we face today, due to humanity's modern sedentary lifestyle. Because of the multiple side effects of nonsteroidal anti-inflammatory drugs, search for new remedies and selection of the best dosage forms remains one of the major challenges of modern medicine. Papain is a complex of plant-derived proteolytic enzymes found naturally in papaya (*Carica papaya* L.) manufactured from the latex of raw papaya fruits and is currently used in the treatment of musculoskeletal disorders. The topical administration of drugs, including enzyme-based drugs, in order to achieve optimal cutaneous and percutaneous drug delivery has recently gained an importance and gels, among the other semi-solid dosage forms, have multiple advantages. Ethosomes are the ethanolic phospholipid vesicles which are used mainly for transdermal delivery of drugs/

The aim of this study was to develop ethosomal gel from papain. The ethosomes were prepared by ethanol injection. First, papain and cholesterol were dissolved in ethanol, and the ethanol solution was injected into a phosphate buffer solution (pH 6.8) at a rate of 200 µL/min under closed conditions. After the ethanol solution was added, stirred for 10 min. The prepared ethosomes was ultrasonicated for 2 min and the ultrasound power was 35% (the total rated power is 650 W). Then passed through a 0.22 µm filter for three times. Proteolytic activity was used for quantitative assessment while FT-IR spectroscopy allowed identification of the formulated gel. The spreadibility, consistency, pH, thermal and colloidal stability of the gel were satisfactory.

**Keywords:** *Carica papaya*, dosage form, ethosomes, enzyme.

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**INNOVATIVE PHARMACEUTICAL PRODUCTS IN THE GEORGIAN PHARMACEUTICAL MARKET**

***Neli Nikuradze<sup>1</sup>***

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

*ORCID ID: 0000-0002-4614-5075*

***Nana Gorgaslidze<sup>2</sup>***

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

*ORCID ID: 0000-0002-4563-5224*

***Nino Nemsitsveridze<sup>3</sup>***

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

*ORCID ID: 0000-0002-5659-1714*

***Tea Zarqua<sup>4</sup>***

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

*ORCID ID: 0000-0001-7265-4749*

***Mariam Baduashvili<sup>5</sup>***

*Minister Of Internally Displaced Persons From The Occupied Territories, Labour, Health And Social Affairs Of Georgia, Regulation agency for medical and pharmaceutical activities.*

*ORCID ID: 0000-0002-8894-0472*

**ABSTRACT**

The study presents a nomenclature analysis of innovative pharmaceutical products - a retrospective of the dynamic indicators of the last 5 years of the departmental drug register and marketing research of positioning.

Based on which it is established that:

- Out of 2,024 pharmaceutical products registered on the Georgian market during the last 2017-2022, 89 positions are innovations, which is about 4.39% of total pharmaceutical products in this period.
- During the research period, about 480 innovative pharmaceutical products of 62 pharmacotherapeutic groups were registered, among them, antineoplastic drugs (18) and systemic antihistaminic drugs - 16 are represented in the most positions.
- In antineoplastics, a total of 83 positions of monoclonal antibodies are registered (under trade name). For example, one of the chemical substances targeted by the research, Trastuzumab L01XC 03, is positioned with 11 different trade names, the most of which are registered in 2021, and the least in 2020.
- 41 positions were registered through initial registration. With re-registration - 42 positions, (including Trastuzumabs) of which: recombinant pharmaceutical products - 14.
- Medicines are mainly registered from European countries, the three main countries from which innovative pharmaceutical products are imported are Italy, Germany, and France.
- Monoclonal antibodies (mABs) take the leading place; Their prevalence is due to increasingly fewer adverse effects and their high specificity. New approvals continue to accrue for the treatment of immunologic diseases, reversal of drug effects, and cancer therapy;

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- Monoclonals fundamentally change the outcome of not only cancer, but also many other diseases (covid, rheumatoid arthritis, hepatitis, diabetes, sclerosis, and others);
- Correlations of marketing data of monoclonal antibodies, annual increase in imports, repeated registrations, involvement in traditional treatment schemes and transnational research are a condition and an important motivator for Oncology in Georgia to better align with international standards.

**Keywords:** monoclonal antibodies, innovative pharmaceutical products

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**IMPACT OF  $\beta$ -BLOCKERS ON THE IMMUNE STATUS OF PATIENTS WITH ESSENTIAL HYPERTENSION**

***Tamar Sharashenidze***

*David Aghmashenebeli University of Georgia, Doctoral Education Programme -Medicine*

*PhD student, Tbilisi, Georgia*

*ORCID ID: 0000-0001-9494-1351*

***Tamar Sanikidze***

*Tbilisi State Medical University, Faculty of medicine, Tbilisi, Georgia*

***Maka Buleishvili***

*Georgian National University SEU, Faculty of medicine, Tbilisi, Georgia*

**ABSTRACT**

Epidemiological and experimental studies revealed a relationship between biochemical markers of systemic inflammation and diseases of the cardiovascular system, such as atherosclerosis, heart failure, and hypertensive disease. As is known, pro-inflammatory cytokines affect vascular function, cause structural and functional changes in endothelial cells, regulate the release of vasoactive factors by the endothelium (endothelin, nitric oxide, NOS-mRNA and in this way participate in blood pressure regulation).

The balance of cytokines (IL-2, IL-10, IF- $\gamma$ ) in patients with essential hypertension before and after treatment with beta-blockers was studied.

20 patients aged 45-65 years and diagnosed with essential hypertension (12 women, 8 men) were investigated.

For the treatment of hypertension, patients received second-generation beta-selective  $\beta$ -blockers Egilok and Betalok Zok, and third-generation  $\beta$ -blocker Nebilet for one month.

Patients performed their blood pressure measurements daily in the morning during 1 month. The content of interleukins (IL-2, IL-10, IF- $\gamma$ ) in the blood by the immune enzymatic ELISA method on a semi-automatic reader Stat Fax 3200 with RayBio, (USA) reagent was measured.

The results of our studies show an increase in the level of CD4+ (IL-2) cytokines in the blood of the studied hypertensive patients, which coincides with the literature data on the important role of CD4+ pro-inflammatory cytokines in the pathogenesis of hypertension. After 1 month of treatment with  $\beta$ -blockers, the patient's arterial pressure and IL-2 level content in the blood decreased. These data indicate the important role of inflammation in the pathogenesis of hypertension and the anti-inflammatory effects of  $\beta$ -blockers, used in the treatment of hypertension.

**Keywords:** cytokines,  $\beta$ -blockers, systemic inflammation, essential hypertension



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**MANAGEMENT OF DRUG DEVELOPMENT LIFE CYCLE OF THE ORIGINAL ANTI-ALLERGIC "DUALLER-G"**

***Tamaz Chumburidze<sup>1</sup>***

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

*ORCID ID: 0000-0003-1053-6901*

***Ioseb Tomadze<sup>2</sup>***

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia*

*ORCID ID: 0000-0003-2906-2187*

***Nino Nemsitsveridze<sup>3</sup>***

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

*ORCID ID: 0000-0002-5659-1714*

***Tea Zarqua<sup>4</sup>***

*TSMU, Faculty of Pharmacy, Department of Social and Clinical Pharmacy, Tbilisi, Georgia.*

*ORCID ID: 0000-0001-7265-4749*

***Elene Tsitsilashvili<sup>5</sup>***

*TSMU, Faculty of Pharmacy, Department of Biochemistry, Tbilisi, Georgia.*

*ORCID ID: 0000-0001-6511-6088*

**ABSTRACT**

Allergic diseases are the most common chronic conditions lasting throughout the patient's life.

They cause significant deterioration in the quality of life of patients. Effective safe treatment of allergic diseases is therefore one of the main challenges.

The creation of a new generation anti-allergic drug requires great scientific and labor potential, which only the world's leading companies have, and against this background, Dualler-G, a new generation anti-allergic, extended-spectrum drug created by a Georgian scientist Pr. Tamaz Tchumburidze and registered by the Ministry of Health of Georgia, can be considered a unique achievement.

Product - a broad spectrum anti-allergic drug - Dualler-G. The drug is a high-tech product. Indications: Pollinosis, acute and chronic urticaria, Quincke's angioneurotic edema, hay fever, allergic rhinitis, rhinosinusitis, dermatoses, (eczema, neurodermatitis, skin vasculitis, lichen planus, skin itching, etc.), allergic complications caused by medicinal drugs.

Does not cause drowsiness, has a rapid action of 15-30 min, the action lasts (for 12-24 hours depending on the dose, clearly expressed side effects do not appear even if you accidentally take two and a half times more than the recommended single dose of the drug (100 mg).

The conducted research shows that the pharmaceutical product is potentially competitive according to many parameters (drug efficiency, safety, wide spectrum of action, speed and duration of action), but it cannot occupy a suitable place in the pharmaceutical both local and global market, due to the lack of appropriate commercialization activities, which hinders development of the life cycle of the drug. The main reason is the unregulated market, unhealthy competition, pandemic declared in 2020 and most importantly, low trust in fair products.

Prospects for the development of Dualler-G medicinal forms - the development and implementation of technological processes of anti-allergic gel and aerosol pharmaceutical preparation, which will have a

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targeted effect for the treatment of allergic diseases of the skin and respiratory tract, provide the possibility of achieving the maximum effect with a minimum dose.

**Keywords:** Allergic diseases, anti-allergic, Dualler-G

**HOSPITAL-ACQUIRED AND VENTILATOR ASSOCIATED PNEUMONIA IN CHILDREN**

*Natia Chkhaidze*

*Tbilisi State Medical University, Clinical medicine, Pediatrician, Tbilisi, Georgia.*

*Maia Kherkheulidze*

*Tbilisi State Medical University, Clinical medicine, Pediatrician, Tbilisi, Georgia.*

**ABSTRACT**

Hospital acquired pneumonia (HAP) and ventilator associated pneumonia (VAP) cause significant inpatient morbidity and mortality. They are especially challenging to diagnose promptly in the intensive care unit because a plethora of other causes can contribute to clinical decline in complex, critically ill patients. Ventilator associated pneumonia (VAP) is a common complication in mechanically ventilated children and adults. There remains much controversy in the literature over the definition, treatment and prevention of Ventilator associated pneumonia (VAP). The incidence of Ventilator associated pneumonia (VAP) is variable, depending on the definition used and can effect up to 12% of ventilated children. For the prevention and reduction of the incidence of Ventilator associated pneumonia (VAP), ventilation care bundles are suggested, which include vigorous hand hygiene, head elevation and use of non-invasive ventilation strategies. Diagnosis is mainly based on the clinical presentation with a lung infection occurring after 48 hours of mechanical ventilation requiring a change in ventilator settings (mainly increased oxygen requirement, a positive culture of a specimen taken preferentially using a sterile sampling technique either using a bronchoscope or a blind lavage of the airways). A new infiltrate on a chest X ray supports the diagnosis of Ventilator associated pneumonia (VAP). For the treatment of Ventilator associated pneumonia (VAP), initial broad-spectrum antibiotics should be used followed by a specific antibiotic therapy with a narrow target once the bacterium is confirmed. The aim of the review in do presents etiology, epidemiology and risk factors of Hospital acquired pneumonia and ventilator associated pneumonia in children.

**Keywords:** Hospital acquired pneumonia, ventilator associated pneumonia, treatment, antibiotic.

**COMPLEX ANALYSIS OF RHEOLOGICAL, THE ELECTRO-PHYSICAL PROPERTIES OF BLOOD, AND SOME FACTORS OF IRON METABOLISM IN THE BLOOD IN GASTRIC CANCER**

*Ekaterine Labadze<sup>1</sup>*

*<sup>1</sup>Tbilisi State Medical University; Internal Medicine Department, Tbilisi, Georgia.*

*Maia Mantskava<sup>2\*</sup>*

*<sup>2</sup>European University/Tbilisi State Medical University/Ivane Beritashvili Experimental Center of Biomedicine; Tbilisi, Georgia*

*Nugzar Narsia<sup>3</sup>*

*<sup>3</sup>Tbilisi State Medical University; Internal Medicine Department, Tbilisi, Georgia*

*Tamar Khandashvili<sup>4</sup>*

*<sup>4</sup>Tbilisi State Medical University; Internal Medicine Department, Tbilisi, Georgia*

**ABSTRACT**

Research of different clinical parameters of different systems of the body in gastric cancer is much needed because gastric cancer is one of the most terrible diseases cancers of the modern world. The aim of our work was to study the rheological properties of blood in gastric cancer, along with the electro-physical properties of blood and iron metabolism in patients with gastric cancer. The research methods were modern and original. The study included patients with stomach cancer and a control group of healthy volunteers. The average age in the studied groups corresponded to each other. All patients were included in the study according to an informed agreement. In patients with gastric cancer before surgery, the content of iron and hemoglobin was reduced, transferrin and ferritin remained within normal limits. On the 7th day after the operation, ferritin increased twice, hemoglobin was close to control values. Transferrin and iron remained reduced on the 7th postoperative day. The erythrocyte agreeability index in patients with gastric cancer before surgery was increased by one and a half times compared to the control. On the 7th day after the operation, the erythrocyte agreeability index improved and was increased by only 30% compared to the control. The index of electro-physical properties in gastric cancer before surgery was changed compared to control values, on the 7th day after surgery, it was also changed. This approach, along with a thorough study of these routine analyzes in gastric cancer, is very important. It turned out that the seven-day postoperative interval was insufficient to normalize the studied parameters. The analysis of such data will make it possible to personalize the therapy of patients with stomach cancer, which is very important for each patient, their loved ones, and public health in general.

**Keywords:** RBC aggregation; electro-clinical blood property; iron; transferrin; ferritin

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**KNEE JOINT MEDIAL COMPARTMENT OSTEOARTHRITIS TREATMENT WITH HIGH TIBIAL OPENING WEDGE OSTEOTOMY AND ARTHROSCOPIC CHONDROPLASTY**

*Irakli Khabeishvili, Tornike Nozadze, Levan Chikvatia*

*Tbilisi State Medical University, Medicine faculty, Trauma and Orthopedic Surgery Department, Tbilisi, Georgia.*

**ABSTRACT**

Osteoarthritis is a disorder involving movable joints characterized by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates maladaptive repair responses including pro-inflammatory pathways of innate immunity. The disease manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodeling, osteophyte formation, joint inflammation and loss of normal joint function), that can culminate in illness. Globally, as of 2010, approximately 250 million people had osteoarthritis of the knee (3.6% of the population). Hip osteoarthritis affects about 0.85% of the population. Together, knee and hip osteoarthritis had a ranking for disability globally of 11th among 291 disease conditions assessed. In the United States, there were approximately 964,000 hospitalizations for osteoarthritis in 2011, a rate of 31 stays per 10,000 population. With an aggregate cost of \$14.8 billion (\$15,400 per stay), it was the second-most expensive condition seen in U.S. hospital stays in 2011. By payer, it was the second-most costly condition billed to Medicare and private insurance.

Approximately 654.1 million (95% CI, 565.6-745.6 million; aged  $\geq 40$  years) individuals worldwide had knee OA in 2020. The global incidence of knee OA was 203 per 10,000 person-years in individuals aged 20 years or over. Correspondingly, approximately 86.7 million individuals aged 20 years or over had incident knee OA worldwide in 2020. The ratios of prevalence and incidence of knee OA in women and men were 1.69 and 1.39 respectively. There are several types of conservative treatment worldwide. Which includes NSAIDs, intraarticular steroid, hyaluronic acid and prp injections. But these treatment methods can't cure osteoarthritis. In more severe pattern of knee joint osteoarthritis there are several surgical treatment modalities. Worldwide exists two main form of surgical procedures: knee joint salvage procedure and joint replacement surgery.

Nowadays in older than 60 years old population widely used knee joint replacement with artificial endoprosthesis. Revision rates of about 6% after five years and 12% after ten years are to be expected after Knee joint replacement surgery. Revision rate is one of the most important outcome measures of joint replacement surgery. The lifetime risk of requiring revision is 22.4% in those aged between 46 and 50 years at the time of the initial surgery. The three commonest indications for revision are aseptic loosening, infection, and unexplained pain. Young males, aged between 46 and 50 years, have the highest lifetime risk of revision (25.2%). Therefore in young population there is a big challenge to treat knee joint osteoarthritis. Our work philosophy is designated on preserving knee joint and delaying knee arthroplasty procedure in older age. We have performed 40 high tibial osteotomy in combination with knee joint arthroscopy chondroplasty. During high tibial osteotomy we have used puddy LCP locking Titanium Plates. Chondroplasty procedures included microfracture and autologous mosaic chondroplasty intervention. Patients were evaluated before and after operation with The Western Ontario and McMaster Universities Osteoarthritis Index / Knee-WOMAC. Preliminary results showed Roentgenological and functional improvement. We can conclude that combination of these two procedure improves knee joint osteoarthritis treatment outcome and delays or prevents in future knee joint replacement surgery with artificial joint.

**Keywords:** 3-6 words. Knee joint osteoarthritis, High tibial osteotomy, Arthroscopic chondroplasty;

**THE COMPOSITE MASSES ADHESION PECULIARITIES ON THE TOOTH ENAMEL-CEMENT CONNECTION (CEJ) STRIP <sup>1</sup>**

*Professor Marina Mamaladze <sup>1</sup>*

*<sup>1</sup> Tbilisi State Medical University, Department of Odontology, Tbilisi, Georgia*

*Dr., PhD candidate Ekaterine Zarkua <sup>2</sup>*

*<sup>2</sup> Tbilisi State Medical University, Tbilisi, Georgia*

*Assoc. Professor Lia Sanodze <sup>3</sup>*

*<sup>3</sup> Tbilisi State Medical University, Department of Odontology, Tbilisi, Georgia*

**ABSTRACT**

The success of tooth restoration with composite materials depends on many factors. The widespread introduction of new generation composites and adhesive systems significantly increased the long-term operation time of teeth, raised the aesthetic parameters of the restoration and ensured the restoration of not only the anatomical indicators of the tooth, but also its function.

Despite the above, with composites, which belong to the group of plastics, the dentist faces a constant challenge in the process of filling/restoring teeth. This is primarily determined by the eclecticism of the tooth structure and the "content" of the composite. In the later, dentin's water content and especially in cementum is high.

That is why, in the case of diseases and injuries in the area of the tooth neck (cervical), where the cement covering the root is exposed and the dentin uncovered by enamel is visible, the selection of adhesive systems is of crucial importance in the tooth restoration process.

During the research, the condition of 35 human teeth was evaluated. All teeth belonged to the group of lower premolars. In the area of 15 teeth neck, class V - medium caries was diagnosed, in 10 cases of recession and 10 of wedge defects.

In the restoration process, V generation adhesive system Ena bond (Micerium) (for 18 teeth) and VII generation adhesive Peak Universal (Ultradent.corp) (for 17 teeth) were used. The tooth restoration was performed using the composite Enamel+ to ensure the maximum visual identity of the restored tooth. After one year, the quality of the restorations and the areas of depressurization were evaluated using the caries detector Sable Seek (Ultradent). During the implementation of the mentioned method, the perimeter of the marginal connection remained colored, the intensity of which was further adjusted by a specially designed algorithm. During the dental treatment, the restoration protocol was followed: adequate anesthesia, sparing, minimally invasive preparation, isolation of the operative field, restoration and post-restoration treatment of the tooth.

The results of our study revealed the following: it was found that cases of dental feelings depressurization (discoloration, deformation, increased sensitivity, etc.) when using of the VII generation adhesive system were 1.25 times more frequent, than when restoring teeth with the V generation adhesive.

**Keywords:** Composites, adhesive systems, cervical lesion, restoration.

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**DIGITAL HEALTH, CONTEMPORARY CHALLENGES AND PERSPECTIVES**

***Irine Zarnadze***

*TSSU, Department of Public Health, Health care Management, Policy and Economics; Tbilisi, Georgia*

*ORCID ID: 0000-0001-5511-437X*

***Shalva Zarnadze***

*TSSU, Department of Nutrition, Aging Medicine, environmental and occupational health; Tbilisi Georgia*

*ORCID ID: 0000-0002-6895-9205*

***Dali Kitovani***

*TSSU, Department of Public Health, Health care Management, Policy and Economics; Tbilisi, Georgia*

*ORCID ID: 0000-0003-3026-4667*

***Lili Lomtadze***

*TSSU, Department of Public Health, Health care Management, Policy and Economics; Tbilisi, Georgia*

*ORCID ID: 0000-0002-1504-7587*

**ABSTRACT**

**Introduction:** Digital healthcare provides and expands the possibilities of receiving quality medical care in modern medicine. The advantages of digital healthcare can be divided into two groups. The first is the regulation of payments and co-payments for medical services, which are very sensitive, and the second is the possibility of transforming health systems.

**The purpose of the research:** consisted of assessment of digital healthcare implementation and systemic transformation in healthcare systems of different countries.

**Research Methods:** Observational study, the study was retrospective, conducted over a period of 6 months. Papers published in English and Georgian from 2015 to September 2022, a total of 45 papers, were studied and evaluated.

**Results:** An analysis of various studies has shown that: Digital health systems enable in line with the principles of financial sustainability and caring for the disadvantaged, the insurance systems were merged and enlarged to become a social insurance system to cover everyone. To effectively promote various services, in addition to establishing specialized departments and offices for various services and policy promotions. The implementation of the “Family Doctor Integrated Care Program,” the “Patient-Centered Integrated Outpatient Care Program in Hospitals,” the “Integrated Home Health Care Program,” and various programs is aimed at improving medical accessibility and quality of patient-centered medical care system, by providing patients with safe, appropriate, and continuous integrated medical services according to their needs, and to reduce the waste of medical resources.

**Conclusion:** The implementation of digital health programs promotes efforts to safeguard the medical benefits and rights of the patients. Despite the rapid development of various medical technologies, medical expenses have also risen greatly, causing financial burdens on the. Digital health systems have the responsibility with the medical providers on good communication and focuses on seeking the balance between financial and clinical needs

**Keywords:** Digital Health, Challenges, Perspectives

**MEDICAL TOURISM AS A BRANDED PRODUCT IN THE EUROPEAN MEDICAL MARKET**

*Devi Tabidze, Ekaterine Mirvelashvili, Nino Khachapuridze, Marina Kajrishvili*

*Tbilisi State Medical University, Tbilisi, Georgia*

**ABSTRACT**

Today, medical tourism is one of the most competitive players in the country's economy. Tourism is not a new product for Georgia, while medical tourism has been developing since 2000. By 2019, 14% of the total income from tourism in the country belongs to medical tourism. According to Saxstat data, by 2022 it is expected to increase to 30%. Due to the natural and climatic diversity and territorial location of Georgia, it is possible to develop it as a branded product with high tourist potential. In the Caucasus region and beyond, there are mountain and sea resort zones in one "space", which .In general, they represent the best infrastructural environment for carrying out treatment and rehabilitation measures. To date, Georgia has registered about 200 resort zones, about 100 for medical purposes - specific air, waters, sands, mud, medicinal plants. According to WHO definition, medical tourism is the purposeful migration of those who want to receive recreation and treatment, complex high-tech services. Balneological-resort direction has one of the oldest and historical potentials in Georgia. It originated at the turn of the 19th century. Tbilisi, Borjomi, Sairme, Tskaltubo, Nunis, Ureki, Grigoleti, Upsira, Tsaishi, Tsikhisdziri, Tsemi, Tsaghveri, Shovi, Java and many others are worth mentioning among the balneological resorts. In Georgia, there are about 2000 mineral springs, whose Among them, carbonated mineral waters are the most common. Factors hindering the development of medical tourism. In order to maximize the potential of medical tourism in Georgia, it is necessary to analyze the hindering factors that prevent its development. Development of medical tourism is hindered by: poor infrastructure. Problems in the transport system, unsatisfactory sanitary-hygienic conditions. Informative and insufficient advertising activities, inconsistency of the legal base with European standards, less activities of tourist agencies, and many other elements. Based on the retrospective analysis conducted by us, the need for the development of medical tourism was highlighted.



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**ROLE OF NURSES IN IMPLEMENTING INNOVATIVE PROJECTS IN PRIMARY HEALTHCARE SECTOR**

***Miranda Jankhoteli***

*PHD student of business Administration, Tbilisi, Georgia*

***Natalia Tchanturia***

*GTU, Associate Professor of the Department of Business Administration, Tbilisi, Georgia*

***Maka Buleishvili***

*SEU, Faculty Medicine, Associate professor, Tbilisi, Georgia*

***Todadze Murtazi***

*GTU, PHD student of business Administration, Tbilisi, Georgia*

**ABSTRACT**

The basis to improve medical, social and economic efficiency of healthcare system functioning, are rational implementation of innovative technologies of treatment of diseases, diagnostics, prevention and rehabilitation; improvement of management of medical personnel of healthcare institutions at all level and professional training. Innovative approaches play a decisive role in the progressive development of every sector of economy, including the healthcare sector. Among the ongoing reforms in the healthcare sector of Georgia, formation of the activity of medical personnel with secondary education is remarkable, which is preconditioned by negative tendencies of the public health: prevalence of chronic diseases and the mortality of the population is increasing, while life expectancy is significantly shorter than in developed countries. Psycho-emotional tension, decline in level and quality of life are accompanied by worsening of the public healthcare indicators, increasing of morbidity and mortality, changes of pathological characteristics, increasing number of social and infectious diseases. It is obvious, that existing circumstances are result of inadequate assessment of the importance of preventive work with the population and communication, namely, inadequate attention paid to medical examinations. With the nursing reform, the role of a community nurse is dramatically increasing in the medical examination of the population – s/he practices as an independent specialist, who fulfills unique duties by taking into consideration deontological and legal principles. It should be noticed that the role of the nurse personnel is not adequately evaluated and appreciated in a clinical examination, and therefore, their potential is far from being fully used. Organized and high quality, flexible and dynamic work of mid and junior level medical personnel, is a main indicator of efficiency of a doctor or, in general, a clinic.

The article examines main, efficient and safe approaches of implementation of innovative technologies in the primary healthcare institutions. Elaborating of efficient and innovative models of healthcare institutions, which are oriented to the needs of local communities, is substantiated.

**Key words:** primary healthcare, migration, role of nurses, innovative projects.

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**THE SIGNIFICANCE OF POST-OPERATIVE BRACING IN PREVENTING KNEE ARTHROFIBROSIS AFTER ACL RECONSTRUCTION**

***Valeri Akhalkatsi***

*Tbilisi State Medical University, Faculty of Physical Medicine and Rehabilitation, Department of Physical Medicine, Clinical Center of Sports Medicine and Rehabilitation, Tbilisi, Georgia*

***Marine Matiashvili***

*Tbilisi State Medical University, Faculty of Physical Medicine and Rehabilitation, Department of Physical Medicine, Clinical Center of Sports Medicine and Rehabilitation, Tbilisi, Georgia*

***Lela Maskhulia***

*Tbilisi State Medical University, Faculty of Physical Medicine and Rehabilitation, Department of Physical Medicine, Clinical Center of Sports Medicine and Rehabilitation, Tbilisi, Georgia*

*ORCID ID: 0000-0002-8893-374X*

**ABSTRACT**

High-energy injuries of the knee joint can cause ligament damage which may have complications in 4-6% of all cases in the form of movement limitation and arthrofibrosis. There are several intra- and extraarticular factors that could be closely connected with formation of arthrofibrosis. One of the most important factor is the utilization of knee brace as the means of immobilization during the post-operative period. There are various opinions on the matter of using a knee brace after an anterior cruciate ligament(ACL) reconstruction surgery. For instance, 85% members of the American Orthopedic Society for Sports Medicine (AOSSM) support and utilize this method. Despite the fact that movement limitations in the affected joint are rare after the aforementioned surgical procedure, the issue of preventing and eliminating knee extension deficit during the post-operative period is still relevant. The following research is based on the evaluation of the findings in 22 patients with extension deficits 2 weeks after arthroscopic ACL reconstruction surgery and it studies the effectiveness of knee brace in eliminating extension limitation during a 3-week rehabilitation period. After implementation of 5-week rehabilitation program, function of quadriceps muscle was equally improved in all patients, and at the same time, undesired effect of utilization of the knee brace during 3 weeks on the functional status of the quadriceps muscle was modest and didn't exceed 6.4%.

The results of the above mentioned research showed that utilization of knee brace in the rehabilitation process during 3 weeks is significantly effective method ( $P < 0.008$ ) for eliminating knee extension deficit in a way that the negative influence on the function of the quadriceps muscle of the affected limb stays negligible.

**Keywords:** knee injury, arthrofibrosis, knee brace.

**THE NEED TO MAINTAIN A HEALTHY WAY OF LIFE TO ENSURE THE PHYSICAL AND MENTAL HEALTH OF THE POPULATION**

*Marina shakarashvili, manana abuladze, devi tabidze, levan baramidze*

**ABSTRACT**

According to the data of the World Health Organization "WHO", human health is determined: 50-55% by following a healthy way of life, 25% by environmental conditions, 15% by genetic factors and 5% by the activity of the healthcare system. A healthy lifestyle is a way of promoting a person's life, which aims to promote health. It is also considered as the basis of disease, mortality prevention and life expectancy increase. A healthy lifestyle includes all those elements of behavior aimed at improving individual and public health. The research shows that promotion of a healthy lifestyle in Georgia should be strengthened as the primary value of health, prevention of bad habits and unhealthy behavioral attitudes. At present, a large part of the population is unaware of the positive and negative effects of a healthy lifestyle and bad habits. Based on the relevance of the problem, the aim of the work and the task of the research is the physical and mental health of a person, which is an integral part of health. As it is known from the definition of health - health is complete physical, mental and social well-being. It is important to correctly analyze the state of health, which unconditionally reflects the ability of the body to adapt to the living environment. During physical and mental health of a person, there are no violations of structural, functional and adaptive mechanisms. . Studies have established that during the onset of the disease, there is a decrease in the functional states of the organism, exhaustion, which has a direct impact on the physical and mental state of a person. Jano defined the criteria of adequacy of physical and mental health: adequate perception of a person, presence of adequate reactions to environmental factors, adequacy of actions committed by a person and the ability to adequately manage actions (response and reaction). Within the framework of the sociological research conducted by us, the following were clearly identified: 1. 723 citizens were interviewed through the social network during the research process. 2. The age distribution is: 1st group - 19-35 years, 2nd group - 55-65 years and the third group is people over 65 with chronic pathologies and under the supervision of a doctor. 3. Only 42% of the surveyed population is interested in and follows a healthy lifestyle. 4. 62% of the population suffers from various types of physical and mental disorders. 5. There is a real need to fill the lack of information in the population. 6. Unhealthy habits of life - tobacco of harmful habits are revealed. Alcohol, drugs, unhealthy diet, unsportsmanlike lifestyle and high percentage of other factors. 7. Avoidance of active involvement of governmental and non-governmental sectors in solving the problem. 8. Activation of information media in promotion of a healthy way of life. All this will actually reduce the statistical data of physical and mental health disorders in the population.

*„ Physical and mental health It is an integral part of health“*

**COVID-19 PANDEMİ SÜRECİNDE SAĞLIK ÇALIŞANLARININ ŞİDDETE MARUZ KALMA DURUMLARI: ŞANLIURFA ÖRNEĞİ**

**EXPOSURE OF HEALTHCARE PROFESSIONALS TO VIOLENCE DURING THE COVID-19 PANDEMIC PROCESS: THE CASE OF SANLIURFA**

**Dr. Öğr. Üyesi Hüseyin ERİŞ**

*Harran Üniversitesi Sağlık Hizmetleri MYO*

*ORCID ID: 0000-0002-1685-9819*

**Doç. Dr. Hasan BÜYÜKASLAN**

*Harran Üniversitesi Tıp Fakültesi*

*ORCID ID: 0000-0002-4714-7347*

**Öğr. Gör. Feray BUCAK**

*Harran Üniversitesi Sağlık Bilimleri Fakültesi*

*ORCID ID: 0000-0002-2453-8310*

**Dr. Aslı KAYA**

*Bursa Ali Osman Sönmez Onkoloji Hastanesi*

*ORCID ID: 0000-0001-6818-3868*

**ÖZET**

Bu araştırma, Şanlıurfa’da kamu, üniversite, özel hastaneler, Aile Sağlığı Merkezleri ve 112’de görev yapan sağlık çalışanlarının pandemi döneminde en az bir kez sözel, fiziksel ve cinsel şiddet türlerinden birine maruz kalıp kalmadıklarını ve bu durumda kalan sağlık çalışanlarının yaşadıkları süreci tespit etmek amacıyla yapılmıştır. Araştırma 01.02.2022 – 30.03.2022 tarihleri arasında yapılmış ve araştırmaya toplamda 408 sağlık çalışanı katılmıştır. Araştırmanın güvenilirlik düzeyi 0,861 olarak yüksek güvenilir olarak tespit edilmiştir. Araştırmaya katılan 408 sağlık çalışanından %81,1’i (331 kişi) meslek hayatında şiddete maruz kaldıklarını ifade etmişlerdir. covid-19 pandemi sürecinde ise şiddete uğrayanların oranı %70,4 (234 kişi) olarak tespit edilmiştir. Araştırmaya katılan sağlık çalışanlarının %71,6’sı ( 237 kişi) son bir yıl içerisinde şiddete uğradıklarını belirtmişlerdir. En çok sözlü şiddet (%65,3) gördüklerini, şiddeti genelde hasta yakınlarından ve erkeklerin yaptıklarını ifade etmişlerdir. Ayrıca 112 çalışanı, hastane personeli ile kendi çalıştığı gölümdeki personelden de şiddete maruz kaldıklarını belirtmişlerdir. Sağlık çalışanlarının şiddete uğradıktan sonra hastane yönetiminin genelde yanlarında durmadıklarını, şikayetçi olmalarına rağmen şiddet uygulayan kişilerin serbest kaldıklarını ve herhangi bir yaptırımın olmadığını belirtmişlerdir.

**Anahtar Kelimeler:** Covid-19 Pandemi, Sağlıkta Şiddet, Sağlık Çalışanları

**ABSTRACT**

This research aims to determine whether healthcare professionals working in public, university, private hospitals, Family Health Centers and 112 in Şanlıurfa have been exposed to one of the types of verbal, physical and sexual violence at least once during the pandemic period and the process experienced by healthcare professionals who remain in this situation. was made to do so. The research was carried out between 01.02.2022 – 30.03.2022 and a total of 408 health workers participated in the research. The reliability level of the study was determined as 0.861 and high reliability. 81.1% (331 people) of 408 health workers who participated in the research stated that they were exposed to violence in their professional life. In the covid-19 pandemic process, the rate of those who have been subjected to

violence has been determined as 70.4% (234 people). 71.6% (237 people) of the health workers who participated in the research stated that they had been subjected to violence in the last year. They stated that they were mostly exposed to verbal violence (65.3%), mostly by the relatives of the patients and by men. In addition, 112 employees stated that they were exposed to violence from the hospital staff and the staff in the lake where they worked. They stated that the hospital management usually did not stand by the healthcare workers after they were subjected to violence, and that despite their complaints, the perpetrators were released and there was no sanction.

**Key Words:** Covid-19 Pandemic, Violence in Health, Healthcare Professionals

## **GİRİŞ**

Şiddet ilkçağlardan beri insanoğlunun maruz kaldığı ve bu durumdan oldukça rahatsız olup hatta ölümüne neden olan bir zorbalıktır. Şiddet kavramının genel kabul görmüş bir tanımını yapmak oldukça zordur. Şiddet Dünya Sağlık Örgütü tarafından genel bir tanımla “*kendisine, başka bir kimseye, bir gruba veya topluluğa kasti olarak yönelmiş fiziki gücün; yaralanma, ölüm, psikolojik zarar, körelme veya mahrumiyet ile sonuçlanmış veya yüksek sonuçlanma ihtimali oluşturması*” olarak tanımlanabilir (DSÖ, 1998). Başka bir tanımda ise şiddet; kişinin kendisine ya da bir başkasına, gruba veya topluluğa yönelik olarak yaralama, ölüm, psikolojik zarar, gelişimsel bozukluğa yol açabilecek fiziksel zorlama, ya da tehdidin amaçlı olarak uygulanması olayıdır (Bıçkıcı, 2013).

Şiddet türlerine bakıldığında genelde 3 şekilde tanımlanmaktadır (Yıldız ve Arkadaşları, 2011):

1. Kişinin kendisine uyguladığı şiddet
2. Kişiler arası şiddet
3. Toplu şiddet

Şiddetin içeriğine bakıldığında ise fiziksel, cinsel, psikolojik ve ihmal gibi boyutları olduğu görülmektedir (DSÖ, 1998).

Uluslararası Çalışma Örgütü (ILO) tarafından işyerinde şiddet tanımı ise “Çalışanların işe gidiş gelişini de kapsayacak şekilde işleriyle ilgili uğradıkları; sağlık, güvenlik ve refahlarına doğrudan veya dolaylı şekilde yönelen suiistimal, tehdit ve saldırı” şeklinde yapılmıştır (ILO 2002).

Son yıllarda özellikle covid-19 pandemi sürecinde Sağlık kurumlarında artan işyükünün yanısıra, hasta ve yakınları tarafından uygulanan şiddetin giderek yaygınlaştığı görülmektedir. Bu şiddetin yayılması ise ciddi bir halk sağlığı ve iş güvenliği sorunu haline gelmekte, sağlık hizmetlerinin aksaması ve diğer sağlık talebinde bulunan hastaların zamanında sağlık hizmeti alamaması gibi sorunlara yol açtığı görülmektedir (Yıldız, 2019). Covid-19 pandemi sürecinde sağlık çalışanlarına yönelik şiddetin başlıca nedenleri bakıldığında şunlar sıralanabilir (Bıçkıcı, 2013; Ayrancı ve Arkadaşları, 2012; Er ve Arkadaşları, 2021)

- Muayene olmak için uzun bekleme süreleri,
- Hasta ve yakınlarının talepleri
- Hasta ve yakınlarının eğitim seviyelerinin düşük olması,
- Sağlık personelinin işyükünün fazla olması nedeniyle zamanının kısıtlı olması,
- Uzun mesai süreleri,
- Hasta ve yakınları ile iletişim problemleri,
- Sağlık personeli sayısının yetersizliği,
- Basında çıkan provakatif haberler,
- Güvenlik ve polis gücünün yetersiz oluşu,
- Hastane Yönetimlerinin pasifliği,

## **METOD**

### **Araştırmanın Amacı**

Bu araştırmanın amacı, Şanlıurfa’da kamu, üniversite, özel hastaneler, Aile Sağlığı Merkezleri ve 112’de görev yapan sağlık çalışanlarının pandemi döneminde en az bir kez sözel, fiziksel ve cinsel şiddet türlerinden birine maruz kalıp kalmadıklarını ve bu durumda kalan sağlık çalışanlarının yaşadıkları süreci tespit etmektir.

### **Araştırmanın Evreni ve Örneklemi:**

Araştırmanın evrenini Şanlıurfa’da şehir merkezinde yer alan devlet, üniversite ve özel hastanelerde çalışan yaklaşık 5.000 civarındaki personel oluşturmaktadır. Çalışmada basit tesadüfi örneklem yöntemi ile 0,95 güven düzeyi ve 0,05 güven aralığında 377 kişi, araştırmanın örnekleme olarak hesaplanmıştır. Araştırma 01.02.2022 – 30.03.2022 tarihleri arasında yapılmıştır. Araştırmaya toplamda 408 sağlık çalışanı katılmıştır.

### **Veri Toplama Aracı**

Sağlık çalışanlarının Covid-19 pandemi sürecinde şiddete maruz kalıp kalmadıklarını tespit etmek amacıyla literatür taramaları sonucunda hazırlanan 16 ifadeden oluşan bir ankete kullanılmıştır. Ayrıca sağlık çalışanlarının sosyo demografik özelliklerini belirleyebilmek amacıyla 9 adet soru sorulmuştur.

Araştırmada elde edilen veriler SPSS istatistik programı ile analiz edilecektir. Analizlerde yüzde, tanımlayıcı istatistikler kullanılmıştır. Araştırmada kullanılan “Çalışan Sadakati Ölçeği”nin Cronbach's Alpha katsayısı 0,861 olarak tespit edilmiştir.

## **BULGULAR**

Araştırmanın bu bölümünde elde edilen bulgulara yer verilmiştir. Tablo 1’de sağlık çalışanlarına ait sosyo demografik özelliklerine yer verilmiştir.

**Tablo 1. Sağlık Çalışanlarının Sosyo Demografik Özellikleri**

	<b>Gruplar</b>	<b>Sayı</b>	<b>Yüzde</b>
<b>Cinsiyet</b>	Kadın	207	50,7
	Erkek	201	49,3
	<b>Toplam</b>	408	100,0
<b>Yaş Grupları</b>	30 yaş veya altı	214	52,5
	31 yaş veya üstü	194	47,5
	<b>Toplam</b>	408	100,0
<b>Medeni Durum</b>	Bekar	171	41,9
	Evli	237	58,1
	<b>Toplam</b>	408	100,0
<b>Eğitim Durumu</b>	Lise	42	10,3
	Önlisans	65	15,9
	Lisans	190	46,6
	Yüksek Lisans	83	20,3
	Doktora	28	6,9
	<b>Toplam</b>	408	100,0
<b>Çalışılan Hastane</b>	Üniversite	169	41,4
	Devlet	140	34,3
	ASM/Tıp Merkezi	61	15,0
	Özel	18	4,4
	112 Acil	20	4,9
	<b>Toplam</b>	408	100,0
<b>Meslek Grupları</b>	Doktor	121	29,7
	Hemşire	64	15,7
	Hemşire/Ebe	132	32,4
	İdari Personel	51	12,5

	Acil Tıp Tek. / Paramedik / laboratuvar ve radyoloji teknisyeni	40	9,8
	<b>Toplam</b>	408	100,0
<b>Çalışma Süresi</b>	7 yıl veya altı	221	54,2
	8 yıl veya üstü	187	45,8
	<b>Toplam</b>	408	100,0
<b>Birim</b>	Poliklinik	114	27,9
	Yataklı Servis	125	30,6
	Acil Servis	118	28,9
	Diğer	51	12,5
	<b>Toplam</b>	408	100,0
<b>Meslek Hayatınızda Şiddete Maruz Kalma</b>	Evet	331	81,1
	Hayır	77	18,9
	<b>Toplam</b>	408	100,0

Araştırmaya katılan sağlık çalışanlarının %50,7'si kadın ve %52,5'i 30 yaş ve altı grupta yer almaktadır. Sağlık çalışanlarının %58,1'i evli ve %46,6'sı lisans mezunudur. Çalışanlarının %41,4'ü üniversite hastanesinde çalıştıklarını ve %32,4'ü hemşire, %29,7'si ise hekim olduğu belirlenmiştir. Çalışma süreleri bakımından %54,2'si 7 yıl ve altı grubunda yer almaktadır. Sağlık çalışanlarının %30,6'sı yataklı servislerde, %28,9'ü ise acil serviste çalıştıklarını ifade etmişlerdir. Araştırmaya katılan 408 sağlık çalışanından %81,1'i (331 kişi) meslek hayatında şiddete maruz kaldıklarını ifade etmişlerdir.

Tablo 2'de araştırmaya katılan sağlık çalışanlarının karşılaştıkları şiddet süreci ile ilgili bilgiler verilmiştir.

**Tablo 2. Sağlık Çalışanlarının Karşılaştıkları Şiddet Süreci**

		<b>Sayı</b>	<b>Yüzde</b>
<b>Pandemi döneminde şiddete maruz kalma</b>	Evet	234	70,7
	Hayır	97	29,3
	<b>Toplam</b>	331	100,0
<b>Son 1 yılda şiddete maruz kalma</b>	Evet	237	71,6
	Hayır	94	28,4
	<b>Toplam</b>	331	100,0
<b>Şiddet Türü</b>	Sözlü Şiddet	216	65,3
	Fiziksel Şiddet	7	2,1
	Hem Fiziksel Hem de sözel şiddet	98	29,6
	Hiç şiddete maruz kalmadım	10	3,0
	<b>Toplam</b>	331	100,0
<b>Şiddeti uygulayan</b>	Hasta Yakını	256	77,3
	112 Çalışanı	4	1,2
	Hastane Personeli	2	0,6
	Hasta	40	12,1
	Orada bulunan herhangi bir kişi veya grup	10	3,0
	Kendi Çalıştığım Bölüm Personeli	12	3,6
	Şiddete Maruz Kalmadım	7	2,1
	<b>Toplam</b>	331	100,0
<b>Şiddet uygulayanın cinsiyeti</b>	Erkek	280	84,6
	Kadın	43	13,0
	Şiddete Maruz Kalmadım	8	2,4
	<b>Toplam</b>	331	100,0
<b>Fiziksel şiddet türü</b>	Yumruk, tekme, tokat, ısırma, tükürme, Kafa Atma, Boğazımı Sıkma	38	11,5
	Sözlü şiddet	31	9,4

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	Fiziksel Şiddete Maruz kalmadım	154	46,5
	Etraftaki nesnelere fırlatma	49	14,8
	Sertçe itip kalkma	37	11,2
	El-kol bükme	19	5,7
	Kesici alet ile saldırma	1	0,3
	Mobbing	2	0,6
	Toplam	331	100,0
<b>Fiziksel şiddet uygulayan sayısı</b>	1 Kişi	60	18,1
	2 Kişi	53	16,0
	3 Kişi	20	6,0
	4 Kişi ve üzeri	53	16,0
	Şiddete Maruz Kalmadım	145	43,8
	Toplam	331	100,0
<b>Sözlü şiddet türü</b>	Bağırarak/Hakaret/Aşağılamak	206	62,2
	Tehtid Etmek	73	22,1
	Küfür Etmek	49	14,8
	Sözel Şiddete Maruz Kalmadım	3	0,9
	Toplam	331	100,0
<b>Sözlü Şiddet uygulayan sayısı</b>	1 Kişi	48	14,5
	2 Kişi	73	22,1
	3 Kişi	41	12,4
	4 Kişi ve üzeri	168	50,8
	Şiddete Maruz Kalmadım	1	0,3
	Toplam	331	100,0
<b>Yaralanma türü</b>	Psikolojik travma yaşadım	175	52,9
	Kas/doku zedelenmesi oldu	12	3,6
	Vücudumda morluklar oluştu	14	4,2
	Vücudumda kesiler oluştu	2	0,6
	Vücudumda kırıklar oluştu	3	0,9
	Herhangi bir yaralanma olmadı	125	37,8
	Toplam	331	100,0
<b>Tedavi türü</b>	Ayaktan tedavi gördüm	46	13,9
	Herhangi bir tedavi görmedim	283	85,5
	Yatarak Tedavi Gördüm	2	0,6
	Toplam	331	100,0
<b>Şiddete karşı tutum</b>	Sözlü karşılık verdim	68	20,5
	Kendimi fiziksel olarak savundum	57	17,2
	Beyaz kod verdim (Alo 113'e bildirdim)	78	23,6
	Hukuki yollara başvurdum	12	3,6
	Yönetime bildirdim	34	10,3
	Karşılık vermeden işime devam ettim	69	20,8
	Kolluk kuvvetlerine bildirdim	13	3,9
	Toplam	331	100,0
<b>Şiddete verilen tepki</b>	Şiddete Uğramadım	10	3,0
	Şikayetçi oldum	115	34,7
	Şikayetçi olmadım	206	62,2
	Toplam	331	100,0
<b>Şikayetin sonucu</b>	Üzerini kapattılar	54	16,3
	Dava devam ediyor	17	5,1
	Şikayetçi olduğuma pişman oldum	21	6,3
	Şiddet uygulayan kişi ceza almadı	49	14,8
	Şiddet uygulayan kişiyi serbest bıraktılar	27	8,2



	Şiddet uygulayan kişiye tatmin edici bir ceza verildi	8	2,4
	Cevapsız	155	46,8
	Genel Toplam	331	100,0
<b>Şiddete maruz kaldığınızda yönetimin desteği</b>	Evet	84	25,4
	Hayır	166	50,2
	Bazen	81	24,5
	Toplam	331	100,0
<b>Şiddetin olumsuz etkisi</b>	Şiddet ile ilgili anıların tekrarlaması var	2	0,6
	Sürekli hastalar ve yakınları tarafından şiddete uğrayacağım kaygısı oluştu	38	11,5
	Bu mesleği (sağlıkçı) seçtiğime pişman oldum	109	32,9
	Çalışma motivasyonum azaldı	109	32,9
	Yaşam ve insan sevgim azaldı	39	11,8
	Görev yerimi değiştirdim	5	1,5
	Kendimi suçladım	3	0,9
	Kendime zarar vermeyi düşündüm	1	0,3
	Herhangi bir olumsuz etki oluşmadı	22	6,6
	Bir başkasına zarar vermeyi düşündüm	1	0,3
	Cevapsız	2	0,6
	Genel Toplam	331	100,0

Tablo 2’de araştırmaya katılan sağlık çalışanlarının karşılaştıkları şiddet ve tedavileri hakkındaki düşüncelerine yer verilmiştir. Araştırmaya katılan sağlık çalışanlarının %70,7’si pandemi döneminde şiddete maruz kaldığını, %71,6’sının son bir yıl içerisinde şiddet gördüğünü belirtmişlerdir.

Sağlık çalışanlarının %65,3’ü sözlü şiddet, %29,6’sı ise hem fiziksel hem sözlü şiddet gördüklerini ifade etmişlerdir. Şiddeti uygulayanların %77,3 oranında hasta yakınları ve %84,6’sının erkekler olduğu belirlenmiştir.

Fiziksel şiddet türü olarak en fazla etraftaki nesnelere fırlatma oranı %14,8 ve %11,5 ile yumruk, tekme, tokat atma, ısırma gibi fiziksel şiddete maruz kaldıklarını ifade etmişlerdir. Fiziksel şiddet uygulayan kişi sayısı bakımından en fazla %18,1 ile bir ve %16 ile 2 kişi olduğu belirtilmiştir.

Sözlü şiddete maruz kalma bakımından sağlık çalışanlarının %62,2’si bağırma, hakaret/aşağılanmaya maruz kalmışlardır. Sözlü şiddet uygulayanların sayısı bakımından en fazla %50,8 ile 4 kişi ve üzeri grup yer almaktadır. Ayrıca sağlık çalışanlarının yaralanma türü açısından %52,9’u psikolojik travma yaşadıklarını belirtmişlerdir.

Sağlık çalışanlarının %85,5’i herhangi bir tedavi görmediğini ve %13,9’unun ise ayakta tedavi gördüğünü belirtmişlerdir.

Şiddete maruz kalan sağlık çalışanlarının %23,6’sı beyaz kod vermiş, %20,5’i sözlü karşılık ve %17,2’si ise kendilerini fiziksel olarak savunmuşlardır.

Sağlık çalışanlarının %34,7’si uğradıkları şiddet karşısında şikayetçi olduklarını belirtmişlerdir. Bu şikâyetlerinin sonucunda ise %16,3’ü dosyanın üzerinin kapatıldığını ve %14,8’i ise şiddet uygulayan kişinin ceza almadığını belirtmişlerdir.

Diğer önemli bir konu ise şiddete maruz kalan sağlık çalışanlarının %50,2’si hastane yönetiminin desteğini görmediklerini, %25,4’ü ise yönetim desteği gördüklerini belirtmişlerdir.

Sağlık çalışanlarının %32,9’u bu mesleği seçtiklerine pişman olduklarını ve yine 32,9’u çalışma motivasyonlarının azaldığını ifade etmişlerdir.

**Tablo 3. Sağlık Çalışanlarının Şiddet Nedenleri ve Önlemleri Hakkında Düşünceleri**

		Sayı	Yüzde
<b>Şiddetin nedeni</b>	Şiddeti kendinde hak görme	127	31,1
	Hastalık psikolojisi	49	12,0
	Kötü iletişim, yanlış anlama	22	5,4
	Aşırı iş yoğunluğu	32	7,8
	Genel olarak izlenen sağlık politikaları	90	22,1
	İhmal edildiğini düşünme	28	6,9
	Tedaviden memnuniyetsizlik	24	5,9
	Uzun bekleme süreleri	24	5,9
	Kötü haber alma	12	2,9
	Toplam	408	100,0
<b>Şiddete karşı güvenlik önlemleri</b>	Her zaman yeterli	19	4,7
	Bazen yeterli	141	34,6
	Hiçbir zaman yeterli değil	248	60,8
	Toplam	408	100,0
<b>Şiddete karşı kolluk önlemleri</b>	Her zaman alınır	46	11,3
	Bazen alınır	201	49,3
	Hiçbir zaman alınmaz	161	39,5
	Toplam	408	100,0

Tablo 3’de araştırmaya katılan sağlık çalışanlarının şiddet nedenleri ve önlemleri hakkındaki düşüncelerine yer verilmiştir. Sağlık çalışanları şiddete uğrama nedeni olarak, %31,1’i insanların şiddeti kendilerinde hak olarak gördüklerini ve %22,1’i ise genel olarak izlenen sağlık politikalarının sonucu olduğunu düşünmektedirler. Sağlık çalışanları şiddete karşı alınan güvenlik önlemlerinin hiçbir zaman yeterli olmadığını ifade etmişlerdir. Şiddete karşı kolluk önlemlerinin ise yine büyük bir çoğunluk tarafından alınmadığı belirtilmiştir.

### **Sonuç ve Öneriler**

Bu araştırma, Şanlıurfa’da kamu, üniversite, özel hastaneler, Aile Sağlığı Merkezleri ve 112’de görev yapan sağlık çalışanlarının pandemi döneminde en az bir kez sözel, fiziksel ve cinsel şiddet türlerinden birine maruz kalıp kalmadıklarını ve bu durumda kalan sağlık çalışanlarının yaşadıkları süreci tespit etmek amacıyla yapılmıştır. Araştırma 01.02.2022 – 30.03.2022 tarihleri arasında yapılmış ve araştırmaya toplamda 408 sağlık çalışanı katılmıştır. Araştırmanın güvenilirlik düzeyi 0,861 olarak yüksek güvenilir olarak tespit edilmiştir.

Araştırmaya katılan 408 sağlık çalışanından %81,1’i (331 kişi) meslek hayatında şiddete maruz kaldıklarını ifade etmişlerdir. covid-19 pandemi sürecinde ise şiddete uğrayanların oranı %70,4 (234 kişi) olarak tespit edilmiştir. Araştırmaya katılan sağlık çalışanlarının %71,6’sı (237 kişi) son bir yıl içerisinde şiddete uğradıklarını belirtmişlerdir. En çok sözlü şiddet (%65,3) gördüklerini, şiddeti genelde hasta yakınlarından ve erkeklerin yaptıklarını ifade etmişlerdir. Ayrıca 112 çalışanı, hastane personeli ile kendi çalıştığı bölümdeki personelden de şiddete maruz kaldıklarını belirtmişlerdir.

Sağlık çalışanlarının şiddete uğradıktan sonra hastane yönetiminin genelde yanlarında durmadıklarını, şikayetçi olmalarına rağmen şiddet uygulayan kişilerin serbest kaldıklarını ve herhangi bir yaptırım olmadığını belirtmişlerdir.

Sağlık çalışanları, şiddete uğrama nedeni olarak, %31,1’i, hasta yakınlarının şiddeti kendilerinde hak olarak gördüklerini ve %22,1’i ise genel olarak izlenen sağlık politikalarının sonucu olduğunu düşünmektedirler. Sağlık çalışanları şiddete karşı alınan güvenlik önlemlerinin hiçbir zaman yeterli olmadığını ifade etmişlerdir. Şiddete karşı kolluk kuvvetleri tarafından alınan önlemlerinin ise büyük bir çoğunluk tarafından, alınmadığı veya yetersiz olduğu belirtilmiştir.

Özellikle normal dönemlerde Şanlıurfa ilindeki kaynak yetersizliği nedeni ile sağlık hizmetlerinde yaşanan sorunlar yüzünden, hasta ve yakınları tarafından muhatap olarak sağlık çalışanları doğrudan hedef olarak alınmakta ve hasta psikolojisi ile sağlık çalışanlarına yönelik doğrudan sözlü veya fiziksel şiddet uygulanmaktadır.

Bu verilerden sonra alınması gereken tedbirleri şu şekilde sıralayabiliriz:

- Sağlık Bakanlığı tarafından Şanlıurfa'daki özellikle eksik olan nitelikli sağlık insangücü sayısı artırılarak ve yeni sağlık tesisleri açılarak, insanların sağlık hizmetlerine ulaşmada yaşadıkları sorunların ortadan kaldırılması,
- Sağlık kurumlarında yeteri kadar güvenlik görevlisi ile hastane polisi veya jandarma personelinin bulundurulması,
- Sağlık çalışanlarına yönelik şiddeti engelleyecek yeni ceza kanunlarının çıkarılması,

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**THE IMPACT OF GUT MICROBIOTA ON PSORIASIS AND PATHOGENESIS**

***Major Gheorghe GIURGIU<sup>1</sup>***

*<sup>1</sup>Deniplant-Aide Sante Medical Center, Biomedicine, Bucharest, Romania*

*ORCID ID: 0000-0002-5449-2712*

***Prof. dr. Manole COJOCARU<sup>2</sup> SciRes I, EuSpLM***

*<sup>2</sup>Titu Maiorescu University, Faculty of Medicine, Bucharest, Romania*

*ORCID ID: 0000-0002-7192-7490*

**Background** A growing body of evidence highlights that intestinal dysbiosis is associated with the development of psoriasis. The gut-skin axis is the novel concept of the interaction between skin diseases and microbiome through inflammatory mediators, metabolites and the intestinal barrier. The gut microbiome affects skin homeostasis through its influence on the signaling pathways that coordinate epidermal differentiation.

The objective of this study was to synthesize current data on the Deniplant nutritional factors in patients with psoriasis.

**Materials and methods** All studies confirmed the association of psoriasis and gut microbiota dysbiosis. We describe the recent advances regarding the interplay between gut microbiota and the skin. Thus, the microbiome can be considered an effective therapeutical target for treating this disorder.

**Results** This presentation provides a detailed and comprehensive systematic study regarding gut microbiome in patients with psoriasis. These results are supported by clinical observations based on a case serie showing improvement in psoriatic skin lesions after Deniplant nutritional factors. It is still not clear whether psoriasis is an effect or a cause of the observed disbalance between beneficial and pathogenic microbes. In this context, the study provides very interesting results, showing significantly greater changes in the gut microbiome of patients with psoriasis after Deniplant nutritional factors.

**Conclusion** There is a significant association between alterations in gut microbial composition and psoriasis. Gut dysbiosis is a state of imbalanced gut microbiome that eventually has a negative impact on skin function and integrity. Deniplant nutritional factors are a potential therapeutic strategy in psoriatic disease.

**Keywords:** dysbiosis, gut microbiome, psoriasis, gut-skin axis, Deniplant nutritional factors

**CLINICAL SYMPTOMS AND CARE BEHAVIORS USED BY NURSES TO IDENTIFY CHANGES IN THE CONDITIONS OF THEIR PATIENTS**

**HEMŞİRELERİN BAKIM VERDİĞİ HASTALARININ DURUMLARINDAKİ DEĞİŞİKLİKLERİ TANIMLAMAK İÇİN KULLANDIĞI KLİNİK BELİRTİLER VE BAKIM DAVRANIŞLARI**

*Halil İbrahim TUNA<sup>1</sup>*

*<sup>1</sup>Selçuk Üniversitesi Akşehir Kadir Yallagöz SYO, Hemşirelik, Konya, Türkiye*

*<sup>1</sup>ORCID ID: 0000-0003-2119-5874*

*Pınar TUNÇ TUNA<sup>2</sup>*

*<sup>2</sup>Selçuk Üniversitesi Akşehir Kadir Yallagöz SYO, Hemşirelik, Konya, Türkiye*

*<sup>1</sup>ORCID ID: 0000-0001-8559-8774*

**ABSTRACT**

Early recognition of changes in a patient's clinical status enables appropriately targeted care that protects patients from adverse events and promotes recovery. If precautions are not taken by nurses, it can cause many adverse events, including worsening of patients' medical conditions, unplanned hospitalization for intensive care, cardiac arrest, and sudden death. This cross-sectional study aims to determine the clinical symptoms and care behaviors of nurses working in internal and surgical clinics that occur in their patients during their daily patient care and enable them to understand that their health status has changed. The sample of the study was determined by the proportional quota method and the sample consisted of a total of 320 nurses who accepted to participate in the research and filled out the questionnaires between March 2022 and June 2022. The data were collected with the sociodemographic information form developed by the researcher and the patient clinical change form and care behavior scale created by the researcher through literature review. Data analysis was done with SPSS 23.0. Descriptive data are presented as numbers (n), mean and percentage (%). It was determined that 32.8% of the nurses work in intensive care units and 65.6% of them work in chest disease clinics. It was determined that nurses working for 10 years or more were the highest with 30.9%. When the nurses' care behavior scale score averages were examined, it was determined that all scale scores were close to or at the average value. It was determined that the nurses used blood sugar changes with a maximum of 67.5% among the clinical change symptoms in their caregivers, and used the oxygenation status with a minimum of 2.2%. As a result, it was determined that nurses often used basic physical examination methods and objective findings for the clinical status determination of the patients under their care. It is clearly stated in the literature that vital signs should be measured routinely and patients should be evaluated further with a physical examination. Monitoring blood sugar changes plays an important role in nurses' evaluation of patients. Our findings are similar to the literature in this respect.

**Keywords:** acute care, clinical deterioration, cues, nurses, nursing assessment, vital signs systematic review patient safety.

**ÖZET**

Bu kesitsel araştırmanın amacı dahili ve cerrahi kliniklerde görev yapan hemşirelerin günlük hasta bakımları sırasında hastalarında ortaya çıkan ve onların sağlık durumunun değiştiğini anlamalarını sağlayan klinik belirtilerin ve bakım davranışlarının belirlenmesidir. Araştırmanın örneklemi, orantılı kota yöntemi ile belirlenmiştir ve örneklemi Mart 2022 – Haziran 2022 tarihleri arasında araştırmaya katılmayı kabul eden ve anketleri dolduran toplam 320 hemşire oluşturmuştur. Veriler araştırmacı tarafından geliştirilen sosyodemografik bilgiler formu ve araştırmacı tarafından literatür taraması ile oluşturulan hasta klinik değişim formu ve bakım davranışları ölçeği ile toplanmıştır. Veri analizi SPSS 23.0 ile yapılmıştır. Tanımlayıcı veriler sayı (n), ortalama ve yüzde (%) olarak

sunulmuştur. Hemşirelerin 32.8' inin yoğun bakımlarda çalıştığı ve bunların da %65.6' sının göğüs hastalıkları kliniklerinde görev yaptığı belirlenmiştir. 10 yıl ve üstü çalışan hemşirelerin %30.9 ile en fazla olduğu saptanmıştır. Hemşirelerin bakım davranışları ölçek puan ortalamaları incelendiğinde tüm ölçek puanlarının ortalama değere yakın veya ortalama değerde olduğu saptanmıştır. Hemşirelerin bakım verdiği hastalarındaki klinik değişim belirtilerinden en fazla %67.5 ile kan şekeri değişikliklerini kullandıkları en az %2.2 ile oksijenlenme durumunu kullandıkları saptanmıştır. Sonuçta hemşirelerin bakımı altındaki hastalarının klinik durum tespiti için sıklıkla temel fizik muayene yöntemlerini ve objektif bulguları kullandıkları belirlenmiştir.

**Anahtar Kelimeler:** akut bakım, klinik bozulma, ipuçları, hemşireler, hemşirelik değerlendirmesi, yaşamsal belirtiler sistematik inceleme hasta güvenliği.

## **INTRODUCTION**

The most common method used in hospitals to assess whether a patient is improving or deteriorating is usually to evaluate five vital signs. These are blood pressure, blood oxygen saturation (SpO<sub>2</sub>), pulse rate, respiratory rate, and body temperature (Ahrens, 2008). These assessments and simple bedside observations have been reported to predict patient worsening in the hospital (Harrison, Jacques, McLaws, & Kilborn, 2006).

Nurses are primarily responsible for recognizing and evaluating changes in a patient's clinical status (Cardona-Morrell et al., 2016). The clinical condition of patients is expected to alternate between improvement and worsening during their hospital stay. Acute change during clinical care is defined as changes that differ from the last patient assessment or are reported by the patient or others (Rhudy & Androwich, 2013).

Early recognition of changes in a patient's clinical status enables appropriately targeted care that protects patients from adverse events and promotes recovery (Hart, Spiva, Dolly, Lang-Coleman, & Prince-Williams, 2016). If precautions are not taken by nurses, it can cause many adverse events, including worsening of patients' medical conditions, unplanned hospitalization for intensive care, cardiac arrest, and sudden death.

Studies show that nurses detect deterioration in patients mainly through intuitive judgments and pattern recognition (Odell, Victor, & Oliver, 2009). Many patients treated in internal and surgical wards have multiple comorbidities and often require complex nursing care. Effective clinical care can contribute to the early recognition of changes in a patient's clinical status (Cardona-Morrell et al., 2016). It plays an important role in making the right clinical decisions on time, improving the quality of nursing care, and providing safe care to the patient (Sucu, Dicle, & Saka, 2012).

To improve nursing practices and improve the quality of patient care, we need to know in more detail how nurses act and cooperate about bedside monitoring, evaluation, and management of patients in the hospital (Burdeu, Lowe, Rasmussen, & Considine, 2021). Therefore, this study aims to determine the clues to the clinical findings that occur in the nurses working in internal and surgical clinics during their daily patient care and that enable them to understand that their health status has changed.

## **MATERIALS and METHODS**

### **Design**

This research is a relation-seeking and descriptive study. The sample of the study consisted of nurses working in active patient care in public hospitals. The data of the research were collected face to face. The research was conducted with nurses who agreed to participate in the research and filled out the questionnaires between March 2022 and June 2022.

sample

The population of the study consisted of nurses working in the inpatient units of four public hospitals providing health services in a metropolitan city in Turkey (approximately N=900). The sample of the study was determined by the proportional quota method. First, stratification was made according to hospitals to determine the minimum number of nurses to be sampled. The minimum number of nurses

to be sampled was calculated as 269 (n=269), taking into account the 95% confidence interval and 5% margin of error, according to the sampling method whose population is known. Inclusion criteria were determined as taking part in direct patient care and volunteering to participate in the study. The exclusion criteria were determined as working in non-inpatient clinics and not taking part in direct patient care (diabetes education nurse, quality unit nurse, infection nurse, etc.).

**Data Collection Tools**

The data were collected with the sociodemographic information form developed by the researcher and the patient findings clue form created by the researcher through literature review.

*Sociodemographic Information Form:* This form; prepared by the researcher. in form; It was composed of questions including age, gender, educational status, marital status, income level, family structure, place of residence, hospital, clinic and working style of the person.

*Patient Clinical Findings Hint Form:* This form was created in order to determine the general status clinical clues of the patients they care for by nurses. Similar studies in the literature were considered in the creation of the form (Burdeu et al., 2021; Cardona-Morrell et al., 2016; Hart et al., 2016). In this form, clinical clues used by nurses were grouped as physiological findings, neurological findings, respiratory system findings, gastrointestinal system findings, urinary elimination changes, and findings understood through the skin. These groups were also divided into sub-finds within themselves. The nurse marked the clues used only by herself during daily patient care from these tables. For example, the table created for sub-findings of neurological findings is as follows:

Neurological Findings	eyes	Pupil status check
	motor function and sense	unresponsiveness to pain Limb movement and strength - unilateral numbness, limb weakness, limb discord
	level of consciousness	Sleepy, alert, unresponsive, hard to wake Agitation, confusion, inability to follow commands
	Communication and speech	nonverbal, slurred speech, aphasic
	Swallowing	dysphagia , drooling,
	Tools used in the clinic	Glasgow coma scale score

*Caring Behaviors Scale-24:* It was created to analyze nurse care behaviors. When the scale was applied to nurses, it showed high internal consistency, validity and good test-retest reliability. The scale includes a total of 24 items. Kurşun and Kanan (Kursun & Kanan, 2012) stated that the C. Alpha coefficients for the reliability of the scale are 0.97 for the overall scale and between 0.81 and 0.94 for the sub-dimensions. The scale is graded on a 6-point Likert type (1: never, 6: always). In calculating the scale total score, the scores of the 24 items are summed and divided by 24 to obtain a scale score between 1-6. As the total scale score increases, the perception levels of nurses' care behaviors increase. The internal consistency (cronbachalpha) of the scale for both patients and nurses ranged from 0.96 in total and between 0.82-0.92 in sub-dimensions (Klarare et al., 2021; Taylan, Özkan, & Şahin, 2021).

**Application of Research**

All nurses who met the inclusion criteria and agreed to participate in the study were asked to fill in the forms given to them.

**Data analysis**

Data analysis was done with SPSS 23.0. Descriptive data are presented as numbers (n), mean and percentage (%).

**Permissions**

Permission was obtained from the university hospital ethics committee with the number 2022/191. Information was given to the institutions where the nurses work. All principles of the Declaration of Helsinki were complied with throughout the study.

**RESULTS**

**Table 1. Descriptive characteristics of nurses (n=320)**

		n	%
Age	under 25	70	21.9
	26-30	104	32.5
	31-35	98	30.6
	over 35	48	15.0
Gender	Woman	239	74.7
	Male	81	25.3
Educational Status	High school	14	4.4
	Licence graduate	271	84.7
		35	10.9
marital status	married	204	63.8
	single	116	36.2
Working unit	Urgent	76	23.8
	Intensive care	105	32.8
	Operating room	12	3.8
	Internal service	81	25.3
	surgical service	46	14.4
Department he works in	Internal medicine	4	1.3
	Cardiology	9	2.8
	neurology	32	10.0
	Chest	210	65.6
	oncology	41	12.8
	Internal intensive care	5	1.6
	Chest intensive care	13	4.1
neurology intensive care	6	1.9	
Working experience (years)	1-2 years	65	20.3
	3-5 years	81	25.3
	6-10 years	75	23.4
	over 10 years	99	30.9
way of working	perpetual night	83	25.9
	day+watch	126	39.4
	all day long	33	10.3
	24-hour shift	78	24.4
Number of nurses working in the clinic	$\bar{X} \pm SD$ 14.85 ± 8.40		
Number of patients cared for in the clinic	11.78±7.74		

It was determined that 63.1% of the nurses were between the ages of 26-35, the majority of them were women, and 95.6% of them graduated from a bachelor's degree or higher. When the working characteristics of the nurses were examined, it was determined that 32.8% of them worked in intensive care units and 65.6% of them worked in chest diseases clinics. It was determined that the number of nurses working for 10 years or more was the highest with 30.9%, and the nurses worked mostly during the day + on duty. It was determined that the average number of nurses working in the clinics was 14.85±8.40, and the average number of patients cared for was 11.78±7.74.



**Table 2. Nurses' Caring Behaviors Scale**

Total and Sub-Dimensional Scores and Min-Max Values

Care Behaviors Scale	$\bar{X} \pm SD$	Min - Max
Assurance	2.89 ± 1.46	1-5
Knowledge Skill	2.53 ± 1.44	1-5
Being Respectful	3.00 ± 1.37	1-5
Loyalty	3.03 ± 1.41	1-5
Total scale score	2.87 ± 1.31	1-5

When the nurses' care behavior scale score averages were examined, it was determined that all scale scores were close to or at the average value.

**Table 3. Tips nurses use in diagnosing patients in the clinic**

Clinical conditions	n	%
Blood sugar changes	216	67.5
Respiratory rate	201	62.8
Pain	145	45.3
Urine output	94	29.4
Power loss	87	27.2
Pupil status	77	24.1
Nausea-vomiting	76	23.8
Unresponsiveness to pain	62	19.4
Sleeping state	60	18.8
Pulse	50	15.6
Body temperature	34	10.6
Follow up with scale	34	10.6
Blood pressure	28	8.8
Bowel sounds	28	8.8
Oxygenation	7	2.2

It was determined that the nurses used blood sugar changes with a maximum of 67.5% and oxygenation with a minimum of 2.2% among the clinical clues in their caregivers.

## **DISCUSSION**

This research was carried out to determine the clinical findings that occur during the daily patient care of the nurses working in inpatient services and enable them to understand that their health status has changed. According to our findings, the education level of the nurses is good and there is more than one nurse who takes care of each patient in the clinics. At the same time, the care behaviors of nurses are slightly above average. This result is satisfactory in terms of patient care and nursing services.

Patients' clinical status or response to treatment varies between improvement and worsening during the hospital stay. Many patients treated in inpatient wards are acutely unwell, have multiple comorbidities, and often require complex nursing care (Burdeu et al., 2021).

In this study, it was determined that nurses mostly used blood sugar changes and respiratory rate changes to determine the changes in the clinical status of the patients under their care. The most common use of respiratory rate changes is attributed to the fact that nurses often work in chest disease services. Our findings also show that clinical status changes used by nurses are components of routine physical examination. It is clearly stated in the literature that vital signs should be routinely measured (Hogan 2006, Wheatley 2006 ) and patients should be evaluated further by physical examination (Cox, James, & Hunt, 2006). Monitoring blood sugar changes plays an important role in nurses' evaluation of patients (Lopriore, LeCouteur, Ekberg, & Ekberg, 2019). Our findings are similar to the literature in this respect.

## **CONCLUSION**

Nurses are primarily responsible for the routine evaluation of the patient and the identification of the patient's clinical status change. Patients should use clinical clues to prevent their condition from getting worse and to intervene in the early period. In this study, it was determined that the care behaviors of nurses were at an average level. It was determined that nurses frequently used basic physical examination methods and objective findings for clinical status determination.

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YETİŞKİNLERDE İNTRAMÜSKÜLER ENJEKSİYON İLİŞKİLİ AĞRI ÜZERİNE HELFER  
SKIN TAP TEKNİĞİ'NİN ETKİSİ: LİTERATÜR İNCELEMESİ

THE EFFECT OF HELFER SKIN TAP TECHNIQUE ON PAIN ASSOCIATED WITH  
INTRAMUSCULAR INJECTION IN ADULTS: LITERATURE REVIEW

*Sevgi PAKIŞ ÇETİN<sup>1</sup>*

<sup>1</sup> Arş. Gör. Dr., Manisa Celal Bayar Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü,  
Manisa, Türkiye.

<sup>1</sup>ORCID ID: h0000-0001-8330-3493

*Ebru BAYSAL<sup>2</sup>*

<sup>2</sup> Dr. Öğr. Üyesi, Manisa Celal Bayar Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü,  
Manisa, Türkiye.

<sup>2</sup>ORCID ID: 0000-0002-8831-3065

**ÖZET**

**Arka plan ve amaç:** Parenteral ilaç uygulama yollarından birisi olan intramüsküler enjeksiyon, ilacın büyük kas gruplarına iletilmesini sağlamak amacıyla en sık kullanılan uygulamalardan birisidir. Ancak enjeksiyona bağlı çeşitli komplikasyonlar gelişebilmektedir. Ağrı, intramüsküler enjeksiyona bağlı en sık karşılaşılan komplikasyonlardandır. Bireyin ağrısının rahatlatılması en temel insan haklarından biri olmakla birlikte hemşirelik bakım kalitesi ve hasta memnuniyetinin sağlanması açısından oldukça önemlidir. Bu nedenle hemşirenin sorumlulukları arasında yer alan ağrı kontrolünün sağlanması ve etkili prosedürlerin kullanılması hayati önem taşımaktadır. İnamüsküler enjeksiyon sırasında yaşanan ağrının azaltılması amacıyla pek çok geleneksel yöntem bulunmakla birlikte Helfer skin tap tekniği gibi yenilikçi yöntemler de bulunmaktadır. Bu literatür incelemesinin amacı yetişkinlerde intramüsküler enjeksiyon sırasında kullanılan Helfer skin tap tekniğinin etkinliğini değerlendirmektir.

**Yöntem:** Literatür incelemesinin evrenini “Helfer skin tap tekniği”, “inramüsküler enjeksiyon” ve “ağrı” anahtar kelimeleriyle “Scopus”, “Pubmed”, “CINAHL” ve “Google Scholar” veri tabanları taranarak ulaşılan 74 makale oluşturmuştur. Derlemeye yayın dili Türkçe veya İngilizce olan, tam metni bulunan, yetişkin bireyler ile yürütülen ve intramüsküler enjeksiyon sırasında Helfer skin tap tekniğinin etkinliğini değerlendiren araştırmalar dahil edilmiştir. Araştırma kriterlerini karşılayan dokuz makale derlemenin örneklemini oluşturmuştur.

**Bulgular:** Literatür incelemesine dahil edilen araştırmalar incelendiğinde, etken maddeleri birbirinden farklı olan ilaçların intramüsküler enjeksiyonu amacıyla deltoid, dorsogluteal ya da ventrogluteal alanlara uygulandığı saptanmıştır. Araştırma sonuçları incelendiğinde; Helfer skin tap tekniği ile intramüsküler enjeksiyon uygulanan hastaların yaşadıkları ağrı düzeyinin daha düşük olduğu bildirilmiştir. Ayrıca Helfer skin tap tekniğinin hemşirelik bakım kalitesi ile hastaların memnuniyet ve konfor düzeyinin artırılmasına katkı sağlayabileceği belirtilmiştir.

**Sonuç:** Helfer skin tap tekniğinin intramüsküler enjeksiyon sırasında yaşanan ağrının azaltılmasında etkili olduğu bildirilmektedir. Hemşirelik bakım kalitesi, hasta memnuniyeti ve konforunun artırılması amacıyla Helfer skin tap tekniğinin kullanılması yararlı olacaktır.

**Anahtar kelimeler:** Helfer skin tap tekniği, intramüsküler enjeksiyon, ağrı.

**ABSTRACT**

**Background and Aim:** Intramuscular injection, which is one of the parenteral drug administration routes, is one of the most frequently used applications to ensure the delivery of the drug to large muscle groups. However, various complications may develop due to injection. Pain is one of the most common

complications associated with intramuscular injection. Relief of the individual's pain is one of the most basic human rights, and it is very important in terms of ensuring the quality of nursing care and patient satisfaction. For this reason, it is vital to provide pain control and use effective procedures, which are among the responsibilities of the nurse. While there are many traditional methods to reduce the pain experienced during intramuscular injection, there are also innovative methods such as the Helfer skin tap technique. The purpose of this literature review is to evaluate the effectiveness of the Helfer skin tap technique used during intramuscular injection in adults.

**Method:** The universe of the literature review consisted of 74 articles that were accessed by searching the databases of "Scopus", "Pubmed", "CINAHL" and "Google Scholar" with the keywords "Helfer skin tap technique", "intramuscular injection" and "pain". The review included studies that were published in Turkish or English, had full text, were conducted with adults, and evaluated the effectiveness of the Helfer skin tap technique during intramuscular injection. The review sample consisted of nine articles that meeting the research criteria.

**Results:** When the studies included in the literature review were examined, it was determined that drugs with different active ingredients were applied to the deltoid, dorsogluteal or ventrogluteal areas for intramuscular injection. When the research results are examined; it has been reported that the level of pain experienced by patients who received intramuscular injection with the Helfer skin tap technique was lower. In addition, it has been stated that the Helfer skin tap technique can contribute to the quality of nursing care and increase the satisfaction and comfort level of the patients.

**Conclusion:** It has been reported that the Helfer skin tap technique is effective in reducing the pain experienced during intramuscular injection. It will be useful to use the Helfer skin tap technique in order to increase the quality of nursing care, patient satisfaction and comfort.

**Keywords:** Helfer skin tap technique, intramuscular injection, pain.

## **GİRİŞ**

Parenteral ilaç uygulamaları, genellikle sistemik etkinin oluşmasının istenildiği ve ilaç etkisinin hızla başlatılmasına ihtiyaç duyulduğu durumlarda başvurulan ilaç uygulama yoludur (Akbiyık, 2021). Parenteral ilaç uygulama yollarından birisi olan intramüsküler enjeksiyon (IM), ilacın büyük kas gruplarına iletilmesini sağlamak amacıyla en sık kullanılan uygulamalardan birisidir (Kaur ve diğerleri, 2019). Ancak enjeksiyona bağlı ağrı, apse, sinir zedelenmesi, doku irritasyonu, enfeksiyon, emboli, alerjik reaksiyon gibi geniş yelpazede komplikasyonlar gelişebilmektedir (Akbiyık, 2021). Ağrı, enjeksiyona bağlı en sık karşılaşılan komplikasyonlardandır (Kaur ve diğerleri, 2019). Ayrıca ağrı, hemşirelik bakım ortamında hastaların yaşadığı rahatsızlık ve stresin başlıca kaynağını oluşturmaktadır (Arora, 2015). Bireyin ağrısının rahatlatılması en temel insan haklarından biri olmakla birlikte hemşirelik bakım kalitesi, hasta memnuniyeti ve yaşam kalitesinin sağlanması açısından oldukça önemlidir (Çelik ve Khorshid, 2015; El Hapshy ve diğerleri, 2016; Kaur ve diğerleri, 2019). Bu nedenle hemşirenin sorumlulukları arasında yer alan ağrı kontrolünün sağlanması ve etkili prosedürlerin kullanılması hayati önem taşımaktadır (Arora, 2015; Shah ve Narayanan, 2016; Kaur ve diğerleri, 2019).

İntramüsküler enjeksiyon sırasında yaşanan ağrının azaltılması amacıyla ilacın yavaş verilmesi, küçük çaplı iğne boyutunun seçilmesi, dokuya hızlıca girilmesi gibi enjeksiyon tekniklerinin yanı sıra enjeksiyon sonrasında on saniye boyunca enjeksiyon alanına basınç uygulanması, ilacın hazırlanmasında ve uygulanmasında farklı iğnelerin kullanılması, daha uzun boyutta bir iğnenin kullanılması, enjeksiyon bölgesi olarak dorsogluteal yerine ventrogluteal alanın tercih edilmesi, uygulamada "Z" tekniğinin kullanılması, kasların gevşeyeceği rahat bir pozisyon verilmesi gibi yöntemlerin ağrıyı azaltmada etkili olabileceği belirtilmektedir (Akbiyık, 2021). Son yıllarda bu uygulamalara ek olarak, enjeksiyon alanına manuel basınç ve akupresür (Raddadi ve diğerleri, 2017), Helfer skin tap tekniği (Pujari ve diğerleri, 2019), "ShotBlocker" (Wilbeck ve diğerleri, 2021), Buzzy (Şahin ve Eşer, 2018), cilt çekme, basınç ve hızlı kas gevşetme (TPR) (Heshmatifar ve diğerleri, 2022) tekniklerinin kullanımı gibi yenilikçi yöntemlerin ağrının azaltılmasında etkili olduğu bildirilmektedir (Zeyrek, 2022).

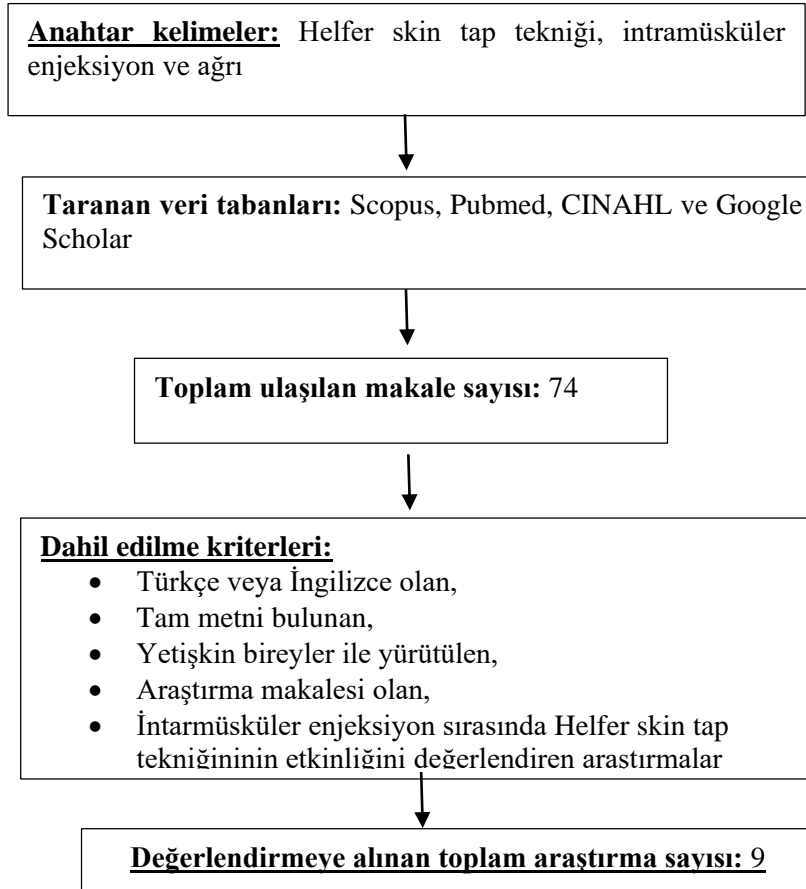
Yenilikçi teknikler arasında yer alan Helfer skin tap tekniği ile kapı kontrol teorisini içeren ağrı teorisinin temel kavramları kullanılmaktadır. Bu teknik sayesinde büyük çaplı kas liflerinin mekanik uyarımıyla, küçük ağrı taşıyan liflerin etkisi azaltılmaktadır. Tekniğin çalışmasında iki temel nokta bulunmaktadır. Bunlardan birincisi iğne girişine karşı direnci fiziksel olarak azaltan kas gevşemesinin sağlanması iken diğeri iğne giriş ve çıkışı sırasında cilde vurularak dikkatin başka yöne çekilmesinin sağlanmasıdır (Helfer, 2000).

Bu literatür incelemesinin amacı yetişkinlerde intramüsküler enjeksiyon sırasında kullanılan Helfer skin tap tekniğinin etkinliğinin değerlendirilmesidir.

## **MATERYAL-METOD**

Literatür incelemesinin evrenini “Helfer skin tap tekniği”, “intramüsküler enjeksiyon” ve “ağrı” anahtar kelimeleriyle “Scopus”, “Pubmed”, “CINAHL” ve “Google Scholar” veri tabanları taranarak ulaşılan 74 makale oluşturmuştur. Derlemeye yayın dili Türkçe veya İngilizce olan, tam metni bulunan, yetişkin bireyler ile yürütülen ve intramüsküler enjeksiyon sırasında Helfer skin tap tekniğinin etkinliğini değerlendiren araştırmalar dahil edilmiştir. Araştırma kriterlerini karşılayan 9 makale derlemenin örneğini oluşturmuştur (Şekil 1).

İlk aşamada, araştırmaya alınma kriterlerinden oluşan bir değerlendirme formu oluşturulmuştur. Oluşturulan bu form doğrultusunda, iki araştırmacı tarafından bağımsız olarak veri tabanı taraması yapılmıştır. Her iki araştırmacı tarafından da araştırmaya alınma kriterlerini karşıladığına karar verilen araştırmalar incelemeye dahil edilmiştir. İkinci aşamada, incelenecek araştırmanın yazar, yıl ve ülke bilgisi, amaç, örneklem ve uygulama, bulgular ve sonuç başlıklarının yer aldığı bir form oluşturulmuştur. Bu form doğrultusunda, araştırmalar, iki araştırmacı tarafından ayrı ayrı okunarak değerlendirilmiştir. Son olarak, her iki araştırmacı tarafından değerlendirilen araştırmalar, tek bir formda birleştirilmiştir.



**Şekil 1: Literatür İncelemesine Dahil Edilen Araştırmaların Şeması**

Tablo 1: Literatür İncelmesine Dahil Edilen Araştırmaların Analizi

Yazar, Yıl ve Ülke	Amaç	Örneklem ve Uygulama	Bulgular ve Sonuç
Therese ve Devi, 2014, Hindistan	İntramüsküler (IM) enjeksiyon uygulanan hastaların ağrısının azaltılmasında Helfer skin tap (HST) tekniği ile rutin yöntemin etkinliğini değerlendirmek.	-Grup 1: 25 hasta 1.-3. enjeksiyon Helfer skin tap tekniği; 2.-4. enjeksiyon geleneksel teknik -Grup 2: 25 hasta 1.-3 enjeksiyon geleneksel teknik; 2.-4. enjeksiyon Helfer skin tap tekniği (çapraz tasarımlı çalışma) -Hastalara ardışık dört gün boyunca IM enjeksiyon uygulanmıştır.	-Helfer skin tap tekniğinin rutin yonteme göre IM enjeksiyona bağılı ağrı düzeyini istatistiksel olarak anlamlı derecede azalttığı ancak bireyin IM enjeksiyon öncesi ve sonrası değerlendirilen fizyolojik parametrelerinde (sistolik ve diyastolik kan basıncı, nabız) değişikliğe neden olmadığı bildirilmiştir. -Helfer skin tap tekniği uygulanan hastaların dört gün boyunca yaşadıkları ağrı puan ortalamaları sırasıyla, 3.36±1.50; 3.12±1.64; 2.80±1.63; 2.80±1.63. -Rutin yöntem uygulanan hastaların dört gün boyunca yaşadıkları ağrı puan ortalamaları sırasıyla, 4.44±2.24; 4.40±2.20; 4.24±2.04; 4.24±2.04. -Sonuç olarak; bakım kalitesinin sağlanabilmesi için Helfer skin tap tekniği'nin intramüsküler enjeksiyon sırasında kullanılabileceği önerilmiştir.
El Hapshy ve diğerleri, 2015, Mısır	İntramüsküler enjeksiyonla ilişkili ağrılarda Helfer skin tap tekniğinin etkinliğini değerlendirmek.	-100 yetişkin hasta -Vitamin ile analjezik tedavisi olan hastaların her birine dört kez IM enjeksiyon uygulaması yapılmıştır. Hastaların her birine uygulama sırasında dorsogluteal enjeksiyon bölgesine iki kez geleneksel ve iki kez Helfer skin tap tekniği kullanılarak enjeksiyon uygulanmıştır (kendi kendinin kontrolü olan çalışma)  -Hastaların enjeksiyon sırasındaki ağrı düzeyleri; Sözel Kategori Ölçeği, Wong Baker Yüz Skalası ve Aktivite Tolerans Skalası olmak üzere üç evrensel ağrı değerlendirme skalası kullanılarak değerlendirilmiştir.	-Değerlendirme sırasında kullanılan üç skala sonucunda; Helfer skin tap tekniğinin geleneksel tekniğe göre intramüsküler enjeksiyon sırasında yaşanan ağrıyı önemli derecede azalttığı saptanmıştır. <b>Sözel Kategori Ölçeği'ne göre;</b> Geleneksel teknik: %17'sinin ağrı yaşamadığı Helfer skin tap tekniği: %40'ının ağrı yaşamadığı <b>Wong Baker Yüz Skalası'na göre;</b> Geleneksel teknik: %21'inin gülümseyen yüz ifadesine sahip olduğu Helfer skin tap tekniği: %48'inin gülümseyen yüz ifadesine sahip olduğu <b>Aktivite Tolerans Skalası'na göre;</b> Geleneksel teknik: %36'sının ağrı yaşamadığı Helfer skin tap tekniği: %57'sinin ağrı yaşamadığı saptanmıştır.  -Sonuç olarak; Helfer skin tap tekniğinin hastaların ağrısının azaltılmasında etkili olduğu; bu nedenle intramüsküler enjeksiyon ilişkili ağrıların azaltılmasında kullanılabilecek bir girişim olarak önerilmiştir.
Kaur ve diğerleri, 2016, Hindistan	İntramüsküler enjeksiyon sırasında Helfer skin tap tekniği kullanımının ağrı düzeyine etkisini değerlendirmek.	-Grup 1: 50 hastaya Helfer skin tap tekniği ile IM enjeksiyon uygulaması (araştırmacı tarafından uygulama öncesinde 2-3 saniye boyunca parmakların palmar yüzü kullanılarak kasa vurulmuş ve enjeksiyon sonrasında iğne çıkarılmadan 1-2 saniye sayılarak beklenmiştir)	-Helfer skin tap tekniği kullanılan bireylerde ağrı puanı ortalamasının (1.60±1.143) kontrol grubu hastalarına göre (4.98±1.755) istatistiksel olarak anlamlı derecede düşük olduğu saptanmıştır (p<0.05).

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		<p>Grup 2: 50 hastaya standart yöntemle IM enjeksiyon uygulaması</p> <p>-Hastalara 21 ya da 23 gauge iğne kullanılarak deltoid, dorsogluteal ya da ventrogluteal bölgelerinden herhangi birine antibiyotik/antipiretik/antihepatik/antiemetik/vitamin D/analjezik tedavilerinden birisi uygulanmıştır.</p> <p>-Ağrı düzeyleri Sayısal Ağrı Ölçeği kullanılarak değerlendirilmiştir.</p>	<p>-Sonuç olarak; intramüsküler enjeksiyon sonrasında yaşanan ağrının azaltılmasında Helfer skin tap tekniğinin etkili olduğu bildirilmiştir.</p>
Hassnein ve Soliman, 2016, Mısır	İntramüsküler enjeksiyonla ilişkili ağrıyı azaltmada Helfer skin tap tekniğinin etkinliğini değerlendirmek.	<p>-100 yetişkin hasta</p> <p>-Vitamin ile analjezik tedavisi olan hastaların her birine dört kez IM enjeksiyon uygulaması yapılmıştır. Hastaların her birine uygulama sırasında dorsogluteal enjeksiyon bölgesine iki kez geleneksel ve iki kez Helfer skin tap tekniği kullanılarak enjeksiyon uygulanmıştır.</p> <p><b>-Helfer skin tap tekniği;</b> araştırmacı tarafından uygulama öncesinde başparmak ile geniş bir V yapıldıktan sonra parmakların palmar yüzü kullanılarak 16 kez kasa vurulması ve enjeksiyon sonrasında iğne çıkarılmadan 1den 3e kadar sayılarak iğnenin çıkarılması işlemidir.</p> <p>-Hastaların enjeksiyon sırasındaki ağrı düzeyleri; Sözel Kategori Ölçeği, Wong Baker Yüz Skalası ve Aktivite Tolerans Skalası olmak üzere üç evrensel ağrı değerlendirme skalası kullanılarak değerlendirilmiştir.</p>	<p>-Değerlendirme sırasında kullanılan üç skala sonucunda; Helfer skin tap tekniğinin geleneksel tekniğe göre intramüsküler enjeksiyon sırasında yaşanan ağrıyı önemli derecede azalttığı saptanmıştır. Ayrıca vitamin ve analjezik tedavisinde yaşanan ağrı düzeylerinde farklılık olmadığı (<b>Geleneksel teknik:</b> vitamin sırasında ağrı ort: 6.9±2.7; analjezik: 7.3±2.9; <b>Helfer skin tap tekniği:</b> vitamin sırasında ağrı ort: 5.04±2.1; analjezik: 5.4±2.4) bildirilmiştir.</p> <p><b>Sözel Kategori Ölçeği'ne göre;</b> Geleneksel teknik: %17'sinin ağrı yaşamadığı Helfer skin tap tekniği: %40'ının ağrı yaşamadığı</p> <p><b>Wong Baker Yüz Skalası'na göre;</b> Geleneksel teknik: %21'inin gülümseyen yüz ifadesine sahip olduğu Helfer skin tap tekniği: %48'inin gülümseyen yüz ifadesine sahip olduğu</p> <p><b>Aktivite Tolerans Skalası'na göre;</b> Geleneksel teknik: %36'sının ağrı yaşamadığı Helfer skin tap tekniği: %57'sinin ağrı yaşamadığı saptanmıştır.</p> <p>-Sonuç olarak; Helfer skin tap tekniğinin hastaların ağrısının azaltılmasında etkili olduğu; bu nedenle intramüsküler enjeksiyon ilişkili ağrıların azaltılmasında kullanılabilecek bir girişim olarak önerilmiştir.</p>
Shah ve Narayanan, 2016, Hindistan	IM enjeksiyon uygulanan hastaların ağrı düzeyi üzerine Helfer skin tap tekniği ile geleneksel tekniğin etkisini karşılaştırmak.	<p>-Grup 1: 41 hasta 1. enjeksiyon geleneksel teknik; 2. enjeksiyon Helfer skin tap tekniği</p> <p>-Grup 2: 41 hasta 1. enjeksiyon Helfer skin tap tekniği; 2. enjeksiyon geleneksel teknik (çapraz tasarımlı çalışma)</p> <p>-Ortopedi ameliyatı geçirmiş hastalara post-op 1. günde anestezinin etkisi geçtikten sonra sabahın erken saatlerinde ilk doz IM analjezik (Diclofenak) tedavisi uygulanırken; ikinci doz IM analjezik tedavisi aynı gün birinci dozdan 8 saat sonra uygulanmıştır.</p> <p>-Hastaların uygulama öncesi ağrı şiddeti Modifiye Kısa Ağrı Envanteri, anksiyete düzeyi Anksiyete Değerlendirme Ölçeği ile değerlendirilmiştir.</p> <p>-Hastaların ilk ve sonraki ağrı düzeyleri Basit Tanımlayıcı Ağrı Şiddeti Ölçeği ve Görsel Kıyaslama Ölçeği kullanılarak değerlendirilmiştir.</p>	<p>-Helfer skin tap tekniğinin IM enjeksiyona bağlı ağrıyı anlamlı derecede azalttığı saptanmıştır. Ayrıca Helfer skin tap tekniği ile IM enjeksiyon uygulanan hastaların anksiyete düzeyi ile ağrı düzeyi arasında anlamlı bir ilişki olmadığı; dolayısıyla anksiyete düzeyinden bağımsız her yaş grubu ve cinsiyette uygulanabileceği bildirilmiştir.</p> <p>-Sonuç olarak; Helfer skin tap tekniğinin IM enjeksiyon sırasında kullanımının oldukça etkili olduğu; bu nedenle hemşirelerin bu tekniği rutin olarak kullanımının hastaların girişimsel ağrısının azaltılarak konfor düzeyinin artırılmasında yardımcı olabileceği önerilmiştir.</p>

Pujari ve diğerleri, 2019, Hindistan	İntramüsküler enjeksiyonla ilişkili ağrıyı azaltmada Helfer skin tap tekniğinin etkinliğini değerlendirmek.	-Ortopedi servisinde tedavi gören 60 hastanın 2*1 uygulanan IM analjezik (Diclofenak) tedavisinde ilk doz rutin yöntemle ikinci doz Helfer skin tap tekniği ile uygulanmıştır.  -Ağrı düzeyleri Sayısal Ağrı Ölçeği kullanılarak değerlendirilmiştir. -Ağrının en iyi göstergelerinden birisi olan nabız değerlendirmesi için enjeksiyon öncesi ve sonrası pulse oksimetre kullanılarak nabız kayıt edilmiştir.	-Helfer skin tap tekniğinin hastaların IM enjeksiyona bağlı ağrı düzeyi ile nabız hızı değişimini azaltmada etkili bir yöntem olduğu bildirilmiştir (Ağrı puan ortalaması Helfer skin tap: 2.45 ±0.938; rutin yöntem: 6.95 ±1.006)  -Sonuç olarak; Helfer skin tap tekniğinin IM enjeksiyona bağlı ağrının azaltılmasında etkili bir nonfarmakolojik yöntem olduğu; bu nedenle bu yöntemin kurumsal politika olarak tanıtılması ve IM enjeksiyonuna bağlı ağrının etkin yönetimi için tüm hastalara rutin bakım olarak uygulanması önerilebilir.
Kaur ve diğerleri, 2019, Hindistan	Helfer skin tap tekniğinin IM enjeksiyona bağlı ağrı üzerine etkinliğini belirlemek.	-110 ortopedi tanısıyla tedavi gören hasta -Grup 1: 1. enjeksiyon Helfer skin tap tekniği; 2. enjeksiyon standart teknik -Grup 2: 1. enjeksiyon standart teknik; 2. enjeksiyon Helfer skin tap tekniği (çapraz tasarımlı, kendi kendinin kontrolü olan çalışma) -Her iki gruba analjezik tedavisi (Diclofenac sodyum) 24 saat arayla iki doz olacak şekilde uygulanmıştır. -Ağrı değerlendirilmesinde Sayısal Ağrı Ölçeği (NRS), Görsel Kıyaslama Ölçeği (VAS) ve Sözel Kategori Ölçeği (VDS) kullanılmıştır.	-Çalışma bulguları, NRS, VAS ve VDS ölçekleri kullanılarak standart ve Helfer skin tap tekniği ile ortalama ağrı değerleri sırasıyla 3.96±1.61, 3.56±1.91, 3.41±1.64 ve 2.55±1.57, 2.32±1.75, 2.22±1.65 olarak belirlenmiştir.  -Sonuç olarak; Helfer skin tap tekniğinin IM enjeksiyona bağlı yaşanan ağrıyı azaltmada etkili olduğu bildirilmiştir.
Güven ve diğerleri, 2020, Türkiye	IM enjeksiyona bağlı olarak gelişen ağrının azaltılmasında Helfer skin tap tekniğinin etkisini belirlemek.	-Grup 1: 50 hasta deney grubu (Helfer skin tap tekniği ile ventrogluteal bölgeye 23 gauge iğne ile IM enjeksiyon uygulanmıştır) -Grup 2: 50 hasta kontrol grubu (Standart teknik ile ventrogluteal bölgeye 23 gauge iğne ile IM enjeksiyon uygulanmıştır)  -Bir devlet hastanesinin enjeksiyon polikliniğine Diklofenak tedavisi için başvuran 100 hasta çalışmaya dahil edilmiştir.  <b>-İşlemi uygularken;</b> *Enjeksiyon alanı belirlendikten sonra kası gevşetmek amacıyla işlem öncesi yaklaşık beş saniye boyunca (yaklaşık 15 vuruş) dominant elin parmak uçlarıyla cilde vurulmuştur. *Cilt alkolle temizledikten sonra iğne kılıfı çıkarılmış, pasif el V şekline getirilerek cilde üç kez vurulmuştur. *Üçüncü vuruş sırasında iğneyle kasa girilmiştir. *Aspirasyon sonrasında pasif elin parmak uçlarıyla cilde vurmaya devam edilmiş, dominant elle ilaç uygulanmıştır. *İlaç enjekte edildikten sonra pasif el V şekline getirilerek cilde üç kez vurulmuş, üçüncü vuruşta enjektör çıkarılmıştır.  -Ağrı değerlendirmesi Görsel Kıyaslama Ölçeği (VAS) kullanılarak IM enjeksiyon sonrası bir dakika içerisinde yapılmıştır.	-Çalışma bulguları, standart teknik uygulanan hastaların ortalama ağrı değeri 2.88±1.02; Helfer skin tap tekniği uygulanan hastaların ortalama ağrı değeri 0.18±0.39 olmakla birlikte aralarındaki farkın anlamlı olduğu bildirilmiştir.  -Sonuç olarak; Helfer skin tap tekniğinin enjeksiyon uygulama yöntemleri arasında yer alabileceği, kanıtları güçlendirmek için ilgili çalışmaların sürdürülmesi ve farklı enjeksiyon uygulama teknikleri ile Helfer skin tap tekniğinin karşılaştırmalı çalışmalarda kullanılması önerilmiştir.
Karabey ve Karagozoglu, 2021, Türkiye	Deltoid kasa IM enjeksiyon uygulamasında yaşanan ağrı üzerine Helfer skin tap	-Grup 1: 40 hasta Helfer skin tap tekniği -Grup 2: 40 hasta standart uygulama (kontrol) -Grup 3: 40 hasta ShotBlocker tekniği -Aile sağlığı merkezine Hepatit B aşısı yaptırmak amacıyla başvuran 180 bireyden	-Çalışma sonucunda, Helfer skin tap tekniği sonrasında ağrı değeri 4.00; standart uygulama sonrasında ağrı değeri 7.00; ShotBlocker tekniği



	tekniki ile ShotBlocker uygulamasının etkisini karřılařtırmak.	arařtırmaya dahil olma kriterlerini karřılayan 120 birey dahil edilmiřtir.  -Ađrı deđerlendirmesi Grsel Kıyaslama leđi (VAS) kullanılarak yapılmıřtır.	sonrasında ađrı deđeri 3.00 olarak belirlenmiřtir.  Sonu olarak; IM enjeksiyona bađlı ađrının azaltılmasında ShotBlocker tekniđinin standart uygulama ve Helfer skin tap tekniđine gre daha etkili olduđu; Helfer skin tap tekniđinin ise standart uygulamaya gre etkili olduđu bildirilmiřtir. Uygulamaları standardize etmek ve kanıt oluřturmak iin Helfer skin tap tekniđi ile ShotBlocker tekniđinin farklı poplasyonlarda kullanılması; sađlık profesyonellerinin ve zellikle hemřirelerin IM enjeksiyonda ađrının azaltılmasında etkinliđi kanıtlanmış nonfarmakolojik yntemleri kullanması nerilmektedir.
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### **BULGULAR VE TARTIřMA**

Literatr incelemesi sonucunda 2014-2021 yılları arasında gerekleřtirilmiř 74 arařtırmaya ulařılmıř olup dokuz arařtırma alıřma kapsamına alınmıřtır (řekil 1). Toplamda 822 hastanın alındıđı ve rneklem byklđ 50 ile 120 arasında deđiřen, Hindistan, Mısır ve Trkiye’de gerekleřtirilen dokuz arařtırma literatr incelemesine dahil edilmiřtir. Literatr incelemesine dahil edilen arařtırmaların yılı-yazarı-lkesi, amacı, rneklem byklđ, uygulama, bulguları ve sonuları Tablo 1’de yer almaktadır.

Therese ve Devi’nin (2014) alıřmasında, 25 hastada 1.-3. enjeksiyonlar Helfer skin tap tekniđi ile 2.-4. enjeksiyonlar geleneksel teknik ile uygulanmıř olup diđer 25 hastada 1.-3. enjeksiyonlar geleneksel teknik ile 2.-4. enjeksiyonlar Helfer skin tap tekniđi ile apraz tasarım kullanılarak ardıřık drt gn boyunca uygulanmıřtır. alıřmada ađrıya bađlı fizyolojik parametrelerde deđiřiklik yařanabileceđi gz nnde bulundurularak iřlem ncesi ve sonrası sistolik ve diastolik kan basıncı ile nabız deđerlendirilmiřtir. Helfer skin tap tekniđinin geleneksel ynteme gre IM enjeksiyona bađlı ađrı dzeyini istatistiksel olarak anlamlı derecede azalttıđı ancak bireyin IM enjeksiyon ncesi ve sonrası deđerlendirilen fizyolojik parametrelerinde (sistolik ve diastolik kan basıncı, nabız) deđiřikliđe neden olmadıđı bildirilmiřtir. alıřma sonucunda bakım kalitesinin sađlanabilmesi amacıyla Helfer skin tap tekniđi’nin intramskler enjeksiyon sırasında kullanılabileceđi belirtilmiřtir (Therese ve Devi, 2014)

El Hapshy ve diđerlerinin (2015) alıřmasında, vitamin ile analjezik tedavisi olan 100 hastanın her birine iki kez geleneksel ve iki kez Helfer skin tap tekniđi kullanılarak dorsogluteal alana IM enjeksiyon uygulaması yapılmıřtır. Deđerlendirme sırasında kullanılan  lek sonucunda Helfer skin tap tekniđinin geleneksel ynteme gre intramskler enjeksiyon sırasında yařanan ađrıyı nemli derecede azalttıđı saptanmıřtır. Deđerlendirmede kullanılan leklerden biri olan Szel Kategori leđi’ne gre; geleneksel teknikle IM enjeksiyon uygulamasında hastaların %17’sinin ađrı yařamadıđı, Helfer skin tap tekniđi ile IM enjeksiyon uygulamasında hastaların %40’ının ađrı yařamadıđı bildirilmiřtir (El Hapshy ve diđerleri, 2015).

Kaur ve diđerlerinin (2016) alıřmasında, IM enjeksiyon 50 hastaya Helfer skin tap tekniđi ile uygulanırken, 50 hastaya standart yntemle uygulanmıřtır. Uygulama sırasında 21 ya da 23 gauge iđne kullanılarak deltoid, dorsogluteal ya da ventrogluteal blgelerinden herhangi birine antibiyotik/antipiretik/antihepatik/antiemetik/vitamin D/analjezik tedavilerinden birisi yapılmıřtır. Helfer skin tap tekniđi kullanılan bireylerde ađrı puanı ortalamasının (1.60±1.143) kontrol grubu hastalarına gre (4.98±1.755) istatistiksel olarak anlamlı derecede dřk olduđu saptanmıřtır (p<0.05) (Kaur ve diđerleri, 2016).

Hassnein ve Soliman’ın (2016) alıřmasında, vitamin ile analjezik tedavisi olan 100 hastanın her birine iki kez geleneksel ve iki kez Helfer skin tap tekniđi kullanılarak dorsogluteal alana IM enjeksiyon uygulaması yapılmıřtır. Helfer skin tap tekniđi ile enjeksiyon uygulaması, arařtırmacı tarafından iřlem ncesinde bařparmak ile geniř bir V yapıldıktan sonra parmakların palmar yz kullanılarak 16 kez kasa vurulmasını ve enjeksiyon sonrasında iđne ıkarılmadan birden e kadar sayılarak iđnenin ıkarılmasını iermektedir. Deđerlendirme sonucunda; Helfer skin tap tekniđinin geleneksel tekniđe

göre intramüsküler enjeksiyon sırasında yaşanan ağrıyı önemli derecede azalttığı saptanmıştır. Ayrıca çalışmada vitamin ve analjezik tedavisinde yaşanan ağrı düzeyleri arasında farklılık olmadığı (Geleneksel teknik ile uygulanan vitamin tedavisinde ağrı puanı ortalaması  $6.9 \pm 2.7$ ; analjezik tedavisinde  $7.3 \pm 2.9$ ; Helfer skin tap tekniği ile uygulanan vitamin tedavisinde ağrı puan ortalaması  $5.04 \pm 2.1$ ; analjezik tedavisinde  $5.4 \pm 2.4$ ) bildirilmiştir (Hassnein ve Soliman, 2016).

Shah ve Narayanan'ın (2016) çalışmasında, ortopedi ameliyatı geçirmiş olan hastalara post-op birinci günde anestezinin etkisi geçtikten sonra sekiz saat arayla iki doz analjezik (Diclofenak) tedavisi uygulanmıştır. 41 hastaya ilk enjeksiyon geleneksel teknik ile ikinci enjeksiyon Helfer skin tap tekniği ile uygulanmış olup, diğer 41 hastaya ilk enjeksiyon Helfer skin tap tekniği ile ikinci enjeksiyon geleneksel teknik ile çapraz tasarım kullanılarak uygulanmıştır. Helfer skin tap tekniğinin IM enjeksiyona bağlı ağrıyı anlamlı derecede azalttığı saptanmıştır. Ayrıca Helfer skin tap tekniği ile IM enjeksiyon uygulanan hastaların anksiyete düzeyi ile ağrı düzeyi arasında anlamlı bir ilişki olmadığı; dolayısıyla anksiyete düzeyinden bağımsız her yaş grubu ve cinsiyette uygulanabileceği bildirilmiştir (Shah ve Narayanan, 2016).

Pujari ve diğerlerinin (2019) çalışmasında, ortopedi servisinde tedavi gören 60 hastaya  $2 \times 1$  IM analjezik (Diclofenak) tedavisinin ilk dozu rutin yöntemle ikinci dozu Helfer skin tap tekniği ile uygulanmıştır. Çalışmada Helfer skin tap tekniğinin hastaların IM enjeksiyona bağlı ağrı düzeyi (Helfer skin tap tekniği ile uygulanan enjeksiyonda ağrı puan ortalaması  $2.45 \pm 0.938$ ; rutin yöntem ile uygulanan enjeksiyonda ağrı puan ortalaması  $6.95 \pm 1.006$ ) ile nabız hızı değişimini azaltmada etkili bir yöntem olduğu bildirilmiştir (Pujari ve diğerleri, 2019).

Kaur ve diğerlerinin (2019) çalışmasında, 110 ortopedi tanısıyla tedavi gören hastaya 24 saat arayla iki doz analjezik tedavisi (Diclofenac sodyum) uygulanmıştır. Çalışmada birinci gruba ilk enjeksiyon Helfer skin tap tekniği ile ikinci enjeksiyon standart teknik ile; ikinci gruba ilk enjeksiyon standart teknik ile ikinci enjeksiyon Helfer skin tap tekniği ile yapılmış olup, çapraz tasarımlı, kendi kendinin kontrolü olan araştırma şeklinde yürütülmüştür. NRS, VAS ve VDS ölçekleri kullanılarak standart ve Helfer skin tap tekniği ile ortalama ağrı değerleri sırasıyla  $3.96 \pm 1.61$ ,  $3.56 \pm 1.91$ ,  $3.41 \pm 1.64$  ve  $2.55 \pm 1.57$ ,  $2.32 \pm 1.75$ ,  $2.22 \pm 1.65$  olarak belirlenmiştir. Helfer skin tap tekniğinin IM enjeksiyona bağlı yaşanan ağrıyı azaltmada etkili olduğu bildirilmiştir (Kaur ve diğerleri, 2019).

Güven ve diğerlerinin (2020) çalışmasında, bir devlet hastanesinin enjeksiyon polikliniğine analjezik (Diklofenak) tedavisi için başvuran 100 hasta dahil edilmiştir. Deneysel grubunda olan 50 hastaya Helfer skin tap tekniği kullanılarak ventrogluteal bölgeye 23 gauge iğne ile IM enjeksiyon uygulanmış, kontrol grubunda olan 50 hastaya standart teknik ile ventrogluteal bölgeye 23 gauge iğne ile IM enjeksiyon uygulanmıştır. Çalışma sonucunda, standart teknik uygulanan hastaların ağrı puan ortalaması  $2.88 \pm 1.02$ ; Helfer skin tap tekniği uygulanan hastaların ağrı puan ortalaması  $0.18 \pm 0.39$  olmakla birlikte aralarındaki farkın anlamlı olduğu bildirilmiştir (Güven ve diğerleri, 2020).

Karabey ve Karagozolu'nun (2021) çalışmasında, Aile Sağlığı Merkezi'ne Hepatit B aşısı yaptırmak amacıyla başvuran 180 bireyden araştırmaya dahil olma kriterlerini karşılayan 120 birey dahil edilmiş, Helfer skin tap tekniği, standart uygulama (kontrol), ShotBlocker tekniği ile uygulama yapılmıştır. Çalışma sonucunda, Helfer skin tap tekniği sonrasında ağrı puanı 4.00; standart uygulama sonrasında ağrı puanı 7.00; ShotBlocker tekniği sonrasında ağrı puanı 3.00 olarak belirlenmiştir. Sonuç olarak; IM enjeksiyona bağlı ağrının azaltılmasında ShotBlocker tekniğinin standart uygulama ve Helfer skin tap tekniğine göre daha etkili olduğu; Helfer skin tap tekniğinin ise standart uygulamaya göre etkili olduğu bildirilmiştir (Karabey ve Karagozolu, 2021).

## **SONUÇ**

Literatür incelemesi sonucunda, Helfer skin tap tekniğinin yetişkin hastaların IM enjeksiyona bağlı yaşadığı ağrı yönetiminde etkili olduğu, dolayısıyla konfor düzeyinin artırılmasına katkı sağladığı belirlenmiştir. Bu nedenle Helfer skin tap tekniğinin ülkemizde kurumsal politika olarak tanıtılması, IM enjeksiyona bağlı ağrının etkin yönetimi için tüm hastalara rutin bakım olarak uygulanması, kanıtları güçlendirmek amacıyla konuyla ilgili çalışmaların yürütülmesi, farklı popülasyonlarda ve farklı enjeksiyon uygulama teknikleri ile Helfer skin tap tekniğinin karşılaştırmalı çalışmalarda kullanılması önerilmektedir.

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**GENÇLER ARASINDA BAĞIMLILIĞIN BİR BOYUTU KRİPTO PARALAR  
CRYPTOCURRENCIES AS ONE DIMENSION OF ADDICTION AMONG YOUNG PEOPLE**

**Selma KAHRAMAN**

*Harran Üniversitesi, Sağlık Bilimleri Fakültesi, Halk Sağlığı Hemşireliği ABD., Şanlıurfa, Türkiye*

*ORCID ID: 0000-0002-4486-6629*

**Suzan HAVLİOĞLU**

*Harran Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu, Şanlıurfa, Türkiye*

*ORCID ID: 0000-0001-5593-5688*

**ÖZET**

Kripto paralar insanların kolay para kazanma arzusu ile rağbet görmesi ve doğal olarak da aşırı talep ile sınırlı sayıdaki Bitcoin kripto parasının değerinin beklenenden çok daha kısa bir sürede, beklenmedik meblağlara yükselmesi ve bu durumun da temelinde yatan kolay para kazanma arzusunun katlanarak ve bir hastalık gibi yayılarak büyümesine neden olmuştur. Bu çalışma gençlerin kripto para oynama sebeplerini ve oynama düzeylerini tespit etmek amacıyla yapılmıştır. Tanımlayıcı tipte bir araştırma olarak planlanan çalışmanın evrenini Sağlık Hizmetleri Meslek Yüksekokulunda öğrenim gören 2600 öğrenci oluşturmuştur. Çalışmada örneklem yöntemine gidilmemiş ve evrenin hepsine ulaşılması hedeflenmiştir. Araştırmaya çalışmaya katılmayı kabul eden 268 öğrenci dahil edilmiştir. Verilerin toplanmasında online olarak hazırlanan tanıtıcı sosyodemografik bilgi formu kullanılmıştır. Verilerin istatistiksel analizi SPSS 22.0 paket programında tanımlayıcı istatistikler, değişkenler arasında ilişki olup olmadığını göstermek için ki-kare testi kullanılmıştır. 0,05'ten küçük bir p değeri istatistiksel olarak anlamlı kabul edilmiştir. Çalışmaya katılan öğrencilerin %20.9'unun kripto para oynadığını, % 13.4'ü ailesinin kripto para ile ilgilendiğini, %52.2'si arkadaşlarının kripto para ile ilgilendiğini, %9.7'sinin arkadaş önerisi ile kripto para oynamaya başladığı saptanmıştır. Öğrencilerin %53.6'sı kısa sürede para kazanmak için, %76.8'i gece uyandığında ya da sabah kalktığında telefon uygulamasını kontrol ettiğini, %82.1'i herhangi bir ortamda ya da ziyaret sırasında kripto para uygulamasına bakma isteği olduğunu ifade etmiştir. Öğrencilerin kripto para oynayıp oynamama durumları ile cinsiyet, gelir durumu, herhangi bir işte çalışma durumu, sigara ve alkol kullanma durumu, aile ve arkadaş çevresinde kripto parayla ilgilenme durumu arasında ilişki olduğu saptanmıştır ( $p<0.05$ ). Çocukluk çağının önemli bir evresi olan ergenlik döneminde; ergenlerin sağlığının korunması, sürdürülmesi, risklerin erken fark edilmesi ve gerekli girişimlerin yapılması çok önemlidir. Kripto paralar gençler arasında bağımlılık düzeyine gelmeden önlenmesi gereken bir halk sağlığı sorunudur. Gençler arasında bu konuda farkındalığı arttırılacak çalışmalarının yapılması önerilmektedir.

**Anahtar Kelimeler:** Genç, Bağımlılık, Kripto Para

**ABSTRACT**

Cryptocurrencies have seen considerable demand due to people's desire to make easy money, and naturally, with excessive demand, the value of the limited amount of Bitcoin crypto money has risen to unexpected levels in a much shorter time than expected, thereby leading to the desire to make easy money, which underlies this issue, grow exponentially and spread like a disease. This study was conducted to determine the reasons for and the level of trading cryptocurrency by young people. The population of this study, in which a descriptive design was used, consisted of 2,600 students from a Health Vocational Higher School. No sampling method was used in the study; it was aimed to reach the entire population. The study sample included 268 students who agreed to participate in the study. An online sociodemographic data form was used to collect data. Statistical analysis of the data was conducted on SPSS 22.0 software package by using descriptive statistics and the chi-square test, which was used to check whether there was a relationship between variables. A p-value of  $<0.05$  was

considered statistically significant. It was determined that 20.9% of the participants in the study traded crypto money, families of 13.4% and friends of 52.2% were interested in it, and that 9.7% of the participants started trading crypto money with the recommendation of a friend. According to participants' responses, 53.6% started trading crypto money to make money in a short time, 76.8% checked the mobile crypto money application when they woke up at night or in the morning, and 82.1 % tended to check the crypto money application in any environment or during a visit. It was determined that there was a relationship between participants' status of trading cryptocurrency and their gender, income status, employment status, smoking and alcohol use, and interest in crypto money in the family and friends circle ( $p<0.05$ ). During adolescence, which is an important stage of childhood, it is very important to protect and maintain adolescents' health, recognize risks early, and carry out necessary interventions. Trading cryptocurrency is a public health problem that should be prevented before it reaches a level of addiction among young people. It is recommended to carry out studies to increase awareness of young people about this issue.

**Keywords:** Young, Addiction, Cryptocurrencies

## **GİRİŞ**

Kripto para, yepyeni bir alternatif para birimi olarak dijital olan sanal paralardır (Bulut ve menteş, 2022). Kripto Para (Cryptocurrency), günümüzde çokça konuşulan Bitcoin, Ethereum, XRP, EOS, Litecoin gibi kodlarında ve kodlanma şekillerinde kriptografinin kullanıldığı para birimlerine verilen genel isimdir. Kripto para teknolojisi çok yeni sayılabilecek bir geçmişe sahip olmasına rağmen, günümüz insanları çokça ilgi göstermektedir. Çünkü kripto paraların sanal ortamda olması hem küçük hem de büyük yatırımcıları uluslararası piyasalarda hareket edebilme kabiliyeti neden olmuştur (Bulut ve Menteş, 2022; Park ve ark. 2019; Aksoy, 2006; Çukurluöz, 2016). Kripto paralar insanların kolay para kazanma arzusu ile rağbet görmesi ve doğal olarak da aşırı talep ile sınırlı sayıdaki Bitcoin kripto parasının değerinin beklenenden çok daha kısa bir sürede, beklenmedik meblağlara yükselmesi ve bu durumun da temelinde yatan kolay para kazanma arzusunun katlanarak ve bir hastalık gibi yayılarak büyümesine neden olmuştur (Yellowlees ve Marks, 2007; Aksoy, 2006). Özellikle yüksek kazanç veya kayıplar kişilerin ruh hallerini doğrudan etkilemektedirler. Ayrıca dışarıdan müdahaleye açık yatırımlar da ise ani yükseliş ve düşmeler yatırımcıların yoğun takibini zorunlu kılmaktadır. Kripto para teknolojisi her ne kadar 2000'li yılların sonlarına doğru pratik hayata geçmiş olsa da ülkemizde akademik camianın ilgisini 2014 yılı itibarı ile çekmiş ve fakat konu sahip olması gereken öneme henüz kavuşmamıştır. Yapılan çalışmaların genellikle finans alanında yapıldığı görülmüştür (Bulut ve Menteş, 2022; Park ve ark. 2019; Aksoy,2006; Çukurluöz, 2016; Yellowlees ve Marks, 2007) Tüm bunlar dışında çalışmaların genel olarak kripto paraların sağlık üzerine etkisini ya da bağımlılık durumunu araştıran çalışmaya rastlanmamıştır. Bu yüzden bu çalışma en çok kullanan grup olan gençlerin kripto para oynama sebeplerini ve oynama düzeylerini tespit etmek amacıyla yapılmıştır.

## **MATERYAL VE METOD**

**Araştırmanın Amacı ve Türü:** Tanımlayıcı tipte yapılan bu çalışma; gençlerin kripto para oynama sebeplerini ve oynama düzeylerini tespit etmek amacıyla yapılmıştır.

**Araştırmanın Evren ve Örnekleme:** Araştırmanın evrenini Sağlık Hizmetleri Meslek Yüksekokulunda öğrenim gören 2600 öğrenci oluşturmuştur. Araştırmada evrenin tamamına ulaşılmaması hedeflendiği için örneklem seçimine gidilmemiştir. Araştırmanın örneklemini çalışmaya katılmayı kabul eden 268 öğrenci oluşturmuştur.

**Araştırmanın Veri Toplama Araçları:** Veriler araştırmacılar tarafından literatür taranarak hazırlanmış tanıtıcı bilgi formu kullanılarak toplanmıştır. Bu form öğrencilerin tanıtıcı özelliklerini ve kripto para oynama durumlarını içeren 25 sorudan oluşmuştur.

**Verilerin Toplanması:** Veriler 01.06.2022-01.08.2022 tarihleri arasında Sağlık Hizmetleri Meslek Yüksekokulu'nda öğrenim gören öğrencilerle online olarak toplanmıştır. Anketin cevaplanma süresi yaklaşık 10 dakikadır.

**Araştırmanın Bağımlı ve Bağımsız Değişkenleri:** Çalışmanın bağımsız değişkenleri, öğrencilerin yaşı, cinsiyeti, medeni durumu, anne-baba eğitim, gelir durumu, herhangi bir işte çalışma durumu, alkol-sigara kullanma durumu, egzersiz yapma durumu, aile ve arkadaşlarının kripto para ile ilgilenme durumu, kripto para ile yatırım yapma sebebi ve kripto para ile oynama şekilleri, çalışmanın bağımlı değişkeni ise kripto para oynama durumlarıdır.

**Verilerin Değerlendirilmesi:** Verilerin istatistiksel analizi Statistical Package for Social Sciences (SPSS 20.0) paket programı kullanılarak yapılmıştır. Çalışma verilerini değerlendirmek için tanımlayıcı istatistikler (sayı, yüzde, ortalama değerler), ki-kare testi ile katılımcıların kripto para oynama durumlarına ilişkin olarak Odds Ratio'ları (OR) dört gözlü tablolar kullanılarak hesaplanmıştır. 0,05'ten küçük bir p değeri istatistiksel olarak anlamlı kabul edilmiştir.

**Araştırma ile İlgili Etik Bilgi:** Araştırmanın yapılabilmesi için ilgili kurumdan ve Harran Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu'ndan izin alınmıştır. Öğrencilerden çalışmaya katılmayı kabul ettiklerine ilişkin onam alınmış, gönüllü olanlarla çalışma yürütülmüştür.

## **BULGULAR**

**Tablo 1. Öğrencilerin Tanıtıcı Özelliklerinin Dağılımı (N=268)**

<b>Değişken</b>		<b>Sayı</b>	<b>Yüzde</b>
Cinsiyet	Erkek	98	36.6
	Kadın	170	63.4
Yaş (20.28±1.69)	18-21	162	60.4
	22-34	106	39.6
Medeni durum	Evli	12	4.5
	Bekar	256	95.5
Baba öğrenim	Okur- Yazar	22	8.2
	İlkokul	94	35.1
	Ortaokul	56	20.9
	Lise	53	19.8
Anne öğrenim	Üniversite	43	16.0
	Okur-Yazar Değil	57	21.3
	Okur- Yazar	47	17.5
	İlkokul	87	32.5
	Ortaokul	41	15.3
Gelir durumu	Lise	26	9.7
	Üniversite	10	3.7
	Gelir Giderden Az	140	52.2
	Gelir Gidere Denk	110	41.1
	Gelir Giderden Çok	18	6.7
Çalışma durumu	Evet	32	11.9
	Hayır	236	88.1
Barınma durumu	Kyk	88	32.8
	Özel Yurt	4	1.5
	Arkadaşlarıyla Evde	16	6.0
	Ailesiyle	148	55.2
	Diğer	12	4.5
Sigara kullanıyor musunuz?	Evet	57	21.3
	Hayır	212	78.7
Alkol kullanıyor musunuz?	Evet	14	5.2
	Hayır	254	94.8
Egzersiz yapıyor musunuz?	Hergün	14	5.2
	Haftada birkaç kez	57	21.3
	Arasıra	197	73.5

Çalışmaya katılan öğrencilerin sosyodemografik verileri Tablo 1.de verilmiştir. Öğrencilerin %63.4'ü kadın, yaş ortalaması 20.28±1.69' dir. Öğrencilerin % 52.2'si gelirinin giderden az olduğunu, %55.2'si ailesiyle birlikte yaşadığını, % 78.7'si sigara kullanmadığını, %73.5'i ara sıra egzersiz yaptığını ifade etmiştir. Öğrenci aile özelliklerine bakıldığında hem annelerin hem de babalarının çoğunluğunun ilkökul düzeyin eğitim durumuna sahip olduğu görülmüştür. Öğrencilerin %11.9'u herhangi bir yerde çalıştığını ifade etmiştir.

**Tablo 2. Öğrencilerin Kripto Para ile İlgili Bilgi ve Uygulamaları (N=268)**

Değişken		Sayı	Yüzde
Ailenizde kripto para ile ilgilenen var mı?	Evet	36	13.4
	Hayır	232	86.6
Arkadaşlarınızda kripto para ile ilgilenen var mı?	Evet	140	52.2
	Hayır	128	47.8
Kripto para oynama durumu	Evet	56	20.9
	Hayır	212	79.1
Kripto sektörüne nasıl girdiniz?	Arkadaş önerisi	26	9.7
	Sosyal medya	6	2.2
	Kişisel merak	19	7.1
	Oynamıyorum	212	79.1
	Diğer	5	1.9
Yatırım yapma sebebiniz nedir?	Kısa sürede para kazanma	30	53.6
	Uzun vadede bu sektörün daha da büyüyecek olması	14	25.0
	Aileme maddi yardım sağlaması için	12	21.4
Paranızın ne kadarı ile kripto yatırımı yaptınız?	1-25	14	25.0
	25-50	12	21.4
	51-75	10	17.9
	76-100	20	35.7
Uzun vadeli olarak mı yatırım yapıyorsunuz?	Evet	31	55.4
	Hayır	25	44.6
Günlük al sat yapıyor musunuz?	Evet	27	48.2
	Hayır	39	51.8
Yatırım yaptığınız projeleri sosyal medyada takip ediyor musunuz?	Evet	36	64.3
	Hayır	20	35.7
Günlük kaç saat borsaları telefon uygulamasından açıp kontrol ediyorsunuz?	1-3	42	75.0
	4-8	14	25.0
Gece uyandığınızda ya da sabah kalktığınızda telefon uygulamasını kontrol ediyor musunuz?	Evet	43	76.8
	Hayır	13	23.2
Herhangi bir ortamda ya da ziyaret sırasında borsalara bakma isteğiniz oluyor mu?	Evet	46	82.1
	Hayır	10	17.9

Öğrencilerin kripto para ile ilgili bilgi ve uygulamaları Tablo 2'de verilmiştir. Çalışmaya katılan öğrencilerin %13,4'ü ailesinin kripto para ile ilgilendiğini, %52.2'si arkadaşlarının kripto para ile ilgilendiğini, %20.9'unun ise kendisinin kripto para oynadığını belirtmiştir. Öğrencilerin %9.7'sinin arkadaş önerisi ile kripto para oynamaya başladığı görülmüştür. Kripto para oynama nedenini öğrencilerin %53.6'sının kısa sürede para kazanmak için oynadığını belirtmiştir. Öğrencilerin çoğunlu parasının %76-100'ünü kripto paraya yatırdığını ifade etmiştir. Öğrencilerin uzun vadeli olarak kripto parayı yatırım yapma oranı %55,4 olarak hesaplanmıştır. Öğrencilerin %76.8'i gece uyandığında ya da sabah kalktığında telefon uygulamasını kontrol ettiğini, %82.1'i herhangi bir ortamda ya da ziyaret sırasında kripto para uygulamasına bakma isteği olduğunu ifade etmiştir.



Tablo 3. Öğrencilerin Sosyo-Demografik Özelliklerine Göre Kripto Para Oynama Durumlarının Karşılaştırılması

Değişken	Kripto para oynama durumu		p/ X <sup>2</sup> /OR
	Evet n/%	Hayır n/%	
Cinsiyet Erkek kadın	40/40,8 16/ 9,4	58/59,2 154/90,6	<b>0,001</b> X <sup>2</sup> :37,09 <b>OR:6,63</b>
Yaş 18-21 22-34	28/17,3 28/26,4	134/82,7 78/73,6	0,07 X <sup>2</sup> :3,23
Baba eğitim Ortaokul ve altı Lise ve üzeri	30/17,4 26/27,1	142/82,6 70/72,9	0,06 X <sup>2</sup> :3,45
Anne eğitim Ortaokul ve altı Lise ve üzeri	44/19,0 12/33,3	188/81,0 24/66,7	0,25 X <sup>2</sup> :1,32
Gelir Gelir giderden az Gelir gidere eşit veya fazla	20/14,3 36/28,1	120/85,7 33/71,9	<b>0,005</b> X <sup>2</sup> :7,74
Çalışma Durumu Evet Hayır	12/37,5 44/18,6	20/62,5 192/81,4	<b>0,014</b> X <sup>2</sup> :6,06 <b>OR:2,61</b>
Barınma Aile ile Birlikte Yurt/ev	32/21,6 24/20,0	116/78,4 96/80,00	0,74 X <sup>2</sup> :0,10
Sigara kullanma Evet Hayır	32/56,1 24/11,4	25/43,9 187/88,6	<b>0,001</b> X <sup>2</sup> :54,40 <b>OR:9,97</b>
Alkol kullanma Evet Hayır	10/71,4 46/18,1	4/28,6 208/81,9	<b>0,001</b> X <sup>2</sup> :22,82 <b>OR:22,8</b>
Ailede kripto para ile ilgilenme Evet Hayır	24/66,7 32/13,8	12/33,3 200/86,2	<b>0,001</b> X <sup>2</sup> :52,70 <b>OR:12,5</b>
Arkadaş çevresinde kripto para ile ilgilenme Evet Hayır	54/38,6 2/1,6	86/61,4 126/98,4	<b>0,001</b> X <sup>2</sup> :55,40 <b>OR:39,5</b>

X<sup>2</sup>: ki-kare testi OR: Odds Oranı

Öğrencilerin kripto para oynayıp oynamama durumları ile cinsiyet, gelir durumu, herhangi bir işte çalışma durumu, sigara ve alkol kullanma durumu, aile ve arkadaş çevresinde kripto parayla ilgilenme durumu arasında ilişki olduğu saptanmıştır. (p<0.05).

## TARTIŞMA

Gençler arasında kripto para kullanım durumu ve bağımlılık durumunu araştıran bu çalışma bildiğimiz kadarıyla literatürde ilkidir. Bu çalışmada gençlerin %20,9'unun (Tablo 2) kripto para oynadığını belirtmiştir. Bu oran yüksek bir orandır. Çünkü kripto paralar bilgisayar yardımı ile üretilmektedir ayrıca ticareti (alım satımı) internet aracılığı ile yapılmaktadır (Park, Im, Seol ve Paek, 2019). İnternette harcanan zamanın kontrol edilememesi genel olarak internet bağımlılığı olarak ifade edilir (Yellowlees ve Marks, 2007). Bu yüzden çalışmada örneği verilen çalışmalar aslında dikkatli irdelendiğinde bu konularda yapılacak çalışmaların artırılmasında toplum sağlığı açısından yararlar olduğu görülecektir.

Kripto para oynayan gençlerin çoğunluğu oynama nedeninin kısa sürede para kazanma olarak belirtmiştir. Bu önemli bir sorundur. Çünkü 2012 yılında sisteme kaydedilen günlük 7000 işlem sayısı 2021 itibarı ile günlük 1 milyon sayısını aşmıştır (Benzekri ve Özütlü, 2021). Artan işlem sayısına paralel olarak bazı kripto paralarda büyük fiyatlanmalar yaşanmıştır. Kripto paralar içerisinde en yaygın bilineni olan Bitcoin 2016 yılında %122 2017 de ise %1360 artış göstermiştir (Bouri, Shahzad ve Roubaud, 2019). Bu durumun gençler arasında bilinmesi ve kripto paranın bir anda çok yükselmesi kısa sürede para kazanma duygularını pekiştirmiş olduğunu düşündürmektedir.

Bu çalışmada erkekler kızlara göre 6 kat fazla oynamaktadır ( $p < 0.05$ , Tablo 3). Bu bulgu, konuyla ilgili Türkiye’de yapılan birçok çalışmanın sonuçlarıyla benzerlik göstermektedir (Aksoy, 2006; Çukurluöz, 2016; ve Bulut ve Menteş, 2022 ). Bu durum sosyal cinsiyet algısının etkisi, aile baskısının artması, geleneksel olarak kızlara oranla erkeklerin ayrıcalıklı olarak madde deneme riski fazla olan kafe, bar, kahve gibi sosyal ve eğlence ortamlarına daha rahat gidebilme imkanına sahip olması ile açıklanabilir.

Bu çalışmada alkol içenlerde yaklaşık 23 kat ve sigara içenlerde yaklaşık 10 kat kripto para kullanımı artmıştır ( $p < 0.05$ , Tablo 3). Sigara ve alkol kullanımı riskli bir davranıştır ve riskli bir davranışın var olması başka riskli davranışlara neden olacağı düşündürmektedir.

Bu çalışmadan çıkan diğer önemli sonuçlarda ailesinde kripto para ile ilgilenen kişi varsa yaklaşık 13 kat, arkadaşlarından varsa yaklaşık 40 kat daha fazla kripto para oynamaktadır. Kripto para oynama direkt ya da indirekt olarak ergenlerin sağlığını, iyilik hallerini ve yaşamlarını etkileyen potansiyel olarak olumsuz sonuçları olabileceğini düşündürmektedir Toplumun geleceği olan ergenlerin bu zorlu değişim süreci, ergeni, aileyi, arkadaşı, okulu ve hatta bütün toplumu ve geleceği etkilemesinden dolayı bir halk sağlığı sorunu haline gelmiştir. Bu nedenle çocukluk çağına önemli bir evresi olan ergenlik döneminde; ergenlerin sağlığının korunması, sürdürülmesi, risklerin erken fark edilmesi ve gerekli girişimlerin yapılması çok önemlidir.

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**ALTERNATIF TIP TERCİH EDİLME NEDENLERİ: ŞANLIURFA ÖRNEĞİ**  
**REASONS TO PREFER THE ALTERNATIVE MEDICINE: THE CASE OF SANLIURFA**

***Suzan HAVLİOĞLU***

*Harran Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu, Şanlıurfa, Türkiye*

*ORCID ID: 0000-0001-5593-5688*

***Hüseyin ERİŞ***

*Harran Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu, Şanlıurfa, Türkiye*

*ORCID ID: 0000-0002-1685-9819*

***Şevket ÖKTEN***

*Harran Üniversitesi Fen Edebiyat Fakültesi, Sosyoloji Bölümü, Şanlıurfa, Türkiye*

*ORCID ID: 0000-0001-8240-4911*

**ÖZET**

Bu çalışma Şanlıurfa'da yaşayan 18 yaş ve üzeri bireylerin alternatif tedavi tercihlerinin saptanması amacıyla planlanmıştır. Çalışma tanımlayıcı tipte olup evrenini Şanlıurfa'da yaşayan 18 yaş ve üzeri bireyler oluşturmaktadır. Çalışma da 01.07.2022 – 01.09.2022 tarihleri arasında çalışmaya katılmaya gönüllü 482 kişiye ulaşılmıştır. Çalışmada amaçlı örneklem yöntemi kullanılarak veriler yüz yüze görüşme tekniği ile toplanmıştır. Verilerin toplanmasında 30 soruluk sosyo-demografik bilgi formu kullanılmıştır. Araştırmaya katılan bireylerin %72,2'si alternatif tedavi yöntemlerinden attara gittiğini belirtmiştir. Daha sonra sırasıyla %57,7'si dua yöntemini ve %28'i hacamat yöntemini kullandıklarını ifade etmişlerdir. Araştırmaya katılan bireylerin %66,6'sı bel, diz ağrısı ve kireçlenme için, %42,8'i mide/bağırsak rahatsızlığı attara gittiğini belirtmişlerdir. Araştırmaya katılan ve çıkıcıya gidenlerin %96,9 kırık çıkık için, %27,3'ünün bel kayması için gittiklerini ifade etmişlerdir. Şeyh/hocaya gidenlerin %70,2'si ziyaret etmek için, %41,8'i muska yazdırmak ve %21,3'ü ise psikolojik rahatsızlıkları için gittiklerini ifade etmişlerdir. Şeyhe/hocaya çocuğunun olması için gidenlerin oranı %7,1 iken, büyü yaptırmak için gidenlerin oranı ise %7,8'dir. İnsanlar alternatif tedavi uygulamalarına doğal ve zararsız olduklarını düşündükleri için ve erişimin kolay olmasından dolayı daha fazla yönelmektedirler. İnsanlar en çok attar, dua okuma yöntemi, hacamat ve bitkisel yöntemleri kullanmakta olduğunu belirtmişlerdir. Geleneksel ve tamamlayıcı tıp merkezlerine (GETAT) başvuru oranları oldukça düşüktür. İnsanların alternatif tedavi yöntemlerini doğru ve etkin kullanmaları için GETAT merkezlerinin yaygınlaştırılarak halkın bilinçlendirilmesi gerekmektedir. Bu sayede profesyonel kişiler tarafından, ihtiyaç sahiplerine alternatif tıp hizmetleri daha yaygın sunulabilir. Ayrıca tedavi alan bireylerin zarar görmeleri engellenebilir.

**Anahtar Kelimeler:** Alternatif Tıp, Tamamlayıcı Tıp, Halk sağlığı

**ABSTRACT**

This study was planned to determine the alternative treatment preferences of individuals aged 18 and over living in Şanlıurfa. The study is of descriptive type and the population of the study consists of individuals aged 18 and over living in Şanlıurfa. In the study, 482 people who volunteered to participate in the study were reached between 01.07.2022 and 01.09.2022. In the study, the data were collected by face-to-face interview technique using the purposeful sampling method. A 30-question socio-demographic information form was used to collect data. 72.2% of the individuals participating in the study stated that they went to the herbal healer from alternative treatment methods. Afterwards, 57.7% of them stated that they used the prayer method and 28% used the cupping method, respectively. 66.6% of the individuals participating in the study stated that they went to the herbal healer for low backache,

knee pain and arthritis, 42.8% for stomach/intestinal discomfort. 96.9% of those who participated in the research and went to the ascendant healer stated that they went for fracture-dislocation, 27.3% of them went for back slippage. 70.2% of those who went to the sheikh/hodja stated that they went to visit, 41.8% to have amulets written and 21.3% to psychological disorders. While the rate of those who go to the sheikh/hodja to have a child is 7.1%, the rate of those who go to have magic is 7.8%. People tend to prefer alternative treatment applications because they think they are natural and harmless and because they are easy to access. People stated that they mostly use herbal healer, prayer reading method, cupping and herbal methods. Application rates to traditional and complementary medicine centers (GETAT) are very low. In order for people to use alternative treatment methods correctly and effectively, GETAT centers should be expanded and public awareness should be raised. In this way, alternative medicine services can be offered more widely by professionals to those in need. In addition, individuals receiving treatment can be prevented from being harmed.

**Key Words:** Alternative Medicine, Complementary Medicine, Public Health

## **GİRİŞ**

Dünya Sağlık Örgütü (DSÖ) sağlığı "bir bireyde sadece hastalıkların ve rahatsızlıkların olmayışı değil, bireyin bir bütün olarak değerlendirildiğinde fiziksel, ruhsal ve sosyal açıdan iyi olma hali" olarak tanımlamıştır (WHO, 2014). Tarihsel yolculuğunda da sağlık sürekli olarak insan hayatının merkezinde yer almıştır. İlkel dönemde insanlar bozulan sağlık durumlarını iyileştirmek ve geliştirmek için daha çok dini inanış ve dogma eksenli yetişen rahip veya rahip-hekim kişilere başvurma yoluna gitmiştir. Hekimler de bu hastaları bağlı bulunduğu inanışa göre değerlendirmiş ve tanı ve tedavi süreçlerini bunlara göre harekete geçirmiştir (Demir ve Balçık, 2022).

Günümüzde de insanlar hem sağlığı koruma hem de sağlık sorunlarının çözümü konusunda modern tıptan "halk tıbbi" olarak isimlendirilen yöntemlere kadar çeşitli yollara başvurumaktadırlar. (Furnham, 2002; Araz, Harlak ve Meşe, 2007). Bu yollar genel olarak tamamlayıcı veya alternatif tıp (TAT) olarak isimlendirilmektedir. Tamamlayıcı ve alternatif tıp (TAT) terimi iki ana başlıktan oluşmaktadır. Alternatif tıp, günümüz modern tıbbi tarafından kabul görmeyen ve modern tıbbi tedavilerin yerine kullanılan uygulamaları, tamamlayıcı tıp ise modern tıbbi tedavilere ek olarak uygulanan tedavi yöntemlerini temsil etmektedir. (O'Connor ve ark., 1997.)

Dünya Sağlık Örgütü'ne göre, Avrupa'da tahmini 100 milyon TAT kullanıcısı vardır. Amerika Birleşik Devletleri'nde (ABD), yaklaşık 33,2 milyon ABD'li yetişkin ve çocuk bir tür TAT kullanıyor. Avustralya, Kore, Kanada, Singapur ve Japonya gibi diğer gelişmiş ülkelerde de TAT kullanımının yüksek yaygınlık gösterdiği bildirilmektedir. (Veziari, Leach ve Kumar, 2017). Türkiye'de kırsal kesimde yapılan bir çalışmada geriatric bireylerde TAT kullanımının %98.3 olduğu, başka bir çalışmada ise yaşlı bireylerin %54,3'ünün TAT yöntemlerini uyguladığı belirtilmiştir (Dedeli ve Karadakovan, 2011; Sağlık ve ark., 2013).

Modern tıbbın gelişmesine rağmen, TAT kullanımı dünya çapında giderek artmaktadır. Alternatif tedavi yöntemlerinin uygulanmasının artmasına yönelik pek çok etmen sayılabilir. Yöntemlerin hasta-terapist ilişkisi sağlaması, modern tıbbın tedavi edemediği psikiyatrik, kronik ve son dönem hastalıklarda umut vermesi, daha az invaziv prosedürler içermesi, özellikle tedavi uygulayıcıların hasta ile fazla zaman geçirmesi, yöntemlerin kolay kabul görmesi, toplumun geleneğiyle uyumlu olması, tıbbi sağlık hizmetlerinden memnun kalmama, sağlık hizmetlerinde çok fazla talep olması kaynaklı bekleme sürelerinin uzun olması, tıbbi tedaviden ve yan etkilerden korkma, ulaşılabilirliğinin daha kolay olması, teknoloji reddi, ümitsizlik, hekim veya kurum güvensizliği, modern sağlık hizmetlerinden hoşnutsuzluk gibi nedenler bunlardan bazılarıdır (Kaptanoğlu ve Tosun, 2022; Şahin, 2017; Ünal ve Dağdeviren, 2019; Furlan ve ark., 2010).

Kullanım sebepleri ne olursa olsun, bu uygulamalara başvuranlar için en çok endişe edilecek durum, hastalıklarına tanı koydurmada ve tıbbi tedavi almada gecikebilmeleri ya da ehil olmayan kişilerin müdahaleleri veya kullanılan yöntemin yan etkileri sonucu zarar görebilmeleridir. Bu nedenle, toplumda geleneksel ve alternatif uygulamaların hangilerinin ne ölçüde ve ne amaçla kullanıldığının bilinmesi

önem kazanmaktadır (Özer, Turan ve Bakır, 2020). Bu çalışma Şanlıurfa’da yaşayan 18 yaş ve üzeri bireylerin alternatif tedavi tercihlerinin saptanması amacıyla planlanmıştır.

## **MATERYAL VE METOD**

Çalışma tanımlayıcı tipte olup evrenini Şanlıurfa’da yaşayan 18 yaş ve üzeri bireyler oluşturmaktadır. Şanlıurfa’nın 2020 Adrese Dayalı Nüfus kayıt sistemine göre 18 yaş ve üstü nüfusu 1.353.461’dir. Evreni bilinenden örneklem büyüklüğü 384 olarak hesaplanmıştır. Çalışma da 01.07.2022 – 01.08.2022 tarihleri arasında çalışmaya katılmaya gönüllü 482 kişiye ulaşılmıştır. Çalışmada amaçlı örneklem yöntemi kullanılarak veriler yüz yüze görüşme tekniği ile toplanmıştır Verilerin toplanmasında literatür taranarak tarafımızdan oluşturulmuş 30 soruluk sosyo-demografik bilgi formu kullanılmıştır.

Çalışmanın yapılabilmesi için Harran Üniversitesi Sosyal ve Beşeri Bilimler Etik Kurulu’ndan, Şanlıurfa Valiliği’nden ve çalışmaya katılacak olan bireylerden izin alınmıştır. Araştırmada elde edilen veriler SPSS istatistik programı ile analiz edilmiştir. Verilerin analizinde tanımlayıcı istatistikler (sayı, yüzde, ortalama) kullanılmıştır.

## **BULGULAR**

Çalışmaya katılan bireylerin yaş ortalaması  $33.6 \pm 11.7$  (min 18-max 83), % 44,6’sı ortaokul ve öncesi eğitim almış, %58,5’i evli ve %47,5’i gelir durumunun giderden az olduğunu ifade etmiştir.

**Tablo 1. Katılımcıların Sosyodemografik Özellikleri (n=482)**

<b>Değişkenler</b>	<b>Gruplar</b>	<b>N</b>	<b>%</b>
Yaş	18-34	279	57,9
	35-83	203	42,1
Cinsiyet	Kadın	195	40,5
	Erkek	287	59,5
Eğitim	Ortaokul ve öncesi	215	44,6
	Lise	146	30,3
	Üniversite ve üzeri	121	25,1
Medeni durum	Bekar	200	41,5
	Evli	282	58,5
Meslek	Ev hanımı	105	21,8
	İşçi	151	31,3
	Memur	49	10,2
	Emekli	14	2,9
	Diğer	163	33,8
Gelir durumu	Gelir giderden az	235	48,8
	Gelir gidere eşit	174	36,1
	Gelir giderden çok	73	15,1
Sigara kullanma durumu	Evet	217	45,0
	Hayır	265	55,0
Alkol kullanma durumu	Evet	53	11,0
	Hayır	229	89,0
Sürekli ilaç kullanma durumu	Evet	87	18,0
	Hayır	395	82,0
Kronik hastalık durumu	Var	72	14,9
	Yok	410	85,1
Aile üyeleri arasında sağlık personeli var mı?	Var	127	26,3
	Yok	355	73,7
Sağlıkla ilgili bilgilere nerden ulaşırsınız	İnternet	196	40,7
	Sağlık Personeli	198	41,1
	Aile	72	14,9
	Komşu/Arkadaş	16	3,3

Tablo 1’de arařtırmaya katılan bireylerin sosyo-demografik özellikleri verilmiştir. Tablo incelendiğinde bireylerin %57,9’u 18-34 yaş aralığında, %59,5’inin erkek, %44,6’sının ortaokul ve öncesi eğitime sahip oldukları, %58,5’inin evli olduğu ve %31,3’ünün işçi olduğu belirlenmiştir. Katılımcıların %48,8’inin gelirinin giderinden az olduğu, %55’inin sigara kullanmadığı, %89’unun alkol almadığı, %82’sinin sürekli ilaç almadığı tespit edilmiştir. Katılımcılar arasında kronik hastalığı olmayanların oranı %85,1’dir. Arařtırmaya katılan bireylerin aile üyeleri arasından sağlık personeli olanların oranı %26,3 olduğu belirlenmiştir. Katılımcıların %41,1’i sağlıkla ilgili bilgilere sağlık personelinden aldıklarının belirtmişlerdir.

**Tablo 2. Katılımcıların Alternatif Tedavi Tercihlerine İlişkin Görüşleri (n=482)**

Değişkenler		N	%
Daha önce doktora gittiniz mi?	Evet	422	87,6
	Hayır	60	12,4
Doktorun uyguladığı tedaviden fayda gördünüz mü?	Evet	316	65,6
	Hayır	88	18,3
	Kısmen	78	16,2
Alternatif/Tamamlayıcı tedavi yöntemleri için kime gittiniz?	Attar	348	72,2
	Çıkıcı	165	34,2
	Şeyh/Hoca	141	29,2
	Getat	33	6,8
Gittiyseniz kim tavsiye etti?	Arkadaş/komşu	377	78,2
	Akraba	178	35,3
	Sağlık personeli	53	10,9
	Diğer	66	13,7

Tablo 2’de arařtırmaya katılan bireylerin alternatif tedavi tercihlerine ilişkin görüşleri verilmiştir. Arařtırmaya katılan bireylerin %87,6’sı daha önce doktora gittiğini, %65,6’sının doktorun uyguladığı tedaviden fayda gördüğünü belirtmiştir. Bununla birlikte katılımcıların Alternatif tedavi yöntemi olarak en çok attara gittiklerini ve alternatif tedavi yöntemlerini kullanmalarını çoğunlukla arkadaş/komşuları tarafından tavsiye edildiğini ifade etmişlerdir.

**Tablo 3. Katılımcıların Alternatif Tedavi Kullanımına İlişkin Görüşleri (n=482)**

Değişkenler	Gruplar	N	%
Alternatif/Tamamlayıcı tıp yöntemlerinden hangilerini kullandınız?	Attar	348	72,2
	Dua	278	57,7
	Hacamat	135	28,0
	Sülük Uygulaması	57	11,8
	Akupunktur	7	1,5
	Ozon	6	1,2
	Apiterapi	3	0,6
	Fitoterapi	2	0,4
	Kaplıca Tedavisi	50	10,3
	Larva Uygulaması	0	0
	Mezoterapi	4	0,8
	Proloterapi	1	-
	Refleksoloji	4	0,8
	Muska	60	12,4
	Müzik Terapi	22	4,6
	Homeopati	2	0,4
	Osteopati	0	0
	Kayropraktik	1	-
	Hipnoz	2	-
	Diğer	5	1,0
Bitkisel	125	25,9	

Attara gelme amacınız	Bel, Diz Ağrısı, Kireçlenme	232	66,6
	Mide / Bağırsak rahatsızlığı	149	42,8
	Çocuğumun olması için	71	20,4
	Kırık ve çıkık İçin	53	15,2
	Romatizmal rahatsızlıklar	39	11,2
	Kanser (Akciğer, Kolon Vb.)	4	1,1
	Şeker,	14	4,0
	Kolesterol	5	1,4
	Hipertansiyon	3	0,8
	Migren	26	7,4
	Psikolojik rahatsızlıklar	16	4,5
	Kadın hastalıkları	13	3,7
	Diğer	37	10,6
Çıkıcıya gitme amacınız	Kırık ve çıkık	160	96,9
	Bel Kayması	45	27,3
	Ameliyattan korkma	16	9,7
	Tedavi süresinin hastanede uzun olması	8	4,8
	Sakat kalma korkusu	30	18,2
	Alçı yapılmasını istememe	23	13,9
	Diğer	32	19,4
	Şeyh/Hoca yagıtme amacınız	Ziyaret İçin (bir şey için istek, talep)	99
Muska		59	41,8
Psikolojik rahatsızlıklar		30	21,3
Çocuğumun olması için		10	7,1
Büyü		11	7,8
Diğer		39	27,6
Alternatif/Tamamlayıcı tıp yöntemleri tercih nedenleriniz	Bu yöntemler tamamen zararsızdır ve doğaldır	224	46,4
	Erişmek kolaydır	175	36,3
	Çevremde kullanıp faydasını görenler vardır	126	26,1
	Daha hızlı iyileştiriyor	125	25,9
	Tıbbi tedavi kadar etkilidir	123	25,4
	İnanç/Dini nedenler	62	12,8
	Hastalıklara karşı koruyucu olduğunu düşünüyorum	51	10,5
	Modern tıp ile çözüm bulamadım	39	8,0
	Diğer	62	12,8
Buralardan aldığımız tedaviden şifa buldunuz mu?	Evet	252	52,3
	Hayır	75	15,6
	Kısmen	155	32,1

Tablo 3’de araştırmaya katılan bireylerin alternatif tedavi kullanımına ilişkin görüşleri verilmiştir. Araştırmaya katılan bireylerin %72,2’si alternatif tedavi yöntemlerinden attara gittiğini belirtmiştir. Daha sonra sırasıyla %57,7’si dua yöntemini ve %28’i hacamat yöntemini kullandıklarını ifade etmişlerdir. Araştırmaya katılan bireylerin %66,6’sı bel, diz ağrısı ve kireçlenme için, %42,8’i mide/bağırsak rahatsızlığı, %15,2’sinin kırık ve çıkık için attara gittiğini belirtmişlerdir.

Araştırmaya katılan ve çıkıcıya gidenlerin %96,9 kırık çıkık için, %27,3’ünün bel kayması için gittiklerini ifade etmişlerdir.

Şeyh/hocaya gidenlerin %70,2’si ziyaret etmek için, %41,8’i muska yazdırmak ve %21,3’ü ise psikolojik rahatsızlıkları için gittiklerini ifade etmişlerdir. Şeyhe/hocaya çocuğunun olması için gidenlerin oranı %7,1 iken, büyü yaptırmak için gidenlerin oranı ise %7,8’dir.

Alternatif tedavi yöntemini kullananların %46.4'ü bu yöntemin tamamen zararsız ve doğal olduğunu, %36,3 bu yöntemlere erişimin kolay olduğunu ifade etmiştir. Bu katılımcıların %52,3'ü buralardan aldıkları tedavilerden şifa gördüklerini belirtmişlerdir.

## **TARTIŞMA**

Modern tıp etkili ve geçerli olsa da yaşam süresinin uzamasına paralel olarak kronik hastalıkların, tedavisi mümkün olmayan veya zor olan hastalıkların artması, kronik ve son dönem hastalıklarda umut vermesi, ilaçların yan etkilerinin ortaya çıkardığı sorunlar, doğallığın yan etkiden uzak olduğu düşüncesi, ulaşılabilirliğinin daha kolay olması, daha az invaziv girişim içermesi, yeni teknolojilerin yüksek fiyatlarının olması, sağlık personellerinin hastalara yeteri kadar zaman ayıramaması gibi sebeplerle alternatif tedavi uygulamaları popüler hale gelmiştir (Şahin, 2017; Öztürk, Akman ve Ünal, 2020).

Sağlık Bakanlığı da gelişmelere kayıtsız kalmayarak Geleneksel ve Tamamlayıcı Tıp Uygulamaları (GETAT) Yönetmeliği ile bu alanda yapılacak çalışmalarla ilgili düzenlemeler getirmiştir. Bu amaçla Türkiye'de en son 27 Ekim 2014 tarihli "Geleneksel ve Tamamlayıcı Tıp Uygulamaları Yönetmeliği" yayınlanmıştır. Bu yönetmelikte 15 yöntem kabul görmüş ve kullanım alanları ifade edilmiştir. Bunlar fitoterapi, mezoterapi, larva uygulaması, proloterapi, kupa uygulaması, müzik terapi, hipnoterapi, homeopati, sülük tedavisi, ozon uygulaması, osteopati, refleksoloji, akupunktur, apiterapi, kayropraktiktir (Ünal ve Dağdeviren, 2019).

Çalışmamızda katılımcıların kullandıkları tamamlayıcı ve alternatif tıp yöntemlerine bakıldığında en sık kullanılan yöntemlerin sırasıyla attar (%72.2), dinsel ve spirituel yöntemler (dua: %57,7), hacamat (%28,0), ve bitkisel ilaçlar (%25,9) olduğu saptanmıştır. Güvelinin çalışmasında bitkiler (%41,4), bitkisel ilaçlar (%29,7) ile dinsel ve spirituel yöntemler (dua: %32,5, şifalı su: %27,9, türbe ziyareti: %21,6) olarak bulunmuştur (Güveli ve ark., 2021). Şanlıurfa'da ki bireylerin kullandıkları alternatif tedavi yöntemleri literatürle benzerlik göstermekle beraber dua yöntemi daha aktif olarak kullanılmaktadır. Bunun nedeni olarak da bu şehirde yaşayan insanların dini olarak inançlarının daha yoğun olarak yaşandığı düşünülmektedir.

Çalışmamızda bireylerin tamamlayıcı ve alternatif tıp yöntemlerini tercih nedenlerine baktığımızda; bu yöntemler tamamen zararsızdır ve doğaldır (% 46,4), erişmek kolaydır (% 36,3), çevremde kullanıp faydasını görenler var (%26.1), daha hızlı iyileştiriyor (%25,9), tıbbi tedavi kadar etkilidir (%25,4) olarak tespit edilmiştir. Karayağızın çalışmasında medikal tedaviden fayda görmeme, ilaç yan etkilerinden korkma ve tat yöntemlerinin daha zararsız olduğunu düşünme hastaların TAT kullanımına yönelten yaygın nedenler olarak bildirilmektedir, Çekicin çalışmasında da TAT yöntemlerinin daha zararsız olduğunu düşünmeleri kullanım nedenleri olarak bildirilmiştir. (Karayağız ve ark., 2008; Çekiç ve ark., 2021). Literatürle uyumlu olarak insanlar alternatif tedavi yöntemlerine yönelmişlerdir.

## **SONUÇ VE ÖNERİLER**

Eski çağlardan beri hastalanan bireylerin tedavi edilmesi için geliştirilen ve kullanılan alternatif tedavi yöntemleri, günümüzde modern tıbbin yanında tamamlayıcı tıp uygulamaları olarak kullanılmaktadır. Bu geleneksel ve tamamlayıcı tıp uygulamaları hastalar tarafından bazen doğrudan tercih edilirken bazen de modern tıp uygulamalarının yanında tedaviye yardımcı olsun diye tercih edilmektedir. Alternatif tedavi yöntemleri insanlar tarafından özellikle doğal ve zararsız olduklarını düşündükleri için kullanılmaktadır. Ayrıca bu tedavi yöntemlerine erişimin kolay olması ve fiyat bakımından daha ucuz olmasından dolayı tercih edilmektedir. Bu çalışmada Şanlıurfa'da yaşayan katılımcıların çoğunluğu attara giderek, doğal bitkisel tedavi yöntemlerini kullandıklarını belirtmişlerdir. Ayrıca insanların dua okuma (Kuran'dan ayetler okunması gibi) yöntemi, hacamat ve şeyh/hocalara giderek tedavi olma yöntemlerini de tercih ettiği belirlenmiştir.

Şanlıurfa'daki katılımcılar tarafından GETAT merkezlerine başvuru oranları oldukça düşüktür. Bunun en önemli nedenlerinden biri GETAT merkezlerinin bilinmemesi ve Şanlıurfa ilinde sadece Mehmet Akif İnan Araştırma ve Uygulama Hastanesi'nde sadece bir polikliniğin olması nedeniyle ulaşımın zor olması düşünülmektedir. Alternatif tedavi yöntemlerinin doğru ve etkin kullanımın sağlanması için GETAT merkezlerinin yaygınlaştırılarak halkın bilinçlendirilmesi gerekmektedir. Bu sayede ehli



olmayan kişiler tarafında yürütülen bu yöntemlerin önüne geçilerek bireylerin yan etkiler sonucu zarar görmeleri engellenebilir.

Attar dükkanı açmak için herhangi bir yeterlilik belgesi istenmemektedir. Bitkilerin yanlış kullanımı, hastalara daha ciddi zararlar vereceği bilindiğinden, Sağlık Bakanlığı tarafından attarlara bitkiler ve içerikleri hakkında ciddi bir eğitim verilmesi ve bu eğitimden başarı ile geçenlere attar dükkanı açmaları için verilmesi faydalı olacaktır.

Ayrıca profesyonel olmayan kişiler tarafından yapılan hacamat, sülük gibi tedaviler, faydadan daha çok zarar sağlamaktadır. Bu gibi uygulama yapanların denetim altına alınması, eğitim verilmesi önemlidir.

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**HEMŞİRELİK ÖĞRENCİLERİNİN ŞİZOFRENİYE BAKIŞ AÇISI: NİTEL BİR ÇALIŞMA  
THE PERSPECTIVE OF NURSING STUDENTS ON SCHIZOPHRENIA: A QUALITATIVE STUDY**

*Arş. Gör. Sevda UZUN<sup>1</sup>*

<sup>1</sup> *Gümüşhane Üniversitesi Sağlık Bilimleri Fakültesi, Gümüşhane, Türkiye*

*ORCID NO: 0000-0002-5954-717X*

*Doç. Dr. Nilgün ULUTASDEMİR<sup>2</sup>*

<sup>2</sup> *Gümüşhane Üniversitesi Sağlık Bilimleri Fakültesi, Gümüşhane, Türkiye*

*ORCID NO: 0000-0002-2231-5236*

**ÖZET**

**Amaç:** Bu araştırmanın amacı hemşirelik öğrencilerinin şizofreniye yönelik bakış açısının belirlenmesidir.

**Gereç ve yöntem:** Araştırmada nitel araştırma modeli kapsamında durum çalışması deseni kullanılmıştır. Çalışmaya 16 hemşirelik öğrencisi katılmıştır. Verilerin analiz edilmesinde içerik analizi kullanılmış ve veriler kategorilere göre yorumlanmıştır.

**Bulgular:** Çalışma sonucunda öğrencilerin şizofreniye yönelik bakış açısının yoğunlaştığı temaların şizofreninin özellikleri, şizofreninin oluşma nedenleri, şizofrenili bireyleri topluma kazandırmak için yapılması gerekenler ve şizofreninin tedavisi olduğu tespit edilmiştir. Öğrencilerin şizofreninin özelliklerine yönelik düşünceleri temasında daha çok halüsinasyon, sanrı ve saldırganlık alt temaları ilk sıralarda yer alırken, şizofrenili bireyleri topluma kazandırmak için yapılması gerekenler temasında onları soyutlamamak, onları ötekileştirmemek ilk sıralarda yer almaktadır. Şizofreninin oluşma nedenleri arasında beyinde nörotransmitterlerin yetersizliği, çocuklukta yaşanan travmalar ve beyin fonksiyonlarında değişim alt temaları yer almaktadır.

**Sonuç:** Yapılan araştırma sonucuna göre, öğrencilerin şizofreni hastalığını tanıdıkları ancak özellik ve tedavisine ilişkin yanlış bilgilere sahip oldukları belirlendi. Öğrencilerin büyük bir kısmının şizofreni hastalarına ilişkin damgalayıcı tutum sergiledikleri şizofreni hastalarını saldırgan buldukları ve şizofrenili bireylerin topluma kazandırılması konusunda önemli oranda olumsuz düşünce, inanç ve duyguya sahip oldukları sonucuna varıldı. Hemşirelik öğrencileriyle şizofreni hakkında bilgilerini artırmak ve tutumlarını olumlu hale getirmek için çeşitli etkinlikler düzenlenmesi ve eğitim müfredatında verilen derslerin içeriklerine psikiyatrik hastalıklara yaklaşım konusu yerleştirilmesi önerilmektedir.

**Anahtar Kelimeler:** Şizofreni Algısı, Bakış açısı, Hemşirelik

**ABSTRACT**

**Objective:** The aim of this study is to determine the perspective of nursing students towards schizophrenia.

**Materials and methods:** The case study pattern was used in the study within the scope of the qualitative research model. 16 nursing students participated in the study. Content analysis was used to analyze the data and the data were interpreted according to the categories.

**Results:** As a result of the study, it was determined that the themes on which the students' point of view towards schizophrenia is concentrated are the characteristics of schizophrenia, the causes of schizophrenia, what needs to be done to bring people with schizophrenia into society, and the treatment of schizophrenia. Thoughts students are in contact on the features of schizophrenia hallucinations,

delusions and aggression, while the themes in the first place, individuals with schizophrenia in contact to provide the society with what needs to be done for them, divide them, and to otekilestirmem ranks in the first tier. The causes of schizophrenia include the decency of neurotransmitters in the brain, traumas experienced in childhood, and sub-themes of changes in brain function.

**Conclusion:** According to the results of the research, it was determined that the students recognized schizophrenia but had incorrect information about its characteristics and treatment. Schizophrenia patients with schizophrenia exhibit their patients, the majority of students stigmatizing attitudes they find their offensive, and reintegration of individuals with schizophrenia significant negative thoughts, beliefs and feelings that they have concluded. It is proposed to organize various events with nursing students to increase their knowledge about schizophrenia and make their attitudes positive, and to include an approach to psychiatric diseases in the content of the courses given in the educational curriculum.

**Keywords:** Schizophrenia Perception, Perspective, Nursing

## **GİRİŞ**

Şizofreni; erken yaşlarda başlayan bireyin gerçeklerden uzaklaşıp kendine özgü bir içe kapanım dünyasında yaşadığı düşünce, algı ve davranışlarda birtakım bozuklukların görüldüğü bir ruhsal bozukluktur (Öztürk ve Uluşahin, 2011).

Şizofreni, çağlar boyu sağlık profesyonellerine ve bilim adamlarına konu olmuştur (Çam ve Engin 2014, Öztürk ve Uluşahin 2011). M.S. birinci ve ikinci yüzyıllarda yaşamış olan Areteus ve Soranus, şizofrenide görülen bozukluklardan bazılarını ve özellikle kuşkucu türdeki bozuklukları günümüzdekine benzer olarak tanımlamışlardır. 17.yy'da Willis'in, 18.yy'da Pinel'in şizofreniye ilişkin yazıları mevcuttur. Özellikle Ortaçağ'da şizofreni batıl inançlarla birlikte üstü kapatılan bir hastalık olmuş ve 19.yy'ın ortalarına doğru bilimsel anlamda incelenmiştir (Yüksel 2006, Çam ve Engin 2014).

Hemşirelikte lisans eğitimine baktığımızda ana amaç her bir öğrencinin eğitimini tamamlamış bir hemşire olarak sağlık sektöründe farklı dallarda donanımlı olarak çalışmaya hazır hale gelmesidir (Happell,1999). Geleceğin sağlık profesyonellerinin ruhsal hastalığa sahip bireylere en kaliteli bakım hizmetini sunması oldukça önemlidir. Bu araştırmanın elde edilen sonuçlar açısından, konuyla ilgili alan yazında yeni araştırmalara ışık tutacak şekilde nitelikli veriler kazandıracağı düşünülmektedir. Ayrıca ruhsal hastalığa sahip bireylerin bakım ve tedavisinde önemli görevler üstlenecek olan hemşirelik son sınıf öğrencileriyle yapılmış olması çalışmaya çok daha anlam katmaktadır.

## **GEREÇ VE YÖNTEM**

### **Araştırmanın Amacı ve Tipi**

#### **Araştırmanın amacı**

Bu araştırmada nitel araştırma yaklaşımlarından durum çalışması deseni kullanılmıştır. Durum çalışması, bir olguyu, bir durumu ayrıntılı olarak ele alan bir araştırma yöntemidir. Başka bir tanıma göre durum çalışması araştırmacının zaman içerisinde sınırlandırılmış bir veya birkaç durumu çoklu kaynakları içeren veri toplama araçları (gözlemler, görüşmeler, görsel-işitseller, dokümanlar, raporlar) ile derinlemesine incelediği, durumların ve duruma bağlı temaların tanımlandığı nitel bir araştırma yaklaşımıdır. (McMillan, 2000; Yin 2003).

#### **Çalışma Grubu**

Araştırma bir devlet üniversitesinin hemşirelik bölümünde öğrenim gören 16 öğrenci ile yapılmış ve çalışma konusunda gönüllü katılım sağlama şartı aranmıştır.

#### **Veri Toplama Araçları**

Hemşirelik öğrencilerinin şizofreniye bakış açısına ilişkin görüşlerinin belirlenmesi amacıyla planlanan bu çalışmada öğrencilere şizofreni ile ilgili dört tane açık uçlu soru yöneltilmiştir. Hazırlanan soruların inanılabilirliği uzman görüşüne başvurulmuş ve yapılmıştır. Psikiyatri hemşireliği ve cerrahi hemşireliği alanında uzman üç öğretim elemanından soruların araştırma problemine uygunluğu, açıklığı ve

anlaşılabilirliği ile ilgili görüş alınmış görüş birliğinin sağlandığı sorular görüşme formuna dahil edilmiştir. Görüşme formunun katılımcılara, anlama ve ifade rahatlığı sağlayacağı düşünülerek, soruların açıklık ve anlaşılabilirliği gözden geçirilmiş ve son hali verilmiştir.

### **Veri Toplama Süreci**

Öğrencilere çalışma öncesi bilgilendirme yapılmış ve gönüllülük esasına dayandığı bildirilmiştir. Çalışmada öğrencilere birer A4 kâğıdı dağıtılarak öğrencilerin sorulara cevap vermesi istenmiştir. Öğrencilerden açık uçlu soruları cevaplandırmaları istenmiştir. Öğrencilerden bilgi verildikten sonra bir hafta süre tanınmış ve daha sonra formlar geri toplanmıştır.

### **Araştırmanın Etik Boyutu**

Araştırmanın yapılabilmesi için X Üniversitesi Bilimsel Araştırma ve Yayın Etiği Kurulu'ndan (2020/3 sayılı) onam alınmıştır.

### **Verilerin Analizi**

Araştırmada verilerin analizinde içerik analizi yöntemi kullanılmıştır. İçerik analizinde temel amaç, birbirine benzeyen verileri belirli kavramları bir araya getirmek ve bunları okuyucunun anlayabileceği biçimde düzenleyerek sunmaktır (Kurt ve Ekici., 2014). Bu işlem birtakım aşamalardan oluşmaktadır. Bu çalışmada; kod, kategori ve temaların oluşturulması aşamaları izlenmiştir. Uygun kodlar bir araya getirilerek kategoriler oluşturulmuştur. Uygun kategorilerin bir araya getirilmesiyle araştırmanın temaları belirlenmiştir (Yıldırım ve Şimşek, 2009;Burns, 2007).

## **BULGULAR**

**Tablo 1. Şizofreni kavramı konusunda elde edilen bulgular**

<b>Kategoriler</b>	<b>Alt kategoriler</b>
<b>1.Şizofreninin özellikleri</b>	Sanrılar
	Halüsinasyonlar
	Saldırganlık
	Suicid riski
	Yalnızlık
<b>2.Şizofreninin oluşma nedenleri</b>	Beyinde nörotransmitterlerin yetersizliği
	Çocuklukta yaşanan travmalar
	Aile ve yaşanmışlıklar
	Genetik faktörler
<b>3.Şizofrenili bireyleri topluma kazandırmak için yapılması gerekenler</b>	Onları soyutlamamak
	Onları ötekileştirmemek
	Onlardan korkmamak
	Onlara değer vermek
<b>4. Şizofreninin tedavisi</b>	İlaç tedavisi
	Aile terapisi
	EKT
	Tedavisi yok

Tablo 1'de görüldüğü gibi "Şizofreninin özellikleri" temasında en yüksek değerlerde olduğu ortaya çıkmıştır. Bu temada en fazla sanrılar, halüsinasyonlar ve saldırganlık kavramlarının ifade edildiği görülmektedir. Hemşirelik öğrencilerinin şizofreninin özellikleri temasına yönelik örnek ifadelerine aşağıda yer verilmiştir.

*"Şizofreni sanrılar ve halüsinasyonlar bütünüdür.(Ö54).*

*"Şizofrenili birey gerçeği kavrayamayan insandır.(Ö64).*

*"Şizofreni sosyal ilişkileri bozan bir hastalıktır."(Ö29).*

Şizofrenili bireyleri topluma kazandırmak için yapılması gerekenler temasında onları soyutlamamak, onları ötekileştirmemek ilk sıralarda yer almaktadır. Hemşirelik öğrencilerinin şizofrenili bireyleri topluma kazandırabilmek için yapılması gerekenler temasına yönelik örnek ifadelerine aşağıda yer verilmiştir.

*“Şizofrenili bireyler toplumda uzak durulması gereken değil kazanılması gereken bireylerdir.” (Ö2)*

Şizofreninin oluşma nedenleri temasında arasında beyinde nörotransmitterlerin yetersizliği, çocuklukta yaşanan travmalar ve beyin fonksiyonlarında değişim alt temaları yer almaktadır. Hemşirelik öğrencilerinin şizofreninin oluşma nedenleri temasına yönelik örnek ifadelerine aşağıda yer verilmiştir.

*“Şizofreni serotonin ve diğer nörotransmitterlerin azalması ya da yaşanmış travmaların etkili olduğu psikotik bir hastalıktır” (Ö1),*

*“Şizofreni beyin fonksiyonlarının gelişmemesi sonucu oluşur.” (Ö26).*

Şizofreninin tedavisi temasında ilaç tedavisi ve aile tedavisi alt temaları ilk sıralarda yer almaktadır. Hemşirelik öğrencilerinin şizofreninin tedavisi temasına yönelik örnek ifadelerine aşağıda yer verilmiştir

*“Şizofreninin tedavisi yoktur fakat ilaçla yatırılır.” (Ö6);*

## **TARTIŞMA**

Çalışmada öğrencilerin şizofreninin özelliklerini çoğunlukla halüsinasyon olarak tanımladıkları belirlenmiştir. Alpan ve arkadaşlarının (2018)' de yaptıkları çalışmada ise öğrencilerin büyük bölümü şizofreninin özelliklerini “Şizofreni bir ruhsal zayıflık halidir” ifadesi olarak tanımlamıştır (Alpan ve ark., 2018). Ayrıca çalışmada öğrencilerin bir kısmının şizofreninin özelliklerini saldırgan kişilik olarak ifade ettikleri saptanmıştır. Çalışma sonuçlarına benzer olarak Yanık ve arkadaşlarının (2003) yaptığı “Tıp Fakültesi Öğrencilerinin Şizofreniye Karşı Tutumları ve Psikiyatri Eğitiminin Etkisi” başlıklı çalışmaya baktığımızda “şizofrenler saldırgan olur” ifadesine tıp ve hemşirelik öğrencileri büyük oranda katılmışlardır (Yanık ve ark., 2003).

Araştırmada katılımcıların şizofreninin oluşma nedenini çocuklukta yaşanan travmaları olarak gördükleri belirlenmiştir. Çalışmamıza paralel olarak Kayahan (2009) Hemşirelik Öğrencilerinin Şizofreniye Karşı Tutumları Ve Psikiyatri Eğitiminin Etkisi başlıklı çalışmada şizofreninin oluşma nedenlerine ilişkin yanıtlara 4.sınıf öğrencilerinin %34.5'i “kisilik yapısının zayıflığından kaynaklanmaktadır”, %37.9'u “sosyal sorunlar nedeniyle ortaya çıkar”, yanıtını vermişlerdir (Kayahan ve ark., 2009). Alpan ve arkadaşlarının (2018) yaptıkları “Sağlık Bilimleri Fakültesi Öğrencilerinin Şizofreni Hastalığına Karşı Tutumları” başlıklı çalışmada şizofreni hastalığının etiyojisine ilişkin, öğrencilerin görüşleri incelendiğinde; öğrencilerin, yarıya yakını şizofreninin kişilik yapısının zayıf olmasından ve yarısının yaşadığı sosyal sorunlardan kaynaklandığına katıldığı belirlenmiştir (Alpan ve ark., 2018).

Araştırmada öğrencilerin şizofrenili bireyleri topluma kazandırmak için yapılması gerekenler temasında en çok onları toplumdan soyutlamamak ifadesi yer almıştır. Alpan ve arkadaşlarının (2018) yaptıkları çalışmada öğrencilerin çok azının şizofreni olan bir kişiyle evlenebileceği, iş arkadaşı olmasını ve kiracısı olmasını isteyebileceği belirtilmiştir (Alpan ve ark., 2018). Arslantaş ve arkadaşlarının (2019) “Lise Öğrencilerinin Ruhsal Hastalıklara Yönelik İnanç ve Sosyal Mesafelerini Etkileyen Faktörler” başlıklı çalışmada ruhsal hastalığı olan bireylerin toplumda yer alması gerektiğini ve bireylerle yakın olması gerektiğini düşünen öğrencilerin oranı %59.4 olarak saptanmıştır (Arslantaş ve ark., 2019).

## **SONUÇ**

Araştırma sonuçlarına göre öğrencilerin şizofreni hastalığı konusunda eksik veya yanlış bilgilere sahip oldukları belirlenmiştir. Şizofreni hastalığı olan bireylerin topluma kazandırılması gerektiği göz önüne alındığında şizofrenili bireylerin sağlığının korunması, geliştirilmesi ve tedavi edilmesinde önemli görevler üstlenecek hemşire adaylarının şizofreni konusunda pozitif bakış açısı geliştirmeleri oldukça önemlidir. Elde edilen bulgular doğrultusunda aşağıdaki şu öneriler yapılabilir;

✓ Hemşirelik öğrencilerinin pozitif bakış açısı geliştirebilmeleri için teorik derslerde şizofreni hastalığı konusunda sosyal boyutta da bilgilendirme yapılmalıdır.

✓ Öğrencilerin bireylere hasta merkezli bütüncül bakım verebilmeleri için psikiyatri kliniklerinin öğrencilerin en iyi şekilde yararlanabilecekleri şekilde düzenlenmesi sağlanmalıdır.

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**PSİKİYATRİ HEMŞİRELİĞİ VE TERAPÖTİK İLİŞKİ**  
**PSYCHIATRIC NURSING AND THERAPEUTIC RELATIONSHIP**

**Arş. Gör. Sevda UZUN<sup>1</sup>**

<sup>1</sup> *Gümüşhane Üniversitesi Sağlık Bilimleri Fakültesi, Gümüşhane, Türkiye*

*ORCID NO: 0000-0002-5954-717X*

**Doç. Dr. Nilgün ULUTASDEMİR<sup>2</sup>**

<sup>2</sup> *Gümüşhane Üniversitesi Sağlık Bilimleri Fakültesi, Gümüşhane, Türkiye*

*nulutademir@yahoo.com, ORCID NO: 0000-0002-2231-5236*

**ÖZET**

Sosyal bir varlık olan insan sosyal yaşamı içerisinde diğer insanlarla iletişimde bulunurken iletişim becerilerini etkili kullanabilmek oldukça önemlidir. Uğraş alanı insan üzerine olan hemşirelik mesleğinde zaman çok büyük önem taşır ve bu bağlamda, iletişimi kolaylaştıran tekniklerin bilinmesi ve uygulanması çok önemlidir. Her hastanın psikolojisi; uygulanan tedaviyi, hastane ortamını, tıbbi tanısını, uygulamaları kaldırabilecek kadar uygun olmayabilir. Böyle durumlarda hem tedavinin aksamaması hem de hastanın psikolojisinin normal ayarlarda tutulması için etkili ve kolaylaştırıcı iletişim kurulmalıdır. Psikiyatri hemşireliği birey, aile ve toplumun ruhsal hastalıklara karşı korunmasında, toplumun ruh sağlığının geliştirilmesinde, hastalığın getirdiği yük ile baş etme ve bu yaşantılarından anlam bulmasında yardımcı olan profesyonel bir hemşirelik sürecidir. İşlevleri arasında sağlığı geliştirme ve koruma, tarama, değerlendirme, triaj, vaka yönetimi, terapötik ve güvenli ortam oluşturma, öz-bakım aktivitelerinin öğretilmesi ve desteklenmesi, psikobiyolojik tedavilerin rejimini yönetmek ve izlenmesi, krize müdahale ve psikiyatrik rehabilitasyon yer almaktadır. Terapötik kelime olarak tedavi edici, tedavi sanatı gibi anlamları içermektedir. Terapötik ilişki karşılıklı etkileşime dayalı, kapsamlı, karmaşık ve özgün bir nitelik taşımaktadır. Literatür incelendiğinde özellikle hümanistik (insancıl) yönelimli terapötik yaklaşımları benimseyen terapistlerin yardım sürecinde insan olmaktan kaynaklanan faktörleri daha çok dikkate aldıkları görülmektedir. Terapötik ilişkiyi bazı durumlar etkileyebilmektedir. Terapistin kendi yaşantıları, terapötik süreçte cinsiyet ve cinsiyet rolü, eşitlik, kültürel değerler, ahlaki tutum, sınır koyma gibi durumlar bazı zamanlarda danışan ile danışman arasındaki ilişkiyi olumsuz etkileyebilmektedir. Danışanların pek çoğu dıştan denetimli, yalnız, mutsuz ve düşük benlik saygısına sahip bireylerdir ve aynı zamanda terapiye duygusal, psikolojik, fiziksel veya cinsel yönden istismar edilmiş olarak gelebilmektedirler. Bundan dolayı da terapötik süreçte danışan ile danışman arasındaki ilişki profesyonel olmalı ve bu şekilde ilerlemelidir. Danışan ve danışan arasındaki ilişkinin formal bir ilişki olduğu unutulmamalıdır.

**Anahtar Kelimeler:** Terapötik ilişki, psikiyatri hemşireliği, terapötik etkileşim

**ABSTRACT**

Being a social being, it is very important to use communication skills effectively when communicating with other people in human social life. Time is of great importance in the nursing profession, whose field of activity is human, and in this context, it is very important to know and apply techniques that facilitate communication. The psychology of each patient; the treatment applied, the hospital environment, the medical diagnosis may not be suitable enough to remove the applications. In such cases, effective and facilitating communication should be established so that both the treatment is not disrupted and the patient's psychology is kept in normal settings. Psychiatric nursing is a professional nursing process that helps an individual, family and society to protect against mental illnesses, improve the mental health of the community, cope with the burden of the disease and find meaning from these lives. Functions include health promotion and prevention, screening, Assessment, Triage, case management, therapeutic and create a safe environment, self-care activities and teaching support,



managing and monitoring a regime of psychobiological therapy, crisis intervention, and psychiatric rehabilitation centre. Therapeutic as a word, therapeutic includes meanings such as therapeutic, therapeutic art. The therapeutic relationship is based on mutual interaction, has a comprehensive, complex and original nature. When the literature is examined, it is seen that therapists who adopt humanistic (humane) oriented therapeutic approaches especially take into account the factors arising from being human more in the help process. Some situations may affect the therapeutic relationship. Situations such as the therapist's own life, gender and gender role in the therapeutic process, equality, cultural values, moral Decency, setting boundaries can sometimes negatively affect the relationship between the client and the consultant. Many of the clients are externally supervised, lonely, unhappy and low self-esteem individuals, and they may also come to therapy as emotionally, psychologically, physically or sexually abused. Therefore, the relationship between the client and the consultant during the therapeutic process should be professional and proceed Decisively. It should be remembered that the relationship between the client and the client is a formal relationship. Dec.

**Keywords:** Therapeutic relationship, psychiatric nursing, therapeutic interaction

## **GİRİŞ**

Psikiyatri hemşireliği birey, aile ve toplumun ruhsal hastalıklara karşı korunmasında, toplumun ruh sağlığının geliştirilmesinde, hastalığın getirdiği yük ile baş etme ve bu yaşantılarından anlam bulmasında yardımcı olan profesyonel bir hemşirelik sürecidir (Çam,2014). Amerikan Hemşireler Birliği (ANA)'ne göre "Psikiyatri hemşireliği; sanat olarak kendiliğince amaçlı kullanımı, bilim olarak ise psikososyal ve nörobiyolojik kuramların, araştırma bulgularının ve hemşireliğin çeşitli rollerinin kullanımı ile hizmet veren ruh sağlığı profesyonelidir (Varcarolis and Halter,2004).

Psikiyatri klinik hemşiresi: Üniversitelerin hemşirelik bölümlerinin lisans programlarından mezun olarak hemşire ünvanını almış ve Sağlık Bakanlığınca onaylanan "psikiyatri birimlerinde hemşirelik hizmetleri" sertifikalı eğitimini tamamlamış meslek mensubudur. İşlevleri;

- Sağlığı geliştirme ve koruma
- Tarama, değerlendirme, triaj
- Vaka yönetimi
- Terapotik ve güvenli ortam oluşturma
- Öz-bakım aktivitelerinin öğretilmesi ve desteklenmesi
- Psikobiyolojik tedavilerin rejimini yönetmek ve izlenmesi
- Krize müdahale
- Psikiyatrik rehabilitasyon

## **HEMŞİRE HASTA ETKİLEŞİMİNİ KOLAYLAŞTIRAN TEKNİKLER**

İletişim "Bilgi alışverişi bilgi üretme ve anlamlandırma sürecidir". İletişimin önemi hemşirelik mesleğinde insan ilişkisi içinde sürdürülmesi nedeniyle artmaktadır (Babadağlı ve ark 2006).

Hemşirenin hastayla kurduğu terapötik iletişimin hastanın tedavi sürecine oldukça olumlu etkileri bulunmaktadır. Bunlar:

- ✓ Zaman, işgücü ve maliyet kaybını önlemektedir.
- ✓ Hastanın bakıma dahil olmasını sağlamaktadır.
- ✓ Yapılan uygulamaların yanlış anlaşılmasını önlemektedir.
- ✓ Farmakolojik tedaviye destek sağlamaktadır.
- ✓ Hastanın yatış süresini azaltmaktadır.
- ✓ Ekip ve hasta arasında güven oluşturmaktadır.

- ✓ Problemlerin çözümüne katkı sunmaktadır (Özcan, 2006) .

### **TERAPÖTİK İLİŞKİ**

Terapötik kelime olarak tedavi edici, tedaviye ait, tedavi sanatı gibi anlamları içermektedir. Terapötik ilişki karşılıklı etkileşime dayalı, kapsamlı, karmaşık ve özgün bir nitelik taşımaktadır (Corsini ve Wedding, 1986; Xiangyi, 2009).

Kendiliğın katıldığı gerçeklik, iki kişinin de insan olmasından kaynaklı olarak ortaya çıkan ve özellikle terapist tarafından sağlanan karşılıklı eşitlik ve saygıya dayalı bir etkileşim sürecidir (Heid and Parish, 1997; Weishaar, 2007).

### **TERAPÖTİK İLİŞKİYİ ETKİLEYEN FAKTÖRLER**

- ✓ Cinsiyet ve Cinsiyet Roller
- ✓ Eşitlik
- ✓ Kültürel Değerler
- ✓ Ahlaki Tutum
- ✓ Sınır Koyma
- ✓ Terapistin Kendi Yaşantıları

### **TERAPÖTİK İLİŞKİDE EŞİTLİK**

Danışan ve danışman ilişkisinin terapötik süreci etkileyen en önemli özelliklerinden birisi, danışmanın ve danışanın her ikisinin de birey olarak eşit olmasıdır. Literatür incelendiğinde hümanistik yönelimli tedavi edici yaklaşımları benimseyen danışmanların yardım sürecinde insancıl faktörleri daha çok dikkate aldıkları görülmektedir (Gelso and Mohr, 2001).

Danışmanların danışma sürecinde kendilerini açmaları da danışma sürecinde eşitlik olarak algılanabilir (Ain and Chipping, 2008; Sady and Vaughn, 2005).

### **TERAPÖTİK İLİŞKİDE SINIR KOYMA**

Terapist, danışanın terapötik sürecin istenmedik yönde ilerlemesini sağlayan tutumları ile başa çıkmak oldukça önemlidir. Bu bağlamda hem kendisinin hem de danışanın süreçteki rollerini yerine getirebilmesi için danışanıla arasına sınır koyması oldukça önemlidir (Johntson, 2001).

Sınır danışmanlara göre farklılıklar göstermektedir ve bu sınırın kuramsal yaklaşım nedeniyle mi yoksa danışanın ihtiyacı olduğu için mi olduğu çok önemlidir. Bu noktada terapist terapötik süreçte danışan ve danışman arasındaki ilişkiyi iyi kurmalıdır (Johntson, 2001).

### **TERAPÖTİK İLİŞKİDE CİNSİYET VE CİNSİYET ROLLERİ**

Terapötik etkileşimde cinsiyet ve cinsiyet rolü üzerine yapılan araştırmalarda bu iki özelliğın terapötik etkileşim sürecini olumlu ya da olumsuz etkilediğı saptanmıştır (Berzins, 1979; Gelderman, 1998). Danışanların birçoğı yalnız, mutsuz ve öz güveni düşük bireyler oldukları için psikolojik, fiziksel veya cinsel yönden istismara açık olabilmektedirler. Bundan dolayı da terapötik süreçte danışan ile danışman arasındaki ilişki profesyonel olmalı ve bu şekilde ilerlemelidir. Danışan ve danışan arasındaki ilişkinin formal bir ilişki olduğu unutulmamalıdır (Denial, 2006).

### **TERAPÖTİK SÜREÇTE KÜLTÜREL DEĞERLER, DİN VE AHLAKİ TUTUM**

Terapötik süreçte kültürel değerleri, dini inançları ile ahlaki değer ve tutumları terapötik süreci etkileyen önemli elemanlardır. Kültürel özellikler bireylerin psikolojik yardım arama davranışlarını da etkilemektedir (Chojan, 2007).

Terapötik etkileşimde danışmanların en az kültürel değerler kadar dini değerlerin de farkında olması gerekmekte ve bu bağlamda hizmet sunması beklenmektedir (Young and Fuller, 2009; Walker ve ark., 2002).

## **TERAPÖTİK İLİŞKİDE TERAPİSTİN KENDİ YAŞANTILARI**

Danışmanların kendi yaşantıları çoğunlukla terapötik süreç esnasında ortaya çıkmakta ve danışmanlık sürecini negatif yönde etkileyebilmektedir. Kendi hayatında kayıpları ve ambivalans durumları olan danışmanların, terapötik süreçte başarısız oldukları saptanmıştır (Coleman ve ark., 1986; Gelso ve ark., 2002).

Terapistin kendi gelişim süreçlerinin, anne babasıyla özdeşimlerinin farkında olması terapistte süreçte fayda sağlayacaktır (Ametrano ve ark., 2005).

### **SONUÇ**

Psikiyatri hemşireliği birey, aile ve toplumun ruhsal hastalıklara karşı korunmasında, toplumun ruh sağlığının geliştirilmesinde, hastalığın getirdiği yük ile baş etme ve bu yaşantılarından anlam bulmasında yardımcı olan profesyonel bir hemşirelik sürecidir. Terapötik ilişki karşılıklı etkileşime dayalı, kapsamlı, karmaşık ve özgün bir nitelik taşımaktadır. Literatür incelendiğinde özellikle hümanistik (insancıl) yönelimli terapötik yaklaşımları benimseyen terapistlerin yardım sürecinde insancıl faktörleri daha çok dikkate aldıkları görülmektedir. Terapötik ilişkiyi bazı durumlar etkileyebilmektedir. Terapistin kendi yaşantıları, terapötik süreçte cinsiyet ve cinsiyet rolü, eşitlik, kültürel değerler, ahlaki tutum, sınır koyma gibi durumlar bazı zamanlarda danışan ile danışman arasındaki ilişkiyi olumsuz etkileyebilmektedir. Danışanların birçoğu yalnız, mutsuz ve öz güveni düşük bireyler oldukları için psikolojik, fiziksel veya cinsel yönden istismara açık olabilmektedirler. Bundan dolayı da terapötik süreçte danışan ile danışman arasındaki ilişki profesyonel olmalı ve bu şekilde ilerlemelidir. Danışan ve danışan arasındaki ilişkinin formal bir ilişki olduğu unutulmamalıdır

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**İÇME SULARINDAN İZOLE EDİLEN ANTİBİYOTİK DİRENÇLİ *ESCHERİCHIA COLI* SUŞLARINDAKİ İNTEGRON GEN KASETLERİNİN BELİRLENMESİ**  
**IDENTIFICATION OF INTEGRON GENE CASSETTES IN ANTIBIOTIC RESISTANT *ESCHERICHIA COLI* STRAINS ISOLATED FROM DRINKING WATER**

**Erva RAKICI**

*Öğr. Gör. Dr., Recep Tayyip Erdoğan Üniversitesi, Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı, Rize, Türkiye.*

ORCID NO: 0000-0002-4464-4882

**Elif AYDIN**

*Öğr. Gör., Kütahya Sağlık Bilimleri Üniversitesi, Dezenfeksiyon Sterilizasyon ve Antisepsi Bölümü, Kütahya, Türkiye.*

ORCID NO: 0000-0003-0877-453X

**Osman Birol ÖZGÜMÜŞ**

*Prof. Dr., Recep Tayyip Erdoğan Üniversitesi, Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı, Rize, Türkiye.*

ORCID NO: 0000-0002-3665-6584

**ÖZET**

Van ilinin farklı bölgelerinden toplanan içme suyu örneklerinden elde edilen *Escherichia coli* suşlarının, T.C. Sağlık Bakanlığı Van Halk Sağlığı Laboratuvarı'nda yapılan antibiyotik hassasiyet testleri sonucunda birçok antibiyotiğe dirençli olduğu belirlenen suşlarda sınıf 1 ve sınıf 2 integronların varlığının ve antibiyotik direnci gen kasetlerinin analizini gerçekleştirmektedir. Van ilinin farklı bölgelerinden 2018 yılı Ocak-Mayıs ayları arasında cami, ilköğretim okulu, lojman, sağlık ocağı, su deposu ve ev gibi insanların kullanımındaki alanlardaki içme sularından membran filtre yöntemi ile 244 adet *E. coli* suşu izole edilmiştir. Van Halk Sağlığı Laboratuvarı'nda, standart disk difüzyon test yöntemiyle bakterilerin 12 farklı antibiyotiğe karşı hassasiyetleri tespit edilmiştir. Kaynatma yöntemi ile DNA izolasyonu yapılarak, polimeraz zincir reaksiyonu (PZR) yöntemi ile sınıf 1 ve sınıf 2 integronların varlığı araştırılmış, gen kaseti taşıyan suşlar belirlenmiştir. Antibiyotik hassasiyet deneylerinde suşların %61,47'sinin ampisiline, %19,67'sinin tetrasikline, %13,93'sinin trimetoprim/sulfametoksazole, %14,75 streptomisine, %10,65'inin nalidiksik aside dirençli olduğu belirlendi. Polimeraz zincir reaksiyonu analizlerinde 244 suşun 37 tanesinin (%15,16) sınıf 1 integron, bir tanesinin (%0,4) hem sınıf 1 hem de sınıf 2 integron taşıdığı belirlendi. İntegronun değişken bölgelerinin PZR ile çoğaltılması sonucunda, sınıf 1 integronlardan 14'ünün ve sınıf 2 integron taşıyan bir suşun gen kasetleri (yaklaşık 500-1000bp aralığında) taşıyor olduğu görüldü. Bu çalışmada içme sularından elde edilen *E. coli* lerde integron varlığı çevre orijinli suşların çoklu ilaç direncinin potansiyel bir rezervuarı olabileceğini düşündürmekte olup, ulusal ve uluslararası düzeyde moleküler epidemiyolojik çalışmalarla takip edilmesi gerektiği kanısındayız.

**Anahtar Kelimeler:** İçme Suyu, *Escherichia coli*, İntegron, Gen Kaseti.

**ABSTRACT**

*Escherichia coli* strains obtained from drinking water samples collected from different regions of Van province, analyze the presence of class 1 and class 2 integrons and antibiotic resistance gene cassettes in strains determined to be resistant to many antibiotics as a result of antibiotic susceptibility tests performed at the T.R. Van Public Health Laboratory of the Ministry of Health. Between January and May 2018, 244 strains of *E. coli* were isolated from drinking water in areas used by people such as

mosques, primary schools, lodgings, health centers, water tanks and houses from different regions of Van province by the membrane filter method. In Van Public Health Laboratory, the susceptibility of bacteria to 12 different antibiotics was determined by the standard disk diffusion test method. DNA isolation was made by boiling method and the presence of class 1 and class 2 integrons was investigated by polymerase chain reaction (PCR) method, and strains carrying gene cassettes were determined. In antibiotic susceptibility experiments, it was determined that 61.47% of the strains were resistant to ampicillin, 19.67% to tetracycline, 13.93% to trimethoprim/sulfamethoxazole, 14.75% to streptomycin, 10.65% to nalidixic acid. In the polymerase chain reaction analyzes, 37 (15.16%) of 244 strains were found to contain class 1 integrons and one (0.4%) carried both class 1 and class 2 integrons. PCR amplification of the variable regions of the integron revealed that 14 of the class 1 integrons and one strain carrying the class 2 integron carried gene cassettes (in the range of about 500-1000bp). In this study, the presence of integrons in *E. coli* obtained from drinking water suggests that environmental strains may be a potential reservoir of multidrug resistance, and we believe that it should be followed up with molecular epidemiological studies at national and international level.

**Keywords:** Drinking Water, *Escherichia coli*, Integron, Gene Cassette.

## **GİRİŞ**

Antibiyotiklerin gereksiz kullanımını dünyada önemli bir problemdir. Son 20 yılda aşırı antibiyotik kullanımının hızlı bir direnç gelişimine yol açtığı bilinmektedir. Antibiyotik direncini kontrol edebilmek için klinik ve pre-klinik değerlendirme ve araştırmaların multidisipliner bir yaklaşımının gerekli olduğu rapor edilmektedir (Hoşoğlu, 2011). Ülkemiz bölgesel antimikrobiyal direnç sürveyan ağlarına üyedir ve özellikle ülke çaplı klinik orijinli bakteriyel direnç bilgileri düzenli olarak rapor edilmektedir. Fakat raporlarda çevre orijinli direnç ile ilgili çok sınırlı bilgiler vardır. Fakat dirençli bakteriler ve genler insanlar arasında, insanlardan da çevreye ve tekrar insanlara çevre orijinli bakteriler vasıtasıyla yayılabilmektedir.

Antibiyotik direnci sadece hastalık oluşturan bakterilerde değil, karasal ve sucul çevrelerde yaşayan çevre mikroorganizmalarında da gösterilmiştir (Ozgumus ve diğerleri, 2007; Ozgumus ve diğerleri, 2009). Klinik ortamlar olmamalarına rağmen, okyanus sularında, sahillerde, nehirlerde, yüzey suları ve çöktülerinde, göllerde ve içme sularında antibiyotiklere karşı dirençli bakteriler tespit edilmiştir (Mezrioui ve diğerleri, 1994).

Su kirliliği, suyun kalitesinin fiziksel, kimyasal ve biyolojik niteliklerinin suyun herhangi bir kullanımını sınırlayacak şekilde değişim göstermesi olarak tanımlanabilir. Sudaki kirlenme bir su yatağına herhangi bir kirleticinin fazla miktarda girmesi sonucu oluşan durumdur (Karpuzcu, 1994). Su kirleticileri arasında bazı virüsler, hastalık yapan bakteriler, yüksek miktarda metaller, bazı radyoaktif izotopları deterjanlar, fosfor, azot ve sodyum gibi mineraller sayılabilir (Akman ve diğerleri, 2000). İçme ve kullanma suyunda bulunan kirletici maddeler zemine sızan kirliliğinden ve özellikle iyi inşa edilmemiş kanalizasyon sistemlerinden karışabilir (Tickner ve diğerleri, 2004). İçme sularının mikroorganizma yükü ve bu mikroorganizmaların antibiyotik direnci halk sağlığı açısından önem arz etmektedir. Memelilerin bağırsak florasında yaşayan koliform grubu bakterilerin içme suyunda bulunması, bir ya da daha fazla aşamada doğrudan ya da dolaylı olarak suya lağım ile dışkı bulaştığının göstergesidir (Halkman, 2005). Ayrıca içme suyundan izole edilen bakterilerde çoklu antibiyotik direncinin olması bulaşın antibiyotik kullanımı yoğun olan bir yerden olduğunu göstermesi açısından önemlidir (Dinçer ve diğerleri, 2001, Aygün, 2002).

Fekal koliformlar, soğuk ve sıcakkanlı hayvanların bağırsaklarında yaşar, sularındaki dışkı kirliliğinin göstergesi olan total koliformun bir alt grubudur. Bu organizmalar, toplam koliform grubundan yüksek sıcaklıklarda büyüebilmeleriyle ayrılabilirler. Bu grubun en yaygın üyesi *Escherichia coli*'dir (Mandaville, 2002).

*Escherichia coli* ve enterokoklar gibi sıcak ve soğukkanlı hayvanların ve insanın normal mikrobiyota elemanları kolaylıkla direnç genlerini kazanarak transfer edebilir. Patojenik bakteriler için direnç genlerinin bir rezervuarı olan bu kommensal bakteriler antimikrobiyal dirençteki değişimlerin bir indikatörü olarak kullanılabilir (Caprioli ve diğerleri, 2000). Fekal indikatör bakterilerdeki antibiyotik

direncinin birçok akıbeti vardır. Örneğin, *E. coli* ve enterokoklar antibiyotiklere direnç oluşturmada insanın hastane kaynaklı (nozokomiyal) enfeksiyonlarının etken patojenleri olarak daha etkili hale gelebilirler (Jett ve diğerleri, 1994). Bu direnç genlerinin kazanımı ve transferi bazı konjugatif plazmitler, transpozonlar ve integronlar gibi hareketli genetik elemanlar vasıtasıyla gerçekleşir.

İntegronlar, genlere dışardan gen kasetlerinin eklenip orada ifade olmasına izin veren genetik elemanlardır. Bu gen kasetlerinin eklenişi bölgeye spesifik rekombinasyonlarla gerçekleşir. Gen kasetleri bir çeşit hareketli elementlerdir ve üzerinde rekombinasyon bölgeleri bulundurulur. Genellikle antibiyotik direnç genleri taşıyıcı (Hall ve Collis, 1995).

İntegronlar antibiyotik direnci ile ilişkilendirilmişlerdir. (Mazel, 2006). Bu sistem, Gram negatif bakterilerin antibiyotik dirençleri genlerini edinmesi için önemli bir faktördür (Hall, 1998). İntegron sistemi bakterilerde çok-yönlü gen kazanım sistemleri olarak tanımlanabilirler. Farklı evrimsel zaman dilimlerinde, birçok farklı çevre ortamında karşımıza çıkmakta, tür ve soylar arasında hareket etme yetenekleri ile önem kazanmaktadır. Bu nedenle, çevresel kaynaklardan elde edilen örneklerden elde edilen integronlar, antibiyotik kullanımı ve bu antibiyotiklerin yeryüzündeki dağılımı hakkında bizlere fikir vermektedir.

Bu çalışmada, Van ilinin farklı bölgelerinden toplanan içme suyu örneklerinden elde edilen 244 *E. coli* suşunun, Van Halk Sağlığı Laboratuvarı'nda yapılan antibiyotik hassasiyet testleri sonucunda dirençli suşların var olduğunun belirlenmesi ile, bu direncin aydınlatılması ve integronların varlığı, belirlenen integronların taşıdığı antibiyotik direnç gen kasetlerinin moleküler biyolojik analizleri amaçlanmıştır.

## **YÖNTEM**

### **Su Örneklerinin Toplanması, Bakteri İzolasyonu ve İdentifikasyonu**

Van ilini coğrafi olarak temsil eden ilçe ve mevkilerinden (Kurubaş mevkii, Başkale ilçesi, Erciş ilçesi, Çaldıran ilçesi, Muradiye ilçesi, Gürpınar ilçesi, Bahçesaray ilçesi, Tuşba ilçesi, Gevaş ilçesi, Özalp ilçesi), 2018 yılı Ocak-Mayıs ayları arasında cami, ilköğretim okulu, lojman, sağlık ocağı, su deposu ve ev gibi insanların kullanımındaki alanlardaki içme sularından örnekler alındı. 500 ml içme suyu örneği soğuk zincirde 24 saatte laboratuvar ortamına getirildi. 100/250 mL su örneği 0,45 µm'lik membran filtreden süzülerek ve Chromogenic Coliform Agar besiyeri üzerine yerleştirildi. İnkübasyon sonrasında, petride pembe-kırmızı renk oluşturan tüm koloniler şüpheli koliform bakteriler olarak değerlendirildi. Doğrulama amacıyla oksidaz testi yapıldı. 36°C'deki petride mavi-mor renk oluşturan tüm koloniler kesin *E.coli*, şüpheli durumda indol testi yapıldı (Bilgehan, 1995). 244 adet *E. coli* suşu elde edildi. Daha sonra bakteri kültürüne %20 steril gliserol eklenip vortekslenildikten sonra -20 ve -80 °C'lik derin dondurucularda saklandı.

### **Antimikrobiyal Hassasiyet Testleri**

Van Halk Sağlığı Laboratuvarında, Standart Disk difüzyon test yöntemiyle bakterilerin antibiyotiklere (ampisilin; AMP, 10µg), (amoksisilin/klavulanat; AUG, 30µg), (amikasin; AK, 30µg), (sefuroksim; CXM, 30µg), (seftazidim; CAZ, 10µg), (meropenem; MRP, 10µg), (tetrasiklin; TE, 30µg), (kloramfenikol; C, 30µg), (streptomisin; S, 10µg), (gentamisin; CN, 10µg), (nalidiksik asit; NA, 30µg), (trimetoprim/sulfametoksazol; SXT, 25µg) karşı hassasiyetleri tespit edildi. Kalite kontrol olarak *E. coli* ATCC 25922 suşu ve değerlendirme için CLSI 2018 (*The Clinical & Laboratory Standards Institute*) rehberi kullanıldı.

### **DNA İzolasyonu**

Bakterilerin DNA izolasyonu kaynatma methodu ile gerçekleştirildi. Bakterilerin bir gecelik sıvı kültürlerinden 1.5 ml'lik kısmı mikrosantrifüjle çöktürüldü. Üç kere steril distile su ile yıkanarak, 1 ml steril distile suda resüspanse edilen bakteri kültürü 15 dk su banyosunda kaynatıldı. Mikrosantrifüj edildikten sonra DNA kalıpları 250 mikrolitrelik alikotlar halinde -20 ve -80 derecede PZR için saklandı (Ausubel, 1995).

### **İntegron Gen Kasetleri için Polimeraz Zincir Reaksiyonu**

*E. coli* suşlarındaki sınıf 1 ve/veya sınıf 2 integron gen kasetlerinin varlığı integrasyon genine spesifik primer çiftlerinin (Tablo 1) kullanılacağı PZR deneyleri ile tarandı. Pozitif örneklerdeki integron gen

kaselerinin deęişken bölgelerindeki antibiyotik gen kasetleri spesifik primer çiftleri ile referanslarda belirtilen şartlarda (Tablo 2) amplifiye edildi ve PZR ürünleri DNA dizi analizleri için derin dondurucuda saklandı.

**Tablo 1:** PZR deneylerinde kullanılan primerler

Primer	Hedef Gen	Nükleotid Dizisi 5'3'	Referanslar
<b>IntI1F</b> <b>IntI1R</b>	Sınıf 1 integron integraz geni	GGTCAAGGATCTGGATTTGG ACATGCGTGTAATCATCGTC	Machado ve diğerleri, 2005
<b>IntI2F</b> <b>IntI2R</b>	Sınıf 2 integron integraz geni	CACGGATATGCGACAAAAAGGT GTAGCAAACGAGTGACGAAATG	
<b>5'CS</b> <b>3'CS</b>	Sınıf 1 integron deęişken bölge	GGCATCCAAGCAGCAAG AAGCAGACTTGACCTGA	Levesque ve diğerleri, 1995
<b>hep51</b> <b>hep74</b>	Sınıf 2 integron deęişken bölge	GATGCCATCGCAAGTACGAG CGGGATCCCGGACGGATGCACGATTTGTA	White ve diğerleri, 2001

**Tablo 2.** PZR master mix reaksiyon bileşenleri ve konsantrasyonları

Reaksiyon bileşenleri	Stok konsantrasyon	Miktar (µL) 1X
Buffer	10X	5
dNTP mix	2.5 mM	1
MgCl <sub>2</sub>	25 mM	3
Primer 1 oligomer	10 pmol/µL	0.5
Primer 2 oligomer	10 pmol/µL	0.5
Taq polimeraz	5 U/µL	0.2
Steril deiyonize su		37.8
Template (Kalıp DNA)		2
Toplam hacim		50

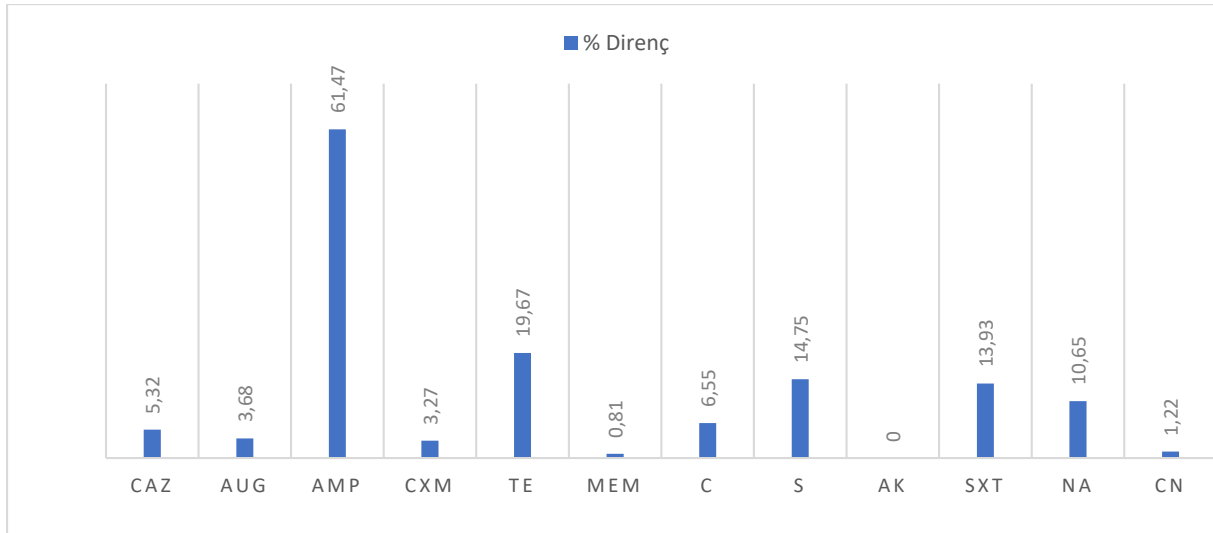
## BULGULAR

Bu çalışma kapsamında, Van ilinin farklı bölgelerinden toplanan içme suyu örneklerinden toplamda 244 *E. coli* suşu izole edildi.

Van Halk Sağlığı Laboratuvarı'nda 12 farklı antibiyotiğe karşı yapılan antibiyotik hassasiyet testleri sonucunda suşların birden fazla antibiyotiğe karşı dirençli olduğu belirlendi. Antibiyotik hassasiyet deneylerinde suşların en yüksek direnç oranları; %61,47 ampisiline, %19,67 tetrasikline, %14,75 streptomisine, %13,93 trimetoprim/sulfametoksazole, %10,65 nalidiksik aside karşı olduğu saptandı (Şekil 1). En düşük direnç oranı ise; meropenem %0,81 ve gentamisin %1,22 antibiyotiğinde olduğu görülmüş, amikasine dirençli olan suşa rastlanmadı.

**Şekil 1.** Suşların antibiyotiklere karşı % direnç dağılımı





\*Ampisilin; AMP, Amoksisilin/klavulanat; AUG, Amikasin; AK, Sefuroksim; CXM, Seftazidim; CAZ, Meropenem; MRP, Tetrasiklin; TE, Kloramfenikol; C, Streptomisin; S, Gentamisin; CN, Nalidiksik asit; NA, Trimetoprim/sulfametoksazol; SXT.

Kaynatma methodu ile DNA izolasyonu gerçekleştirildikten sonra integraz genine ait bölgenin spesifik primerler yardımı ile çoğaltılması sonucunda, 244 suşun 37 tanesinin (%15.16) sınıf 1 integron, bir tanesinin (%0.4) hem sınıf 1 hem de sınıf 2 integron (Tablo 3) taşıdığı belirlendi.

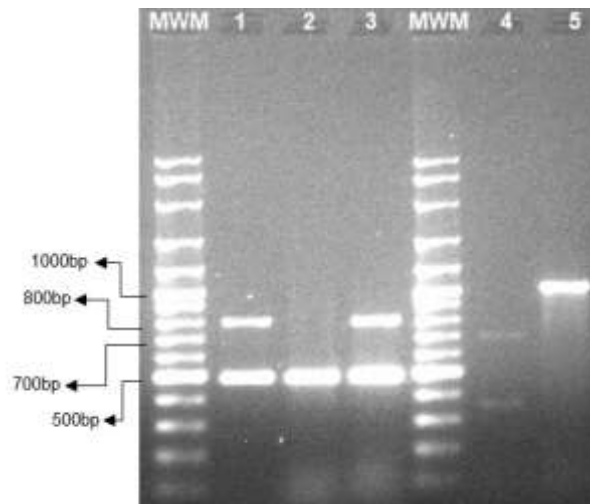
**Tablo 3.** *E. coli* suşlarının izolasyon tarihi, izolasyon yeri, direnç fenotipi ve PZR sonuçları

Suş No	<i>intI1</i>	<i>intI2</i>	İzolasyon Tarihi	Direnç Fenotipi	İzole Edildiği Yer
208-2*	+		31.01.18	CAZ, AMP, NA	ERCIS SALMANAGA KÖYÜ İ.Ö.O.
210-1	+		31.01.18	AUG, AMP, TE, MRP, S, SXT	ERCIS HOCAALI KÖYÜ CAMI
210-2	+	+	31.01.18	AMP	ERCIS HOCAALI KÖYÜ CAMI
213-1	+		31.01.18	AMP, S, SXT	ERCIS HACIKAS KÖYÜ CAMI
213-2	+		31.01.18	AMP, TE, S, SXT	ERCIS HACIKAS KÖYÜ CAMI
213-3	+		31.01.18	AMP, SXT	ERCIS HACIKAS KÖYÜ CAMI
597-1	+		12.03.18	AMP, TE, SXT	GÜRPINAR HAMURKESEN KÖYÜ OK ULU
597-2	+		12.03.18	AUG, AMP, CXM, TE, SXT	GÜRPINAR HAMURKESEN KÖYÜ OK ULU
597-3	+		12.03.18	AUG, AMP, TE, C, S, SXT	GÜRPINAR HAMURKESEN KÖYÜ OK ULU
669-1	+		19.03.18	AMP, TE, S, SXT	GÜRPINAR KUSDAGI KÖYÜ CAMII
669-2	+		19.03.18	AMP, TE, S, SXT	GÜRPINAR KUSDAGI KÖYÜ CAMII
669-3	+		19.03.18	AMP, TE, S, SXT	GÜRPINAR KUSDAGI KÖYÜ CAMII
670-1	+		19.03.18	AMP, TE, S, SXT	GÜRPINAR BAGRIYANIK KÖYÜ CAM I
670-2	+		19.03.18	AMP, TE, S, SXT	GÜRPINAR BAGRIYANIK KÖYÜ CAM I
670-3	+		19.03.18	AMP, TE, S, SXT	GÜRPINAR BAGRIYANIK KÖYÜ CAM I
671-1	+		19.03.18	AMP, TE, S, SXT	GÜRPINAR PARMAKKAPI KÖYÜ CAM II
671-2	+		19.03.18	AMP, TE, S, SXT	GÜRPINAR PARMAKKAPI KÖYÜ CAM II
671-3	+		19.03.18	AMP, TE, S, SXT	GÜRPINAR PARMAKKAPI KÖYÜ CAM II
672-1	+		19.03.18	AMP, TE, S, SXT	GÜRPINAR SAPAKONAK KÖYÜ CAMI I
672-2	+		19.03.18	AMP, TE, S, SXT	GÜRPINAR SAPAKONAK KÖYÜ CAMI I
672-3	+		19.03.18	AMP, TE, C, S, SXT	GÜRPINAR SAPAKONAK KÖYÜ CAMI I

703-1*	+		21.03.18	-	ÇALDIRAN KILIMLI KÖYÜ SAĞLIK O CAGI
719-2	+		21.03.18	-	ERCİS SABANBÜKEN KÖYÜ CAMI
722-2	+		21.03.18	-	ERCİS YÜNÖREN KÖYÜ CAMII
722-3	+		21.03.18	-	ERCİS YÜNÖREN KÖYÜ CAMII
745-1	+		23.03.18	AMP, TE, S, SXT, NA	ERCİŞ MÜNİR TINAZ TEPE KIZ YBO SU DEP OSU
745-2	+		23.03.18	AMP, TE, S, SXT, NA	ERCİŞ MÜNİR TINAZ TEPE KIZ YBO SU DEP OSU
745-3	+		23.03.18	AMP, TE	ERCİŞ MÜNİR TINAZ TEPE KIZ YBO SU DEP OSU
746-1	+		23.03.18	-	ERCİŞ MURAT İŞLER ANADOLU LİSE Sİ SU DEPOSU
773-3	+		26.03.18	TE, S, SXT, NA	İPEKYOLU YALINAGAÇ KÖYÜ CAMII
1038-2	+		11.04.18	AMP, S, SXT	ÖZALP DORUTAY KÖYÜ SAĞLIK OC AGI
1224-1	+		09.05.18	AMP, TE, S, SXT	ÇATAK NARLI KÖYÜ İLKOKULU
1233-1	+		09.05.18	AMP, TE, NA	BASKALE EKECEK KÖYÜ İ.Ö.O
1260-1	+		09.05.18	AMP, TE, C, SXT, NA	ERCİŞ TRAFİKO MERKEZİ TUVALETİ
1260-3	+		09.05.18	AMP, TE, C, S, SXT, NA	ERCİŞ TRAFİKO MERKEZİ TUVALETİ
1252-2	+		09.05.18	AMP, TE, SXT, NA	ERCİŞ ERCİS MAGARA KÖYÜ İ.Ö.O.
1508-1	+		23.05.18	AMP, TE, C, S, SXT, NA, GN	ERCİS YÜNÖREN KÖYÜ CAMII

İntegron taşıyan suşlarda değişken bölgelerinin PZR ile çoğaltılması sonucunda, sınıf 1 integronlardan 14'ünün ve sınıf 2 integron taşıyan bir suşun gen kasetleri (yaklaşık 500-1000bp aralığında) taşıyor olduğu görüldü (Şekil 2).

Şekil 2. *int1* ve *int2* spesifik PZR ampliconları.



\*MWM, Moleküler ağırlık standardı (Vivantis 100bp Ladder); 1, *int1* ve *int2* 500bp, 740 bp pozitif kontrol; 2, *int1* pozitif 500bp; 3, *int1* ve *int2* pozitif 500bp,740bp; 4, sınıf 1 pozitif, ~700bp; 5, sınıf 1 pozitif, ~1000bp.

## SONUÇ VE TARTIŞMA

Antibiyotik direnci dünya çapında önemli bir halk sağlığı problemi olmasına rağmen, çevreyle ilgili çalışmalarda bu olgu büyük ölçüde gözden kaçmıştır. Sucul çevrelerin, antropojenik aktivitelerden dolayı antibiyotik direncinin kazanılması ve yayılması açısından ideal çevreler olabileceği bilinmektedir (Marti ve diğerleri, 2014). Antibiyotikler antibiyotik direncinin uyarıcılarıdır ve hareketli elemanlar aracılığı ile kazanılabilirler (Rodriguez Rojaz ve diğerleri, 2013). Antibiyotik ve diğer kirleticilerin karışımı, dirençli bakteriler ve onların metabolitleri, işlenmiş ve işlenmemiş lağım suları, hastane atıkları, akuakültür atıkları ve tarım deşarjları vasıtasıyla sucul ortamlara ulaşmaktadır. Böylece su ve

çöktellerin antibiyotik direnç genlerinin transferinde, ekolojisinde ve evriminde direksiyon rolüne sahip olduğu düşünülmektedir (Taylor ve diğerleri, 2011).

Bu çalışmada içme sularından elde edilen *E. coli* lerde integronların varlığı çevre orijinli suşların çoklu ilaç direncinin potansiyel bir rezervuarı olabileceğini düşündürmektedir. Daha önce Özgümüş ve Arkadaşları (2009), yaptıkları bir çalışmada, 10 dereeden aldıkları su örneklerinden toplamda 183 bakteri izole etmiş, *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Enterobacter spp.*, *Citrobacter koseri* ve *Proteus vulgaris* türlerini dere sularından elde etmişlerdir. Bu suşların antibiyogram değerlendirmeleri sonucunda, streptomisin (%51,9), neomisin (%46,4), gentamisin (%42) gibi aminoglikozidlere oldukça yüksek olduğunu belirlemişlerdir. PZR deneyleri ile; suşların 14 tanesinin sınıf 1, 5 tanesinin sınıf 2 integron taşıdığı belirlenmiştir.

Canal ve Arkadaşları (2016) Güney Brezilya' da Patos Lagünü'nden 5 farklı noktadan alınan su örnekleriyle yaptıkları benzer bir çalışmada, 441 *E. coli* izolatu elde edilmiş, 17 farklı antibiyotiğe karşı yapılan antibiyotik hassasiyet testlerinde suşların en az 3 farklı sınıfa ait antimikrobiyale dirençli olduğu saptanmıştır. Suşların 157 tanesi en az bir antibiyotiğe dirençli olarak belirlenmiş ve PZR yöntemiyle integraz geni varlığı araştırıldığında, 62 suşun *intI1* geni taşıdığı, 2 ya da daha fazla antibiyotiğe ise karşı dirençli 43 suşa da *intI1* geni tespit edilmiştir.

Shamsizadeh ve Arkadaşları (2021), İran'da; atık su, su veya atık su ile sulanan toprak örnekleri ile yaptıkları benzer bir su çalışmasında, 51 *E. coli* suşu izole edilmiş, PZR ile çeşitli direnç genleri (beta laktam *blaCTX-m-32*, *blaOXA-23*, tetrasiklin *tet-W*, sulfonamid *sul1*, kloramfenikol *cml-A* ve makrolid *erm-B*) ve sınıf 1 integron varlığı araştırılmış, suşların %46' sını sınıf 1 integron taşıdığı belirlenmiştir.

Chang Su ve Arkadaşlarının (2012)' de Dongjiang nehir havzasındaki 38 farklı bölgeden aldıkları su örnekleri ile yaptıkları çalışmada ise, 3456 *Escherichia coli* izole edilmiş ve bu örneklerin 20 farklı antibiyotiğe karşı direnç oranları belirlenmiştir. Suşların %89.1'unun dirençli olduğu, %87.5'inin en az 3 antibiyotiğe direnç gösterdiği belirlenmiştir. Ayrıca sınıf 1, 2, ve sınıf 3 integron varlığını araştırmış, sınıf 1 ve 2 integrona sıklıkla rastlandığı (%82.3) belirlenmiştir. Sınıf 3 integrona rastlanmamıştır. Gen dizilimleri incelendiğinde, 14 gen kasetinde 21 gen direnç geni olduğu görülmüş, 10 farklı direnç geni ailesi tanımlanmıştır. Daha önce su örnekleriyle yapılan çalışmalar çalışmamızı destekler nitelikte sonuçlar içermektedir. İçme suları ve diğer su kaynaklarındaki çevre orijinli suşların çoklu ilaç direncinin altında yatan potansiyel bir rezervuarı konumundadır, ulusal ve uluslararası düzeyde moleküler epidemiyolojik çalışmalarla takip edilmesi gerektiği kanısındayız.

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**THE ROLE OF INFLAMMATORY INTERLEUKINS IN DIAGNOSIS OF NECROTIZING ENTEROCOLITIS**

*Sevinj Nasirova*

*Scientific Research Institute of Pediatrics named after K.Y. Farajova, Baku, Azerbaijan*

*ORCID ID: 0000-0002-3113-3282*

**ABSTRACT**

Necrotizing enterocolitis (NEC) -is infection and inflammation of the intestine of newborn. Recently, particular attention is paid to studying the effects of interleukins in the diagnosis, course and pathogenesis of the disease.

**The aim of our work:** The aim of the research was to study the properties of inflammatory interleukins in newborns with necrotic enterocolitis, depending on the stage of the disease.

**Materials and methods.** Immunological examinations were carried out in the ELISYS UNO-Human EFA full-automatic analyzer using the IFA method of the Institute of Pediatrics. Patients with necrotic enterocolitis (NEC) were divided into 3 groups: Group I - 26 patients with stage I of NEC, group II - 44 patients with stage II of NEC, group III - 30 patients with stage III of NEC.

**Research findings and interpretation.** Looking at cytokine status, changes were observed in all groups. Interleukin-1 $\beta$  increase was the most in group II. Thus, compared to the control group, Interleukin-1 $\beta$  increased 3 times in group I, 3,4 times in group II, and 3,1 times in group III. Interleukin-1 $\beta$  was 1,88 $\pm$ 0,18 in group I, 2,12 $\pm$ 0,07 in group II, and 1,95 $\pm$ 0,10 in group III. Interleukin-6, as well as Interleukin-1 $\beta$ , increased more in group II. Compared to the control group, an increase of 6,9 times in group I, 7,8 times in group II, and 7,1 times in group III was recorded. Thus, the amount of interleukin-6 in group I was 28,4 $\pm$ 1,9, in group II 32,3 $\pm$ 0,9, and in group III 29,4 $\pm$ 0,7.

**Summary:** The main goal of the research is to study of cytokine profile in newborns with necrotizing enterocolitis. Research revealed, that course of NEK clinical-exographic picture is associated with greater disbalance of inflammatory cytokines.

**Key words:** necrotizing enterocolitis, newborn, inflammatory interleukins

**ÇOCUK HASTALARIN HASTANE İÇİ TRANSPORTU: SİSTEMATİK DERLEME  
IN-HOSPITAL TRANSPORT OF PEDIATRIC PATIENTS: SYSTEMATIC REVIEW**

**Selin DEMİRBAĞ**

*Manisa Celal Bayar Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Manisa, Türkiye*

*ORCID NO: 0000-0002-4606-5171*

**ÖZET**

**Giriş ve Amaç:** Hastanede çocuğun kaldığı odada yapılamayan tanı ve tedavi prosedürleri için hastane içi transport gereklidir. Bir hasta için bu durum potansiyel olarak risk barındırmaktadır. Bu riskler hastanın altta yatan hastalığından ziyade sağlık hizmeti yönetiminin neden olduğu tıbbi müdahaleden kaynaklanan yaralanmalar veya komplikasyonlar olarak tanımlanmaktadır. Bu bağlamda bu sistematik derlemenin amacı, hastanede yatan hasta çocukların hastane içi transportunda yaşanan olaylar ve transportun etkilerini belirleyen çalışmalarını incelemek ve tanımlamaktır.

**Yöntem:** Tarama, Ekim 2022 tarihinde Web of Science, Science Direct ve Scopus veri tabanlarından "transport", "çocuk", "pediatri", "hastane içi" anahtar kelimeleri ile yapılmıştır. Çalışma kapsamına alınan makalelerin metodolojik kalite değerlendirilmesinde "Joanna Briggs Enstitüsü (JBI) Eleştirel Değerlendirme Listeleri" kullanılmıştır. Değerlendirme listelerinden ise tanımlayıcı ve kohort araştırma tiplerine uygun listeler kullanılmıştır. Verilerin çekilmesi ve analizinde örneklem, girişim, karşılaştırma, sonuç, çalışma deseni (PICOS) sistemine temellenen bu çalışma için geliştirilen standart bir veri özetleme formu kullanılmıştır.

**Bulgular:** Tarama sonucunda 611 araştırmadan dahil edilme kriterlerine uyan beş araştırma inceleme kapsamına alınmıştır. Değerlendirmeye alınan beş araştırma, 2018-2022 yılları arasında yayınlanmış, tam metnine ulaşılan, pediatri hastalarının örneklem grubunu oluşturduğu araştırmalardır. Toplamda 942 hastanın alındığı ve örneklem büyüklüğü 114 ile 293 arasında değişen, Japonya, Çin, Türkiye, Brezilya ve İsviçre’de gerçekleştirilen çalışmalardır. Araştırmalardan elde edilen bulgular sonucunda, hastane içi transport sonucu hastalarda olumsuz olaylar ve etkiler oluştuğu belirlenmiştir.

**Sonuç:** Çocuk hastalarda hastane içi transport sırasında yaşanan çoğu olayın önlenemez olduğu sonucuna ulaşılmıştır. Geliştirilmiş kontrol listeleri ve çift kontrollere ile olumsuz olayların ve etkilerin önlenebileceği düşünülmektedir.

**Anahtar kelimeler:** Transport, hastane içi, pediatri.

**ABSTRACT**

**Introduction and Aim:** In-hospital transport is required for diagnosis and treatment procedures that cannot be performed in the room where the child is staying in the hospital. For a patient, this poses a potential risk. These risks are defined as injuries or complications from medical intervention caused by healthcare management rather than the patient's underlying disease. In this context, the aim of this systematic review is to examine and describe the events in the in-hospital transport of hospitalized children and the studies that determine the effects of transport.

**Method:** The search was carried out with the keywords "transport", "child", "pediatric", "inhospital" from Web of Science, Science Direct and Scopus databases in October 2022. "Joanna Briggs Institute (JBI) Critical Evaluation Lists" were used in the methodological quality evaluation of the articles included in the study. Among the evaluation lists, lists suitable for descriptive and cohort research types were used. A standard data summary form developed for this study, based on the sample, intervention, comparison, outcome, study design (PICOS) system, was used for data collection and analysis.

**Results:** As a result of the screening, five studies out of 611 that met the inclusion criteria were included in the review. Five studies included in the evaluation were studies published between 2018-2022, the

full text of which was reached, and the sample group of pediatric patients. These are studies conducted in Japan, China, Turkey, Brazil, and Switzerland, with a total of 942 patients and sample sizes ranging from 114 to 293. As a result of the findings obtained from the studies, it was determined that adverse events and effects occurred in patients as a result of in-hospital transport.

**Conclusion:** It has been concluded that most of the events experienced during in-hospital transport in pediatric patients are preventable. It is thought that adverse events and effects can be prevented with improved checklists and double checks.

**Keywords:** Transport, in-hospital, pediatric.

## **GİRİŞ**

Hastanede yatan çocuk hastalar, kaldıkları birimlerde mevcut bulunmayan teknik veya prosedürle ilgili ek bakım, tetkik ve tedavi almaları gerekebilir. Bu nedenle çocuk hastanın, ek bakımın sağlanması, tetkik ve tedavinin yürütülmesi için hastane içindeki bir birimden başka bir birime (örneğin; ameliyathaneye veya özel bakım ünitesine) nakledilmesi gerekebilir veya başka bir hastaneye sevk edilmesi gerekebilir (Warren ve ark, 2001).

Çocuk hastalar, nakil sırasında yüksek morbidite ve mortalite riski altındadır (Warren ve ark, 2001). Dikkatli planlama, uygun kalifiye personel kullanımı ve uygun ekipman seçimi ve mevcudiyeti ile risk en aza indirilmeye çalışılarak sonuçlar iyileştirilebilir. Nakil sırasında hastanın hayati fonksiyonlarının izlenmesinde veya sürdürülmesinde herhangi bir kesinti asla olmamalıdır. Ayrıca, eşlik edecek personelin seçimi ve ekipmanların belirlenmesi, hastanın var olan ve öngörülen akut bakım ihtiyaçlarını karşılamak amacıyla gerçekleştirilir. Özellikle kritik bakıma ihtiyacı olan çocuk hastaların transportunu sağlayacak personelin özel eğitilmiş kişiler arasından belirlenmesi önerilmektedir (Decruq ve ark., 2013).

Kritik durumdaki çocuk hastanın hastane içi nakli, hasta yönetiminin zor ancak önemli parçasıdır. Bu tür hastane içi nakil, hastanın fizyolojik dengesizliği ve karşılaşılan problemler nedeniyle tehlikeli ve oldukça risklidir. En kısa nakil bile yaşamı tehdit eden komplikasyonlara neden olabilir (Lovell ve ark., 2001). Riskler arasında kardiyovasküler sorunlar ve solunum yetersizliği, yetersiz ilaç tedavisi, yetersiz takip ve çok sayıda mekanik problemler yer almaktadır (Papson ve ark., 2007).

Bu çalışmanın amacı hastanede yatan hasta çocukların hastane içi transportu sırasında yaşanan olayları ve transportun etkilerini araştıran çalışmaların belirlenerek araştırma sonuç verilerinin sistematik biçimde sunulmasıdır. Bu amaca yönelik olarak sistematik derleme çalışmasının soruları şu şekildedir:

- (1) Hasta çocukların hastane içi transportu sırasında yaşanan olaylar ve transportun çocuğa etkileri var mıdır?
- (2) Hasta çocukların hastane içi transportu sırasında yaşanan olaylar ve transportun etkileri nelerdir?

## **GEREÇ VE YÖNTEM**

### **Araştırma Dizayını**

Sistematik derleme tipindeki bu çalışmanın hazırlanmasında ve makalenin yazımında PRISMA Bildirimi kullanılmıştır (Moher ve ark., 2009). Bu çalışmada yanlılık riskini azaltmak için literatür taraması, makaleleri seçme, veri çıkarma ve makalelerin kalitesini değerlendirme süreci bir bağımsız araştırmacı tarafından kontrol edilmiştir. Araştırmacılar arasındaki fikir ayrılıkları tartışma yoluyla uzlaşmaya varılarak giderilmiştir.

### **Tarama Stratejisi**

Çalışmada, konu ile ilgili yayınların geriye dönük taranmasında Web of Science, Science Direct ve Scopus veri tabanları kullanılmıştır. Tarama, Ekim 2022 tarihinde 2018-2022 yılları arasında yayımlanmış çalışmaları belirlemek amacıyla "transport", "çocuk", "pediatri", "hastane içi" anahtar kelimeleri kullanılarak yürütülmüştür.

### **Araştırma kapsamına dahil edilme kriterleri**

1. Araştırmaların 2018-2022 yıllarında yapılmış olması,

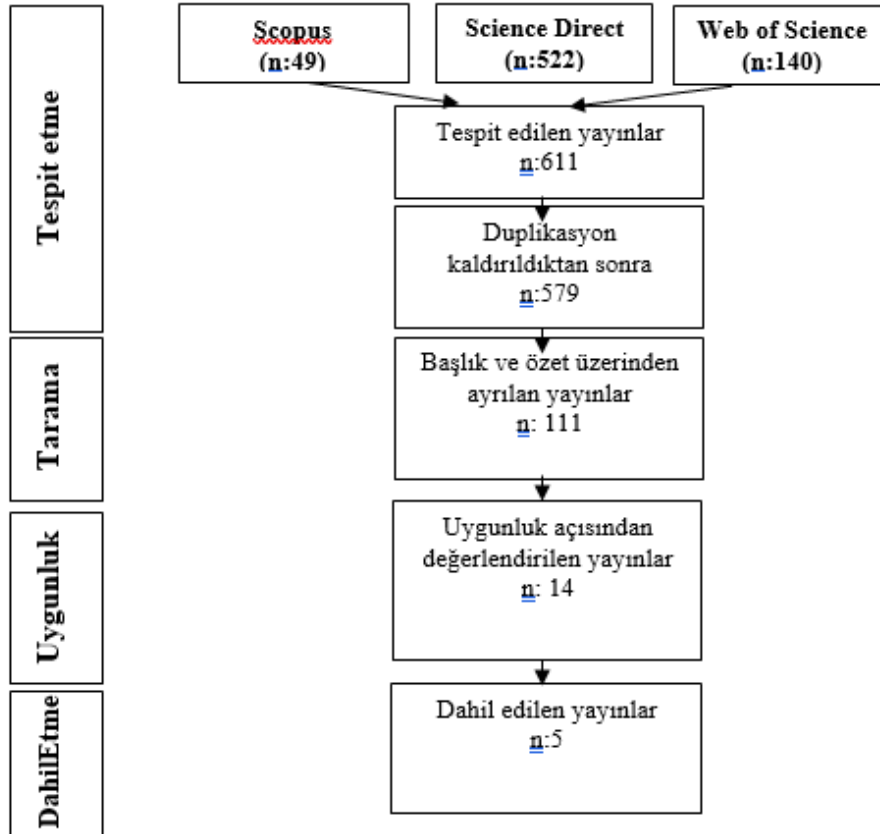
2. Arařtırmaların İngilizce yayımlanmış olması,
3. Pediatrik hasta grubu ile çalışılması,
4. Makalelerin tam metnine ulaşılmış olması,
5. Arařtırma tipinin sistematik derleme ve metaanaliz olmamasıdır.

#### Arařtırma kapsamından veri çıkarma kriterleri

1. Arařtırmaların yayın dilinin İngilizce dışında olması,
2. 2018-2022 yılları dışında bir zaman diliminde yayımlanması,
3. Pediatrik hasta grubu ile çalışılmaması,
4. Makalelerin tam metnine ulaşılamaması,
5. Arařtırma tipinin sistematik derleme ve metaanaliz olmasıdır.

#### Çalışmaların Belirlenmesi ve Seçimi

Verilerin seçimi ve sunulmasında PRISMA Akış Şeması kullanılmıştır (Moher ve ark., 2009). Literatür tarama sonucunda 611 arařtırmaya ulaşılmış ve 32 tanesi duplikasyon nedeniyle çıkarılmıştır. Arařtırmacı tarafından başlık ve özet değerlendirmesi yapılarak 468 arařtırma, dahil edilme kriterlerine uymayan 106 arařtırma çıkarılmıştır. Tarama sonucunda beş arařtırma çalışmaya dahil edilmiştir (Şekil 1).



Şekil 1. PRISMA Akış Şeması

#### Kalite Değerlendirilmesi

Çalışmaya dâhil edilen arařtırmaların metodolojik kalite değerlendirmesinde, Joanna Briggs Enstitüsü tarafından yayımlanan “Joanna Briggs Enstitüsü (JBI) Eleřtirel Değerlendirme Listeleri” kullanılmıştır.



Değerlendirme listelerinden ise tanımlayıcı ve kohort araştırma tiplerine uygun listeler kullanılmıştır. Toplam puanın yüksekliği araştırmanın metodolojik kalitesinin yüksekliğini göstermektedir (Moola ve ark., 2017). Çalışma kapsamına alınan araştırmaların kalite değerlendirmesi Tablo 1’de sunulmuştur. Araştırmaların biri tanımlayıcı ve dördü kohort araştırma tipindedir. Beş çalışma metodolojik kalite değerlendirme puanlarına bakılmaksızın çalışmaya kabul edilmiştir.

### **Çalışmaların çekilmesi ve analizi**

Araştırmaların çekilmesi ve analizinde örneklem, girişim, karşılaştırma, sonuç, çalışma deseni (population, intervention, comparison, outcome, study design PICOS) sistemine temellenen araştırmacı tarafından hazırlanan standart bir veri değerlendirme formu kullanılmıştır (CRD, 2009).

### **Çalışmanın Etik Yönü**

Çalışmanın örnekleme dahil edilen araştırmalar erişime açık olan elektronik veri tabanları ve arama motorlarından alınması ve çalışma sırasında herhangi bir maddi/manevi zarar verme riski bulunmadığından bu çalışma için etik kurul onayı gerekmemektedir. Çalışmaya dâhil edilen araştırmalar kaynakçada gösterilmiştir.

### **Araştırmanın sınırlılıkları**

Bu sistematik derlemede dahil edilme kriterlerinde çalışmaların yayın yılı son beş yıl olarak sınırlandırılmıştır. Konu açısından bakıldığında hastaneler arası transport ile ilgili yayın sayısının fazla olmasına karşın hastane içi transport ile ilişkili çalışma sayısı oldukça sınırlıdır. Ayrıca veri tabanı sayısının üç olması çalışmanın sınırlılıklarındandır.

### **BULGULAR**

Tarama sonucunda 611 araştırmaya tespit edilmiş olup beş araştırma çalışma kapsamına alınmıştır. Beş çalışmanın dördü kohort ve biri tanımlayıcı tipte araştırmalardır (Şekil 1). Toplamda 942 hastanın alındığı ve örneklem büyüklüğü 114 ile 293 arasında değişen, Japonya, Çin, Türkiye, Brezilya ve İsviçre’de gerçekleştirilen beş araştırma sistematik derlemeye dahil edilmiştir. Dahil edilen araştırmalarda pediatri ve yenidoğan hastalarının hastane içi transportu sırasında yaşanan olaylar ve transportun etkileri ile klinik özellikler incelenmiş ve sunulmuştur (Tablo 1).

**Tablo 1. Araştırma Kapsamına Alınan Çalışmaların Özellikleri (n:5)**

Araştırma Adı/Yazar ve Yılı	Araştırma Tipi	Örneklem	Girişim	Sonuç	Kalite
Outcomes of 'unrecognised situation awareness failures events' in intensive care unit transfer of children in a Japanese children's hospital  <b>Aokive ark., 2019, JAPONYA</b>	Kohort araştırma	Hastane içi planlı nakiller  68 hasta: Güvenli olmayan grup  167 hasta: Güvenli olmayan grup dışında kalan grup	Genel çocuk kliniğinden yoğun bakıma nakli olan hastaların tıbbi kayıtlarını geriye dönük olarak incelenmiştir. Güvenli olmayan grubun özellikleri trakeal entübasyon, vazoaktif ilaçların alınması ve YBÜ ilk 60 dakikasında veya yoğun bakıma gelmeden önce 3 sıvı bolusu başlatılması olarak belirlenmiştir. Bu iki grup arasında YBÜ kalış süresi ve mortalite oranları karşılaştırılmıştır.	YBÜ'de kalış süresi ve mortalite güvenli olmayan grupta güvenli olmayan grup dışında kalan gruba göre önemli ölçüde daha kötü olduğu bulunmuştur (YBÜ kalış süresi 9 güne/4 gün, mortalite oranı %13'e/%4.2).	10/11
Effect analysis of in-hospital transfer care based on STABLE technology in critically ill newborns  <b>Fang ve ark., 2022, ÇİN</b>	Kohort araştırma	180 kritik yenidoğan hasta:  88 yenidoğan: kontrol grubu  92 yenidoğan: olgu grubu	Konvansiyonel resüsitasyon ile resüsite edildikten sonra doğumhanede hemşireler tarafından YYBB nakledilenler kontrol grubu olarak, STABLE ile hemşireler tarafından hastane içi nakli gerçekleşen yenidoğanlar girişim grubu olarak belirlenmiştir. Kritik yenidoğanlarda STABLE (glukoz ve güvenli bakım, vücut ısısı, hava yolu, kan basıncı, laboratuvar değerlendirmesi, duygusal destek) tekniğine dayalı hastane içi transfer bakımının etkinliği değerlendirilmiştir.	Nakli gerçekleştirenlerin transfer prosedürü sırasında çeşitli alt süreçleri yürütme süreleri girişim grubunda kontrol grubuna göre daha kısa olduğu bulunmuştur (p<0.05). Nakil kazaların insidansı girişim grubunda kontrol grubuna göre daha düşük olduğu bulunmuştur (p<0.05). Nakilden sonra girişim grubundaki çocukların kan şekeri, kan basıncı, vücut ısısı, solunum ve kan gazı göstergeleri kontrol grubundakilerden daha stabil olduğu bulunmuştur (p<0.05). Girişim grubundaki çocukların ailelerinin memnuniyetleri kontrol grubuna göre daha yüksek bulunmuştur (p<0.05)	9/11
In-hospital pediatric patient transfers to the pediatric emergency department  <b>Güleryüz, 2022, TÜRKİYE</b>	Kohort araştırma	Çocuk Acil Servisi'ne nakledilen 120 çocuk hasta	Çocuk Acil Servisi'ne (PAS) nakledilen 120 çocuk hastanın geçmiş kayıtları incelenerek klinik özellikleri, aciliyetleri ve nakil nedenleri belirlenmiştir. Bunun için Pediatrik Değerlendirme Üçgenine (PDÜ) ve Acil Şiddet İndeksi (AŞİ) kullanılmıştır.	Çocuk hastaların %54,8'i Pediatrik Değerlendirme Üçgenine (PDÜ-3'lü sistem) göre stabil ve %78,6'sı Acil Şiddet İndeksi'ne (AŞİ-5'li sistem) göre kategori 3, 4, 5 idir.  Hastaların 69'u (%57,5) erkek olup ortanca yaşı 42 (0-210) aydır. Hastaların kırk sekizi (%40) altta yatan bir kronik hastalığa sahiptir. Hastaların elli	8/11

				<p>sekizi (%48,33) 14:00-18:00 saatleri arasında acil servise sevk edilmiştir. Hastaların dördü (%3.3) mavi kod ile gelmiştir. Hastaların 50'si (%41,7) genel pediatri polikliniğinden sevk edilmiştir.</p> <p>Hastaların 96'sı (%81,4) sevk edilmeden önce PAS'e bilgi verilmiştir. Hastaların yüz on üçü (%94,2) bir aile üyesi eşliğinde ve herhangi bir sağlık personeli olmadan PAS'e gelirken, beş hasta (%4,2) sağlık personeli eşliğinde gelmiştir. İki hastaya ise bir doktor eşlik etmiştir. Hastaların 65'inde (%54,6) nakil notu bulunmaktadır.</p> <p>PAS'a nakledilen hastaların hastalıkları değerlendirildiğinde; 41 hastanın (%34,16) solunum yolu rahatsızlığı nedeniyle nakledildiği tespit edilmiştir.</p> <p>PAS'a transfer edilen hastaların 78'i (%65) PDÜ'ine göre stabildi. Hastaların doksan dokuzu (%73.1) ESI kategorisi 3, 4 veya 5'te değerlendirilmiştir.</p> <p>Hastaların 84'ü (%70) PAS'da tedavi görmüştür. Hastaların yüz biri (%84,9) takip ve tedavi amacıyla çocuk acil servislerine yerleştirilmiştir. Hastaların 78'i (%67,2) 0-6 saat PAS'da kalmıştır. Hastaların 71'i (%60,2) tedavi sonrası PAS'dan taburcu edilmiş, 32 hasta (%27,1) PAS'dan çocuk servisine transfer edilmiştir.</p> <p>Hastaların dördü (%3.4) AŞI'ye göre hayat kurtarıcı müdahaleler almıştır. Bu hastalardan ikisi PDÜ'ye göre 'stabil', biri 'solunum sıkıntısı/yetersizliği', biri de 'solunum yetmezliği' olarak değerlendirilmiştir. Üç hasta ESI 2 triyaj kategorisinde, bir hasta</p>	
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				AŞİ 3 triyaj kategorisinde değerlendirilmiştir. PAS'e nakil nedenleri ile PDÜ ve AŞİ triyaj kategorileri arasında istatistiksel bir anlamlılık bulunmuştur.	
Prevalence of medication discrepancies in pediatric patients transferred between hospital ward  <b>Alcântara ve ark., 2021, BREZİLYA</b>	Tanımlayıcı araştırma	114 hasta çocuk	Hastalara ait medikal tedaviler incelenmiş ve ilaç uyumsuzluğunun yaygınlığını analiz etmek amaçlanmıştır.	Çalışmaya dahil edilen 114 hastadan 85'inde (%74,5) en az bir kasıtsız olarak ilaç uyumsuzluğu bulunmaktadır; bunların 16'sı (%14,0) hastaneye başvuru sırasında, 42'si (%36,8) hastane içi transferde ve 52 (%45,6) hasta taburcu olurken gerçekleşmiştir. İlacın verilmemesinin oranı ise, hastane kabulünde 20 (%74,1), hastane içi transferde 26 (%37,7) ve hastaneden taburculuktan sonra 80 (%100,0) olarak bulunmuştur.	6/8
Adverse events and associated factors during intrahospital transport of newborn infants  <b>Delacretaz ve ark., 2022 İSVİÇRE</b>	Kohort araştırma	293 yenidoğanın 990 hastane içi nakil verileri	Sonuçlar 293 yenidoğan bebekte gerçekleştirilen 990 hastane içi nakilden elde edilen veriler analiz edilmiştir. Yenidoğan bebeklerin hastane içi nakli sırasında advers olayların sıklığını, tipini ve şiddetini belirlemek ve ilişkili faktörleri belirlemek amaçlanmıştır	Nakil sırasında yenidoğanın yaş ortancası 13 gündür. Olumsuz olaylar, nakillerin %25'inde (248/990) meydana gelmiştir ve esas olarak kardiyovasküler ve solunum sistemlerinin dengesizliği, ajitasyon ve sıcaklık kontrolü ile ilişkilidir. Olumsuz olaylar 207 taşımada zararsız (207/990, %21), 37 taşımada hafif zarar (37/990, %4), 4 taşımada orta derecede zarar (4/990, %0.4) ile ilişkilendirilmiştir. Ciddi veya ölümcül bir advers olay olmamıştır. Katekolaminlerle hemodinamik destek, santral venöz kateter varlığı ve daha uzun taşıma süresi, taşıma sırasında advers olayların ortaya çıkmasında etkili bulunmuştur.	9/11

## TARTIŞMA

Bu sistematik derlemede, pediatri hastalarında hastane içi transport sırasında yaşanan olaylar ve transportun etkileri ile klinik özelliklerini inceleyen beş çalışmaya yer verilmiştir. Çalışmaların sonuçları hastane içi transportun riskli ve tehlike olduğu, hastane içi transportun pediatri hastalarında olumsuz sonuçlar yarattığı görülmüştür. Bu olumsuz sonuçlar hastalarda yaşamsal bulguların

kötüleşmesi, kalış süresinde artış, mortalite oranında artış, ilaç uyumsuzluğunda artış ve advers olaylarda artış olarak sıralanabilir.

Aoki ve ark. (2019) Japonya’da yaptığı çalışmada hastane içi planlı nakillerden güvenli olmayan grup ve güvenli olmayan grup dışında kalan grup olarak ayırarak retrospektif kohort çalışması yürütmüştür. Güvenli olmayan transport yaşayan hastaların yoğun bakımda kalış sürelerinin daha uzun ve mortalitesinin daha yüksek olduğu görülmüştür.

Fang ve ark. (2022) Çin’de yaptığı çalışmaya 180 kritik yenidoğanı dahil etmiştir. STABLE ile hemşireler tarafından hastane içi nakli gerçekleşen yenidoğanlar (n=92) girişim grubu olarak belirlenmiştir. Diğerleri kontrol grubu (n=88) olarak alınmıştır. Hastane içi transfere acil ihtiyaç duyan yenidoğanlar için STABLE teknolojisine dayalı transfer bakımının uygulanmasını, transport hemşirelerinin kapsamlı kalite ve acil müdahale yeteneğini etkili bir şekilde artırabilir olduğu ve hastane içi transport süresini kısaltabilir olduğu ve transfer sırasında advers olayların görülme sıklığını azaltabilir olduğu görülmüştür. Girişim grubunda çocukların yaşam bulguları sabittir ve aile üyelerinin memnuniyeti yüksek tespit edilmiştir.

Güleryüz (2022) hastane içi birimlerden Çocuk Acil Servisi’ne nakledilen 120 çocuk hastanın nakil kayıtlarını incelemiştir. Nakiller sırasında Pediatrik Değerlendirme Üçgenine ve Acil Şiddet İndeksi kullanılmıştır. PAS’e nakil nedenleri ile PDÜ ve ESI triyaj kategorileri arasında istatistiksel bir anlamlılık bulunmuştur. Çalışma sonucunda hastanın durumunu PDÜ’ya göre değerlendirmesi ve bu değerlendirmenin sonuçlarına göre acil servise sevk gerekliliği konusunda karar vermesi önerilir.

Alcântara ve ark. (2021) Brezilya’da tanımlayıcı tipte 114 çocuk hasta ile yürüttüğü çalışmada hastalara ait medikal tedaviler incelenmiş ve ilaç uyumsuzluğunun yaygınlığı değerlendirilmiştir. Pediatri bölümünde kasıtsız uyumsuzlukların meydana geldiği en yaygın kasıtsız uyumsuzluk nedeninin ihmal olduğu ve en fazla oranın hastane içi nakil ve hastaneden taburculukta gerçekleştiği görülmektedir.

Delacretaz ve ark.(2022) İsviçre’de yaptığı çalışmada 293 yenidoğanın 990 hastane içi nakil verileri incelenmiştir. Yenidoğanların hastane içi nakilleri, düşük ila orta şiddette advers olayların önemli bir oranını oluşturmaktadır. Kalite iyileştirme girişimleri ve özel kılavuzların geliştirilmesi advers olayların önlenmesinde gerekli olduğu önerilmiştir.

Çalışma sonuçları incelendiğine hastane içi transportun hastalar için risk ve tehlike barındırdığı görülmektedir. Hastane içi transportun hassas grup olan çocuk hastalardaki sonuçların advers olayların oranında artışın görülmesi nedeniyle oldukça önemlidir. Çocuk hasta bakım ve tedavisinin bir parçası olan hastane içi transport kaçınılmazdır. Bu nedenle bu sürecin takip edilmesi ve iyi yönetilmesi için önlemlerin alınması vurgulanmaktadır.

## **SONUÇ**

Bu sistematik derleme sonucunda pediatri hastalarının hastane içi transportlarında hastayı olumsuz etkileyecek sonuçlar olduğu belirlenmiştir. Çalışmaya dahil edilen araştırmalarda hastane içi transport riskli ve tehlikelidir. Bu riskli eylemin en sorunsuz şekilde gerçekleştirilmesi gereklidir. Bu bağlamda standart bir nakil formu, kontrol listesi ya da prosedürleri içeren değerlendirme araçların uygulanması, hasta transfer sürecinde veri atlanmasını ve olumsuz sonuçların yaşanmasını önlemek için esas olacaktır. Nakil sürecinde uygulananlar taburcu olduktan sonra hastanın ve ebeveynlerin sağlık ekibinden memnuniyeti ve sağlık ekibine duyulan güven üzerinde olumlu bir etkiye sahip olacağı düşünülmektedir.

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**December 09-11, 2022 / Tbilisi, Georgia**

**FLUORESCENCE MICROSCOPY - A METHOD OF STUDYING CELLULAR PROCESSES AND DIAGNOSING DISEASES**

*Davit Mamatsashvili*

*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

*David Kelenjeridze*

*Tbilisi State Medical University, Faculty of Public Health, Tbilisi, Georgia*

*Nikoloz Lobjanidze*

*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

**ABSTRACT**

A fluorescence microscope is an optical microscope that uses the phenomenon of fluorescence instead of scattering, reflection, and attenuation or absorption, which can additionally be used to study the properties of organic and inorganic substances.

Fluorescence was first discovered in 1845 by Friedrich Herschel. He discovered that ultraviolet radiation can cause a solution of quinine (eg, tonic water) to produce blue rays. British scientist Sir George Stokes later studied this discovery and observed that the fluorescence emission from the object represents a longer wavelength than the ultraviolet light that initially excites the object.

The absorption and subsequent re-emission of light by organic and inorganic samples is usually the result of a well-established physical phenomenon described as fluorescence or phosphorescence. The emission of light by the fluorescence process is almost simultaneous with the absorption of the excitation light, since there is a relatively short time delay between the absorption and emission of a photon, usually less than a microsecond. When the emission continues after the excitation light has been extinguished, the phenomenon is called phosphorescence.

"Fluorescence microscope" refers to any microscope that uses fluorescence to produce images, whether it is a simple system such as an epifluorescence microscope (for cell biology) or a more complex design such as a confocal microscope (for life sciences) that uses optical division to obtain better resolution of the fluorescence image. . Fluorescence microscopy has become an essential tool in cell biology. These techniques allow researchers to visualize the dynamics of tissue, cells, individual organelles, and macromolecular assemblies within a cell. Light-emitting diode fluorescence microscopy (LED-FM) is recommended by the World Health Organization for the diagnosis of pulmonary tuberculosis. Fluorescence examination is a fast, simple, non-invasive, selective and sensitive diagnostic tool for evaluating treatment results in oncology. The role of fluorescence microscopy is great, also for other clinical diagnostics.

The role of the mentioned method of microscopy in the process of diagnosing such types of diseases as: tuberculosis, malaria, toxoplasmosis, various types of tumors, etc. is known.

The work presented by us concerns the issues of using fluorescent microscope, the mechanisms of the research method and the structures of the devices, as well as its wide use in the development of cell biology and modern clinical diagnosis processes.

**RECURRENT APHTHOUS STOMATITIS IN CHILDREN**

*Veriko Gergauli*

*Tbilisi State Medical University, Faculty of Dentistry, Tbilisi, Georgia*

*Nana Kipiani*

*Tbilisi State Medical University, Faculty of Dentistry,*

*TSMU Department of Child and Adolescent Therapeutic Dentistry, Tbilisi, Georgia.*

**ABSTRACT**

Chronic recurrent aphthous stomatitis (stomatitis aphtosa chronica recidiva), recurrent benign aphthae is an autoimmune infectious-allergic disease, widespread in both pediatric and adult dentistry. It is characterized by the presence of painful ulcers and aphthae on the non-keratinized oral mucosa (cheek and lip mucosa, tongue, floor of the mouth). The child feels discomfort, which negatively affects his quality of life, eating and speech.

Their clinical presentation is characterized by small, round or ovoid ulcers with erythematous haloes and yellow-gray floors. Recurrent rash with a long course and exacerbation is characteristic. It is less common to involve the highly keratinized mucous membrane of the palate and gums. It mainly occurs in children and adolescents, in 25-50% of the population. The etiology of RAS is still unknown, but several local, systemic, immunologic, genetic, allergic, nutritional, and microbial factors, as well as immunosuppressive drugs, have been proposed as risk factors. Diagnosis is mainly carried out only on the basis of clinical data and complete anamnesis.

We will discuss the risk factors for the development of chronic recurrent aphthous stomatitis and their influence on the course of the disease in children, clinical data and research methods. Much attention will be paid to the main signs characteristic of it, in order to accurately differentiate it from ulcers caused by other causes on the oral mucosa. We will also talk about the basic principles of treatment, a comprehensive choice of treatment measures that will be based on clinical symptoms, data from concomitant diseases, laboratory results and age characteristics, as well as the identification and control of predispositions.

I will inform you of studies found in other PubMed articles describing the correlation of different predisposing factors (e.g., genetic) with chronic recurrent aphthous stomatitis.

**Keywords:** children; pathogenesis; recurrent aphthous stomatitis; treatment; pediatric dentistry; risk factors.



**CRISPR - THE SIMPLEST WAY OF GENE EDITING**

*Elene Didbaridze*

*International Faculty of Physical Medicine and Rehabilitation of Tbilisi State Medical University,  
Tbilisi, Georgia*

*Davit Tskhomelidze*

*Department of Medical Biology and Parasitology of Tbilisi State Medical University, Tbilisi, Georgia*

**ABSTRACT**

The idea of using gene editing to prevent and reverse diseases dates all the way back to 1950. The “old” gene editing technologies and tools that were created back then were very promising, but because of their complexity and inefficiency it made them unsuitable for use for other scientists. But after all the years of research in biotechnology, scientists think that CRISPR is the simplest and most reliable gene editing tool out there, which simplicity lies in its natural immune defence mechanism.

The CRISPR-Cas is a system that cuts off the part of viral DNA that is injected by the virus invading the cell and inserts the viral DNA segment into the chromosome with the help of Cas protein. Cell then makes a copy of that viral DNA into short pieces of RNA, which then binds to cas-9 protein, and forms a complex of free floating material, which searches for its sequence matches. If the same virus invades again, Cas-9 will be able to detect its DNA and cut it. Importantly those bits of DNA will be passed on to the cell's progeny.

The Cas-9 RNA mechanism can be manipulated with our interests as well. To make changes in DNA, scientists can customise a ‘guide’ RNA to match the mutated gene they want to edit and attach it to Cas9. By injecting that, guide RNA will direct Cas9 to target the same sequence gene in the chromosome and cut it, and When cells' ability to repair broken DNA will kick in, scientists will be able to trigger cells to homology directed repair, by incorporation or distribution of new genetic information.

CRISPR technology can be employed not only in adult cells but also in the embryo's organisms. With the ability to repair DNA, scientists will be able to cure or prevent diseases linked to specific genetic errors, like sickle cell anaemia, cystic fibrosis, Huntington's disease, etc. This technology is the fastest, cheapest and easiest way to repair and prevent certain mutations in the DNA by far.

**Key Words:** Crispr, DNA Reparation, Cas-9, Biotechnology

**THE MOST COMMON UROLOGICAL DISEASES IN FEMALES – A BRIEF REVIEW**

***Kochuashvili Nino<sup>1,2</sup>, Zhuzhniashvili Nino<sup>1</sup>***

*<sup>1</sup>Tbilisi State Medical University, Tbilisi, Georgia*

*<sup>2</sup>Student Scientific-Research Club „ENDEAVOR“ of Scientific Research-Skills Center of TSMU, Georgia*

**ABSTRACT**

Urology is a branch of medicine that studies diseases of the male and female urinary systems and male genital organs. Their frequency is different in representatives of different sexes. Among women's urological diseases, the most common are: Urinary incontinence, urinary tract infections, painful bladder syndrome, cystitis, urethritis and pyelonephritis. According to statistics, urological diseases have increased by 20% in recent years.

Urinary tract infections (UTIs) are one of the most common infections worldwide, but little is known about their global scale and long-term trends. Data from the Global Burden of Disease Study 2019 were analyzed to depict the incidence, mortality, and disability-adjusted life years (DALYs) of UTIs in 204 countries and territories from 1990 to 2019 by socio-demographic status, nations, region, sex, and age.

In the United States (US), urinary tract infections (UTI) lead to more than 10 million office visits each year. Temperature and season are potentially important risk factors for UTI, particularly in the context of climate change.

20-25% of women have cystitis, and 10% have a chronic, recurrent form. Of course, cystitis also occurs in men, but with a lower percentage. Statistically, urinary incontinence occur in 72% of women over 50 (and 37% of women over 30)

There are a number of symptoms that help us detect the presence of urological disease in general. They include: pain, urination disorder, quantitative change in urine output, qualitative change in urine, mucous and purulent discharge.

Diseases of the genitourinary system are one of the global health problems. Diseases of the genitourinary system can be caused by infectious agents as well as other conditions and risk factors, including: Irregular sex life, insecurity of personal and sexual hygiene, inflammatory diseases of genital organs, presence of chronic inflammation centers in the body, endocrine pathology and others. The mentioned diseases are characterized by certain features at different ages or physiological conditions. They can be accompanied by various complications, post-defloration cystitis and pyelitis often appear after the start of sexual life.

Diseases of the genitourinary system in Georgia are on the 4th place in terms of prevalence. Among the main causes of death, this group of diseases takes the 11th place. It should be taken into account that the spread of diseases of the genitourinary system is constantly increasing in Georgia in recent years.

Diagnosis of urinary system infection is based on a thorough examination of the patient, detailed collection of data, use of laboratory, endoscopic, ultrasound, X-ray and other methods.

Like any other pathology, many urological diseases are easier to prevent than to treat them. For this, it is recommended to take some preventive measures. Treatment is different for different urological diseases. Urinary stress incontinence is mostly treated surgically, although local treatment is also possible in the initial stage - the use of ointments containing female sex hormones. Antibacterial treatment gives temporary results and becomes ineffective over time. The problem of chronic cystitis is very urgent and the fight against it should be based on modern international principles.

**Key words:** urology, urological diseases, cystitis in women, urethritis, urological problems of pregnant women

**HISTORY OF OPHTHALMOLOGY IN GEORGIA – A LITERATURE RESEARCH**

*Gigi Gorgadze<sup>1</sup>, Ramaz Shengelia<sup>1,2</sup>*

<sup>1</sup>Tbilisi State Medical University

<sup>2</sup>World Society of Historians of Medicine

Ophthalmology - the field of medicine that deals with the treatment of eye diseases, has been an integral part of daily medical activities since time immemorial, because it refers to the organ, the health of which depends on a person's perception of the world, ability to work and integration into society. It has always been an ideal indicator of how medicine was developed at a particular moment in a particular country or in the whole world.

**Purpose:** The research aimed to find information about the Georgian School of Ophthalmology and to systematize them.

**Materials and methods:** within the framework of the research, monuments of ancient Georgian medical literature, works and monographs of historians of medicine, newspapers and other written sources, Internet materials and modern collections were searched and analyzed.

**Results:** As a result of the research, it was found that the history of the school of ophthalmology in Georgia is quite old and interesting. It is particularly well presented in the works of Zaza Fanaskertel-Tsitsishvili, Sulkhani-Saba Orbeliani and Davit Batonishvili. As for the modern school of ophthalmology, its founder was Giorgi Tarsaidze, information about which can be found in many Georgian and foreign language (mainly Russian) medical and non-medical sources. It is worth noting that the first operation in the Caucasus was performed by the important founder of modern medicine and its teaching, Nikoloz Pirogov, which is not surprising, if we take into account the discovery that the first ophthalmology clinic was opened in the Russian Empire in 1946.

**Discussion:** In the Middle Ages, the knowledge of the visual system in Georgia followed the knowledge of the Eastern medical school. From the 10th - 11th centuries, views on the anatomy, physiology and pathologies of the visual system, as well as the methods of treatment of the latter, were already well established. The history of modern ophthalmology in Georgia includes many reports, facts and episodes.

**Conclusion:** the history of Georgian ophthalmology is quite old, high-quality and valuable. Its high level of development in all periods indicates the fact that medicine itself has always stood at the height of vocation in Georgia. It is important to systematize the mentioned discoveries, collect them and properly record them and pass them on to future generations.

**Key words:** Ophthalmology, History of Medicine, monuments of literature.

**THE IMPACT OF THE CORONAVIRUS (COVID-19) ON THE MENSTRUAL CYCLE AND MENTAL HEALTH OF GEORGIAN YOUNG WOMEN**

*Aleksandre Asanidze<sup>1</sup>*

*<sup>1</sup>Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia.*

**ABSTRACT**

The COVID-19 pandemic has caused great damage to humanity and significantly decreased quality of life. Coronavirus affects not only physical health but also causes a significant threat to mental health.

**Objective** of the study was to investigate the impact of coronavirus infection on the menstrual cycle and mental health of Georgian young women and establish the relationship between them.

**Methods:** A cross-sectional study was conducted by administering online questionnaires to young women (18-25 years, n 420) in Georgia, from 8th to 28th May, 2022. The questionnaires were designed by a gynecologist, a psychotherapist, and clinical epidemiologists.

**Results:** 48.2 % of participants reported significant changes in their menstrual cycle after the coronavirus infection. These included changes in menstrual cycle length (48%), the duration of menses (34%), and changes in premenstrual symptoms (25%).

Participants' mean menstrual cycle length significantly increased after 3 months of infection,  $p < 0.05$ . Participants' menstrual cycle length before and 6 months after coronavirus infection did not differ significantly.

Duration of menstruation before the pandemic was significantly lower than after 3 and 6 months of coronavirus infection,  $p < 0.05$ .

The prevalence of premenstrual symptoms (PMS) components and severity of dysmenorrhea was significantly increased during COVID-19 compared with before,  $p < 0.05$ .

78% of participants report various changes in their psychological state after COVID-19. Women related a significant increase in low mood, poor concentration, anxiety, poor sleep, loneliness, depression,  $p < 0.05$ .

Positive correlations between COVID-19-associated mental health disorders and changes of the menstrual cycle, dysmenorrhea severity and PMS were observed,  $p < 0.05$ . The multiple linear regression model revealed that dysmenorrhea severity, PMS symptoms, and changes of the menstrual cycle were associated with worsening of depression and aggravation of anxiety.

**Conclusions:** Coronavirus infection causes significant changes of the menstrual cycle and mental health in Georgian young women. The study showed a link between the COVID-19 pandemic-induced anxiety, stress, depression, and menstrual cycle irregularity among Georgian young woman.

**Keywords:** COVID-19; menstrual cycle; depression; anxiety; stress

**IMPOSTOR SYNDROME AND ITS CORRELATION WITH DEPRESSION AND BURNOUT AMONG MEDICAL STUDENTS IN GEORGIA WITH REGARDS TO THEIR FUTURE CHOICE OF SUBSPECIALTY**

*Mariam Alavidze<sup>1</sup>*

*<sup>1</sup>Tbilisi State Medical University, Medical Faculty, USMD Program, Tbilisi, Georgia.*

*Elene Dolidze<sup>2</sup>*

*<sup>2</sup>Tbilisi State Medical University, Medical Faculty, USMD Program, Tbilisi, Georgia.*

*Melita Melikishvili<sup>3</sup>*

*<sup>3</sup>Tbilisi State Medical University, Medical Faculty, USMD Program, Tbilisi, Georgia.*

*Lia Khorbaladze<sup>4</sup>*

*<sup>4</sup>Neurosurgeon, JCX Evex, Neurosurgery department, Tbilisi, Georgia.*

**ABSTRACT**

Impostor syndrome (IS) is becoming more widely recognized as a disorder among medical students. Impostor syndrome is especially problematic because it has been linked to an increase in suicide. Few studies have discovered a relationship between IS and depression and/or burnout. Our study will look into the correlation of IS with depression and burnout in a local population and its risk factors, such as students' preferred medical specialization.

**Materials and Methods**

A cross-sectional web-based study was conducted. 91 medical students were investigated in Georgia using questionnaires that included information about sociodemographics, sleep length, frequency of studying, and medical specialty of choice, as well as the Patient Health Questionnaire-9 (PHQ-9), the Maslach Burnout Inventory (MBI), the Clance IP scale.

**Results:**

Among the 91 subjects, 71 had depression and 88 had IS. Imposter syndrome was found to be substantially related to depression (OR = 15.96, 95% CI 2.98, 0.8545, P-value-0.0141).

Medical students, according to the findings, were ten times more likely to feel burnout and imposter syndrome. (OR=9.874, 95% CI 1.22, 79.94, P=0.058)

Suicidal ideation was linked with imposter syndrome (OR=2.49, 95% CI 0.238, 23.77, p-value-0.647).

Pediatrics showed the strongest correlation with IS (OR=6.818, 95% CI 0.238, 195.3) among all subspecialties.

Internal medicine had the second largest correlation with IS (OR=5.95, 95% CI 0.256, 138.4), while cardiology had the strongest correlation with depression and IS.

Imposter syndrome in correlation with depression in the clinical years of medical school (OR=17.27, CI 95%, 0.791, 37.68, p-value-0.0366) was much greater than in the preclinical years. (OR=4.254, CI 95% 0.1959, 92.36, p-value-0.498)

**Conclusion:**

The study's findings indicate that impostor syndrome is common among medical students. It is greater throughout clinical years and connected with burnout. IS may predispose students to depression. Imposter syndrome is most common among students who choose pediatrics as a subspecialty. This brings up new possibilities for preventing, managing, and screening medical student populations for potential mental health illnesses.

**Keywords:** Imposter syndrome, burnout, depression, suicide, subspecialty

**Table 1: Imposter syndrome risk factors and correlations**

<b>Imposter syndrome its Associations and risk factors (RF)</b>	<b>Odds ratio (OR)</b>	<b>P Value</b>	<b>Confidence interval (CI 95%)</b>
Depression	15.96	0.0141	0.8545, 298
Preclinical years	4.254	0.498	0.1959, 92.36
Clinical years	17.27	0.0366	0.791, 37. a 68
Surgery with anesthesiology as subspecialty	5.37	0.48	0. a 236, a 122.4
Internal Medicine as subspecialty	5.95	0.478	0.256, 138.4
Psychiatry and Neurology as subspecialties	5.4	0.381	0.195, 149.9
Pediatrics as subspecialty	6.818	0.33	0.238, 195.3
Burnout	9.875	0.058	1.22, 79.94
Daily studying as RF	0.8	1	0.127, 5.05
Suicidal ideations as RF	2.491	0.647	2.67, 23.77
Bad Family Relationships as RF	1.038	1	0.052, 20.66
Sleep duration as RF	13.17	0.0118	2.17, 79.91

**DEPRESSION RATE IN FIRST-YEAR MEDICAL STUDENTS - A SINGLE CROSS-SECTIONAL STUDY ACCORDING TO THE ZUNG QUESTIONNAIRE**

*Ani Gorgadze*

*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

*Mariam Bokhua*

*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

*Gigi Gorgadze*

*TSMU student scientific-research organization "Endeavor", Tbilisi, Georgia*

*<https://orcid.org/0000-0002-7885-639X>*

*Luiza Gabunia*

*TSMU scientific Research-Skills Center, Tbilisi, Georgia*

*<https://orcid.org/0000-0003-0856-2684>*

**ABSTRACT**

The life of medical students is characterized by a busy study schedule, which is often associated with various psychological and psycho-somatic pathologies. Their psychological status is not so rarely characterized by an increased rate of neuroticism and an increase in the depressive background. All this is especially the problem of first-year students, which is probably associated with the new environment and study mode.

**Materials and Methods:** A single cross-sectional study was conducted. Zung questionnaire was used, which was developed for differential diagnostics of depressive states and screening-diagnosis of states close to depression. The questionnaire consists of 20 questions, the answers of which are evaluated with 1-4 points. The total score varies from 20 to 80 points. Each has a corresponding depressive state. In total, 21% of first-year students (n=95, N=450) were interviewed through an anonymous Google Forms questionnaire.

**Results:** as a result of the survey, it was found that 29.4% of the respondents have a mild depressive state of situational or neurotic origin (n=28). 9.4% of cases were diagnosed with masked or true depression or subdepressive state (n=90). It should be noted that 82.1% mention that they do not live a complete life (n=78). In addition, 70.5% face problems with decision-making (n=67).

**Discussion:** According to the data, students with pre-depressive status or indicators close to it, complain of problems with appetite and fatigue (it should be noted that the latter is expressed even in persons with zero depressive index). Also, there are frequent disorders of motivation, socialization and quality of rest.

**Conclusion:** as the research confirmed, the depressive background is definitely increased in the first-year students in not so rare cases - even severely. The issue requires further study and identification of correlative aspects.

**Key words:** depression, neuroticism, student schedule, stress.

**ORAL CONTRACEPTIVE ASSOCIATED RISKS AND PREVENTION**

*Nuca Karselishvili*

*Tbilisi State Medical University, Faculty of Medicine, Department of Pharmacology, Tbilisi, Georgia.*

*Lika Lavrelashvili*

*Tbilisi State Medical University, Faculty of Medicine, Department of Pharmacology, Tbilisi, Georgia.*

*Luiza Gabunia*

*Director of Scientific Research-Skills Center, Associate Professor of Medical Pharmacology  
Department of the Tbilisi State Medical University*

*ORCID ID: 0000-0003-0856-2684*

**ABSTRACT**

Oral contraceptives, also called birth control pills, at first glance are a safe and reliable option for unwanted pregnancy, but if taken long-term they are associated with a higher risk of developing thromboembolism and breast cancer in women. The pill contains artificial versions of female hormones estrogen and progesterone; Venous thromboembolism (VTE) in the deep veins of the legs or pulmonary vasculature is the most typical clinical manifestation of estrogen-related thrombosis, typically within the first few months of therapy, especially if they have a family history of thrombosis. A retrospective analysis was performed of the case records of women who developed a TEE (thromboembolic event) while on oral contraceptives or HRT (hormone replacement therapy) and were referred for thrombophilia evaluation over 4 years. 65 of the 85 women who experienced a TEE while taking HRT or an oral contraceptive had at least one more thrombophilia risk factor. In addition to arterial thrombosis, estrogen has also been linked to an increased incidence of "unusual location" thromboses. Breast cancer and hormonal contraception use are associated. The Danish cohort study reported a 20% increased risk of breast cancer among current and recent hormonal contraception users. The overall absolute increase in breast cancers diagnosed among current and recent users of any hormonal contraceptive was approximately one extra breast cancer for every 7690 women using hormonal contraception for 1 year. Regarding the estrogen component, ethinylestradiol (EE) dosage reduction helped lessen related adverse effects. It is recommended for women with a family history of breast cancer to avoid hormonal contraceptives and those who have a family history of thrombosis can choose COCs with norethisterone or levonorgestrel, which is shown to have a lower risk for venous thromboembolism. In conclusion there is a piece of evidence that oral contraceptives are related to both venous and arterial thrombosis and breast cancer; Therefore, women with a higher risk of those diseases should avoid birth control pills. In all cases is necessary to control/monitor the dynamics of the functional parameters of the above-mentioned organs regarding avoiding complications.

**Keywords:** oral contraceptives, breast cancer, venous thrombosis.



**COVID-19 AND PROBABLE MECHANISMS OF POST SARS-CoV-2 NEUROLOGICAL CONSEQUENCES**

*Maia Beridze*

*Tbilisi State Medical University, Faculty of Medicine, Department of Neurological Diseases'  
Propaedeutic and Topical Diagnostics, Tbilisi, Georgia*

*ORCID ID: 0000-0002-1295-5360*

**ABSTRACT**

The outbreak of the SARS-CoV-2 has resulted in hundreds of millions of infected individuals and millions of deaths in all over the world. Infected patients experience different severity range of respiratory complications, advanced inflammation, hypoxia or hypoxemia that impacts multiple organs, including the central and peripheral nervous systems.

Neurological symptoms range from impaired taste and/or smell to stroke, encephalopathy, meningoencephalitis, demyelination disorders, seizures, peripheral neuropathies and polyneuropathies suggesting SARS-CoV-2 may contribute to nervous system injury through direct and/or indirect mechanisms. SARS-CoV-2 triggers the proinflammatory cascade, when the production of interleukins ((IL-1, IL-6, IL-12) increases in the blood and cerebrospinal fluid (CSF). The amount of Fibrinogen, D dimer is elevating, complement system is activated, count of thrombocytes is diminished. Prothrombin time is prolonged, vascular endothelium is damaged due to the activation of matrix metalloproteinases (MMP-2, MMP-9) and leakage of the injured blood brain barrier permits the free radicals to rush into the brain. Activation of transmembrane protease Serin-2 (TMPRSS-2) leads to the production of microvascular thrombus. The central mechanisms comprise the direct invasion of SARS-CoV-2 into hypothalamus via olfactory or vascular pathways.

Systemic review of 2021 year discussed totally 2834 post Covid-19 patients admitted in different hospitals of Europe. Among them the highest percent (56.5%) took patients with loss of smell and taste, 25.3% were with cerebrovascular diseases, 5.3%- patients with encephalopathy, 3.3%-peripheral neuropathy and polyneuropathy, 2.9%-inflammatory demyelinating pathologies, and 6.8%- the other neurological pathologies like seizures, insomnia, neurosis, memory problems, depression and etc.

Probably, the direct invasion of the virus in the central nervous system, damage of the microvasculature with toxic reactions and production of autoantibodies are the main mechanisms that take place as a consequence after the surveillance from SARS-Cov-2 infection.

**Key words:** pandemic, inflammation, autoantibodies, stroke, neuropathy, encephalopathy

**RESPIRATORY VIRAL INFECTIONS IN CHILDREN IN GEORGIA IN THE POST- COVID PERIOD**

*<sup>1</sup>Malvina Javakhadze*

*<sup>1</sup>Tbilisi State Medical University, Faculty of Medicine, Infectious Diseases department, Tbilisi, Georgia*

*<sup>1</sup>ORCID ID: 0000-0002-1090-8106*

*<sup>2</sup>Nia Iakobashvili*

*<sup>2</sup>Tbilisi State Medical University, Faculty of Medicine, Georgian Sector, Tbilisi, Georgia*

**ABSTRACT**

**Introduction:** During the period of high morbidity with SARS CoV2, which became the cause of the pandemic, the morbidity with various respiratory viral infections decreased dramatically. The reason for this was the active use of personal protective equipment and social distancing.

**The purpose of the study:** From May 2022 to October 2022, in accordance with the viruses circulating in the country, is to determine the structure of the disease in children under the age of 18.

**Methods:** We studied medical records of the patients who were hospitalized with respiratory viral infections (RVI) or with their complications in the clinic of Acad. V. Bochorishvili from May 2022 to the end of October 2022, in order to determine the structure of the diseases, the etiological agents, severity and complications of the diseases.

**Results:** We analyzed the medical records of 350 patients who were treated at the clinic with RVI. The age distribution is as follows: 24.8% <2 y. 38.2%  $\geq$ 2 - <5 y. 29% 5–15 y. 8% - 16–18 years old. The main clinical symptoms were fever, rhinorrhea, sore throat, cough. 35% of - developed pneumonia, as a bacterial complication following a viral infection.

In the post-pandemic period, the age structure and seasonality of viral infections have changed. Both before and after the pandemic, the two most common agents were rhinovirus and respiratory syncytial virus (RSV). In most, 30% of cases (among those hospitalized), bronchiolitis occurred: disturbing spasmodic cough, difficulty breathing, production of large amounts of mucus. The duration of symptoms was prolonged, especially in children under 2 years of age.

Among other viruses, cases of adenovirus, bocavirus and influenza (last month) were reported. An important feature is the increased frequency in illness due to viral infections, so that the period between illnesses has been significantly shortened. Also, mixed viral infections occur.

There were no patients with Covid-19 in our clinical material, according to the data of the National Center for Disease Control, 18% of the viral population has SARS CoV2, with a mild disease.

**Conclusion:** Thus, in the post-pandemic period, rhinovirus, RSV, adenovirus, bocavirus infections and influenza, cases have increased dramatically among children. The interval between illnesses has shortened, children under 5 years of age have fever almost continuously, and bronchiolitis is relatively more severe under the age of 2 years. Coinfection of different viruses are common.

**Keywords:** Rhinovirus; RSV; Adenovirus; Bocavirus.

**CORRELATION OF THE RESULTS OF THE IMMUNOPHENOTYPIC AND MORPHOLOGICAL ANALYSIS IN DIAGNOSING ACUTE LEUKEMIAS**

*Nino Gogokhia*

*Tbilisi State Medical University, Physical Medicine and Rehabilitation Faculty, Laboratory Medicine Department, Tbilisi, Georgia*

**ABSTRACT**

The necessary algorithm for modern diagnostic studies of acute leukemias is **Hemogram (HMG), Myelogram, Cytochemistry, Immunophenotyping, and Cytogenetic** studies.

HMG - the morphological study of peripheral blood cells by microscopy of the blood smear is a basic, frequently prescribed study, and it appears to be the first indicator of the primary malignant processes of the bone marrow at the initial stage. Then a bone marrow biopsy is performed to confirm the diagnosis with a **myelogram test**. To determine the type of disease in the malignant *cell* substrate, the following are prescribed: **cytochemistry, immunophenotyping, and cytogenetic** studies.

Based on the above, it is the morphological study of peripheral blood and bone marrow cells that is crucial in the diagnosis of acute leukemias at the initial stage, which needs to be supplemented and clarified with the help of the other listed studies.

Performing immunophenotypic and cytogenetic studies may not always be performed or may be delayed for some time, so it is of course interesting how the morphological diagnosis of acute leukemias coincides with the findings of cytochemical, immunophenotypic, and cytogenetic analyses.

For this purpose, we present to you the cases studied in the laboratory of the First University Clinic: the studies were carried out in the emergency department and hematological department of the clinic with patients, whose HMG, and bone marrow examination findings were compared with the results of cytochemistry and immunophenotyping.

In six cases out of ten patients taking part in the study, the interpretation of HMG and myelogram findings were in complete concordance with immunophenotyping results. However, in four cases, the diagnosis of leukemia was confirmed but the type of leukemia appeared to be different from the type that the morphological study had suggested.

The main goal of the research was to determine the concordance of morphological studies with the results of immunophenotyping and to evaluate the reliability of the results of morphological studies.

**Keywords:** Acute leukemia, morphological analysis, immunophenotyping.

**A NEW ERA IN TUBERCULOSIS TREATMENT**

*Irma Bubashvili*

*Tbilisi State Medical University, Department of Phthisiatry and Pulmonology*

*Tamar Levidze*

*Tbilisi State Medical University, Department of Phthisiatry and Pulmonology*

**რეზიუმე**

საქართველოში ახალი ტუბსაწინააღმდეგო მედიკამენტებისა და სამკურნალო რეჟიმების ხელმისაწვდომობამ ეტაპობრივად შესაძლებელი გახდა სენსიტიური და რეზისტენტული ტუბერკულოზის მკურნალობის ხანგრძლივობის და სამკურნალოდ გამოყენებული კომბინაციების/რეჟიმების შეცვლა. კერძოდ, წარმოდგენილი ნაშრომის ფარგლებში განხილული იქნება სენსიტიური ტუბერკულოზის სამკურნალოდ ხელმისაწვდომი 4 თვიანი რიფაპენტინის და მოქსიფლოქსაცინის შემცველი სამკურნალო რეჟიმი.

**ABSTRACT**

Innovations in TB diagnosis and treatment have improved TB management and moved many countries towards elimination by 2019. In particular, from 2019 to 2020, the registration of tuberculosis cases decreased by 18% and returned to the level of 2012, while the annual estimated number of tuberculosis patients in 2020 and 2021 was 10 million, similar to the annual rates of the last decade. Limited access to phthisiatric services has increased the death rate among HIV-negative individuals by 1.2 to 1.3 million. Systematic screening for active tuberculosis is important for the management of tuberculosis, which involves the systematic detection of people at risk of developing active tuberculosis in predetermined target groups by evaluating symptoms using tests, instrumental studies or other procedures that can be quickly implemented. Systemic screening for active tuberculosis reduces the risk of disease transmission by identifying infected individuals and shortening their infectious period. It is not enough to detect active tuberculosis only among persons who refer to a medical institution. The still underdetection of TB cases, delayed diagnosis and resulting prolonged transmission in the community, confirm the need for more active approaches aimed at timely detection and systematic screening of active TB in the selecting risk groups and populations.

Within the framework of the presented topic, tuberculosis screening with updated, latest and modern approaches and methods are discussed; New TB drugs and treatment regimens available programmatically in Georgia, based on which it became possible to change the duration of treatment and the combinations/regimen used for treatment of sensitive and different types of resistant tuberculosis.

In particular, a 4-month treatment regimen containing rifapentine and moxifloxacin has become available for the treatment of sensitive tuberculosis, a 6-month treatment regimen containing bedaquiline, pretomanid, linezolid and moxifloxacin is recommended for the treatment of rifampicin or multidrug-resistant tuberculosis, a 6-9 month 3-component BPaL regimen is programmatically recommended for the treatment of pre-extensively resistant tuberculosis and other. Modern aspects of TB management include and aim to ensure universal access to high-quality, patient-centred treatment for TB patients.

I	მაღალი ხარისხის მტკიცებულება
II	სარწმუნო, კარგი ხარისხის მტკიცებულება
III	საშუალო ხარისხის მტკიცებულება
IV	დაბალი ხარისხის მტკიცებულება
V	ექსპერტთა მოსაზრება/კლინიკური გამოცდილება

**მტკიცებულების დონები**

**სენსიტიური ტუბერკულოზის მკურნალობა**

**სენსიტიური ტუბერკულოზი** - ეს არის ტუბერკულოზის ბაქტერიოლოგიურად დადასტურებული, ან კლინიკურად დიაგნოსტირებული შემთხვევა რიფამპიციინისა და იზონიაზიდისადმი რეზისტენტობის მტკიცებულების გარეშე, რომლის სამკურნალოდაც ათწლეულების განმავლობაში მხოლოდ 6 თვიანი სტანდარტული 2HRZE/4HR რეჟიმი იყო რეკომენდებული. ამჟამად კი სენსიტიური ტუბერკულოზის სამკურნალოდ 6 თვიანი სტანდარტული რეჟიმების ალტერნატივად შესაძლებელია 4 თვიანი მკურნალობა დაინიშნოს.

სენსიტიური ტუბერკულოზის სამკურნალოდ ამჟამად შემდეგი 3 რეჟიმია რეკომენდებული:

- 2HRZE/4HR;
- 2HRZE/2HR;
- 2HPMZ/2HPM.

სენსიტიური ტუბერკულოზის სამკურნალოდ რეკომენდებული რეჟიმები პაციენტების ასაკის და დაავადების სიმძიმის გათვალისწინებით უნდა შეირჩეს:

- 6 თვიანი 2HRZE/4HR რეჟიმი ნებისმიერ ასაკობრივ ჯგუფში, ნებისმიერი სიმძიმის პაციენტთან შეიძლება დაინიშნოს;
- იგივე მედიკამენტებით შემდგარი 4 თვიანი 2HRZE/4HR რეჟიმი 3 თვიდან 16 წლამდე ასაკობრივ ჯგუფში არამძიმე ფილტვის ან ლიმფური კვანძების ტუბერკულოზის შემთხვევაში შეიძლება დაინიშნოს;
- 4 თვიანი რიფაპენტინის და მოქსიფლოქსაცინის შემცველი სამკურნალო 2HPMZ/2HPM რეჟიმი >12 წლის ასაკობრივ ჯგუფში, ნებისმიერი სიმძიმის პაციენტთან შეიძლება დაინიშნოს;

**ცხრილი DS-TB სამკურნალო რეჟიმის შერჩევა**

რეჟიმი	0-3 თვე	3თვე-12 წელი	12-16 წელი	>16 წელი
<b>2HRZE/4HR</b>	<b>დაავადების სიმძიმის და აივ სტატუსის მიუხედავად</b>			
<b>2HRZE/2HR</b>		<b>არამძიმე TB*, &gt; 3 კვ პაციენტი</b>		
<b>2HPMZ/2HPM</b>			<b>დაავადების სიმძიმის და აივ სტატუსის მიუხედავად</b>	

DS-TB სამკურნალო რეჟიმის ხანგრძლივობის შესარჩევად ფილტვის არამძიმე ფორმად ითვლება: მკერდშიდა ლიმფური კვანძების ტუბერკულოზი საჭაერო გზების ობსტრუქციის გარეშე; პლევრის ღრუში გამონაჟონით გართულების გარეშე; ან ბაქტერია არაგამომყოფი, არაკავერნოზული, ერთ წილში ლოკალიზებული და მილირული კერების გარეშე მიმდინარე ფორმა.

ასაკობრივ ჯგუფებს თუ შევხედავთ, გვაქვს გარკვეული ასაკობრივი გადაფარვა. მაგალითად, 3 თვიდან 12 წლამდე ასაკის პაციენტებთან შეიძლება დაინიშნოს მაგ. 2HRZE/2HR და 2HRZE/4HR რეჟიმი; 12–16 წლის პაციენტებთან კი შეიძლება სამივე რეჟიმი (2HRZE/4HR, 2HPMZ/2HPM და 2HRZE/2HR) დაინიშნოს. შესაბამისად სამკურნალო რეჟიმის შერჩევასას ასაკობრივ ჯგუფთან ერთად დაავადების სიმძიმე, თანმხლები მდგომარეობები (მაგ. ჰეპატიტი, თირკმლის უკმარისობა, არაკომპენსირებული შაქრიანი დიაბეტი, აივ სტატუსი) და მედიკამენტების (მაგ. რიფაპენტინის და მოქსიფლოქსაცინის)

ხელმისაწვდომობა უნდა იყოს გათვალისწინებული: 3 თვიდან 16 წლამდე პაციენტებთან 2HRZE/2HR რეჟიმის დანიშვნისას გათვალისწინებული უნდა იყოს, რომ ეს რეჟიმი მხოლოდ ტუბერკულოზის არამძიმე ფორმის შემთხვევებში ინიშნება.

#### **6 თვიანი 2HRZE/4HR რეჟიმი**

ნებისმიერი ასაკობრივი ჯგუფის და ნებისმიერი სიმძიმის ფილტვის სენსიტიური ტუბერკულოზით დაავადებული პაციენტებისათვის 6 თვიანი სტანდარტული სამკურნალო რეჟიმი პირველი რიგის ტუბსაწინააღმდეგო მედიკამენტების - H = იზონიაზიდი, R = რიფამპიცინი, Z = პირაზინამიდი, E = ეტამბუტოლის კომბინაციით ინიშნება. აქედან ფილტვის სენსიტიური ტუბერკულოზის შემთხვევაში პირველი ორი თვის განმავლობაში ოთხივე ეს მედიკამენტი ერთად ინიშნება, შემდეგ კი ოთხი თვის განმავლობაში მკურნალობა რიფამპიცინის და იზონიაზიდის კომბინაციით გრძელდება. სულ ფილტვის სენსიტიური ტუბერკულოზის სტანდარტული მკურნალობა მედიკამენტების ყოველდღიურ რეჟიმში მიღებით 6 თვის განმავლობაში გრძელდება. იგივე 6 თვიანი სტანდარტული სამკურნალო რეჟიმი ასევე რეკომენდებულია ფილტვგარეშე სენსიტიური ტუბერკულოზის სამკურნალოდ, გარდა ცენტრალური ნერვული სისტემის და ძვალ-სახსრის ტუბერკულოზისა. ტუბერკულოზური მენინგიტის და ძვალ-სახსრის ტუბერკულოზის სენსიტიური ფორმების სამკურნალოდ 6 თვეზე ხანგრძლივი რეჟიმები ინიშნება.

სენსიტიური ტუბერკულოზის სტანდარტული 6 თვიანი რეჟიმით მკურნალობის გაგრძელების ფაზაში იზონიაზიდით და რიფამპიცინით (HR სქემით) მკურნალობის ალტერნატივაა რეჟიმის ეტამბუტოლით გაძლიერება და HRE სქემის გამოყენება პაციენტებთან, ვისთანაც:

- პარენქიმის გავრცობილი დაზიანება აღინიშნება, ან
- ინტენსიური ფაზის ბოლოს იზონიაზიდისადმი მგრძობელობა უცნობია, ან
- თუ პაციენტი ინტენსიური ფაზის ბოლოს მგბ(+) რჩება, ამ დროს ჩატარებული მგრძობელობის ტესტი კი პირველი რიგის ტუბსაწინააღმდეგო მედიკამენტებისადმი რეზისტენტობას გამოიჩინებს.

#### **4 თვიანი 2HRZE/2HR რეჟიმი**

3 თვიდან 16 წლამდე >3 კგ წონის ფილტვის არამძიმე სენსიტიური ტუბერკულოზით დაავადებულ პაციენტებთან რეკომენდებულია 4 თვიანი სამკურნალო რეჟიმი პირველი რიგის ტუბსაწინააღმდეგო მედიკამენტების - H = იზონიაზიდი, R = რიფამპიცინი, Z = პირაზინამიდი, E = ეტამბუტოლის კომბინაციით. აქედან, პირველი ორი თვის განმავლობაში ოთხივე ეს მედიკამენტი ერთად ინიშნება, შემდეგ კი ორი თვის განმავლობაში მკურნალობა რიფამპიცინის და იზონიაზიდის კომბინაციით გრძელდება. სულ მკურნალობა 4 თვის განმავლობაში მედიკამენტების ყოველდღიურ რეჟიმში მიღებით ტარდება.

3 თვიდან 16 წლამდე ფილტვის არამძიმე სენსიტიური ტუბერკულოზით დაავადებული პაციენტების 4 თვიანი 2HRZE/2HR რეჟიმით მკურნალობის მკაცრი რეკომენდაცია კვლევის შედეგებს ეყრდნობა, რომელთა მიხედვითაც 4 თვიანი 2HRZE/2HR რეჟიმით მკურნალობა არანაკლებ ეფექტური და უსაფრთხოა 6 თვიან 2HRZE/4HR რეჟიმთან შედარებით.

ტუბერკულოზის არამძიმე ფორმით დაავადებული 3 თვიდან 16 წლამდე ბავშვებთან და მოზარდებთან 4 თვიანი 2HRZE/2HR რეჟიმი გარკვეული კრიტერიუმების გათვალისწინებით ინიშნება.

ბავშვებთან და მოზარდებთან, რომლებსაც ბაქტერიოლოგიური კვლევა და გულმკერდის რენტგენოგრაფია ჩატარდა უნდა დაინიშნოს 4 თვიანი 2HRZE/2HR რეჟიმი თუ ისინი შემდეგ კრიტერიუმებს აკმაყოფილებენ:

➤ გულმკერდის რენტგენოგრამა შეესაბამება ტუბერკულოზის არამძიმე ფორმას, მაგ:

✓ ვლინდება მკერდშიდა ლიმფური კვანძების ტუბერკულოზი საჭკერო გზების ობსტრუქციის გარეშე;

✓ ფილტვის ტუბერკულოზი ლოკალიზებულია ერთ წილში, კავიტაციის და მილიარული კერების გარეშე; ან

✓ პლევრალური გამონაჟონით გართულების გარეშე (პნევმოთორაქსის ან ემპიემის გარეშე);

➤ Xpert Ultra ტესტის შედეგი MTB უარყოფითია, კვალია, ძალიან დაბალი ან დაბალია (ან თუ Xpert Ultra ტესტი ხელმისაწვდომი არ არის, ნახველის ნაცხი არის უარყოფითი); და

➤ ბავშვს ან მოზარდს ტუბერკულოზისათვის დამახასიათებელი საშუალო სიმპტომები და ნიშნები აქვს და არ საჭიროებს ჰოსპიტალიზაციას;

საშუალო ხასიათის სიმპტომები, რომლებიც არ საჭიროებენ ჰოსპიტალიზაციას გულისხმობს შემდეგს:

– საშიში ან მაღალი პრიორიტეტის ნიშნები არ არის;

– ასიმეტრიული სუნთქვა ან პერსისტირებადი ხიხინი არა არის;

– არ არის ფილტვგარეშე ტუბერკულოზის ნიშნები გარდა პერიფერიული ლიმფური კვანძების ტუბერკულოზისა; და

– არ არის არცერთი შემდეგი: მწვავე, მძიმე მალნუტრიცია; რესპირატორული დისტრესი; მაღალი ტემპერატურა; ძლიერი სიფერმკრთალე; მოუსვენრობა; გაღიზიანებადობა ან ლეთარგია.

საშიში ან მაღალი პრიორიტეტის ნიშნებია: 2 კვირაზე გახანგრძლივებული ხველა, ლეთარგია, წონაში კლება, ჰემოფტიზი, ღამით ოფლიანობა, ლიმფური კვანძების შესიება, ტახიკარდია და ტახიპნოე.

მწვავე, მძიმე მალნუტრიციის მქონე ბავშვებთან და მოზარდებთან იმ შემთხვევაშიც კი თუ ტუბერკულოზის პროცესი არამძიმეა, 4 თვიანი სამკურნალო რეჟიმი არ უნდა დაინიშნოს. ამ შემთხვევაში რეკომენდებულია 6 თვიანი მკურნალობა.

#### **4 თვიანი 2HPMZ/2HPM რეჟიმი**

>12 წლის ფილტვის სენსიტიური ტუბერკულოზით დაავადებულ პაციენტებთან, დაავადების ნებისმიერი სიმძიმის შემთხვევაში შეიძლება 4 თვიანი სამკურნალო რეჟიმი H = იზონიაზიდის, P = რიფაპენტინის, M = მოქსიფლოქსაცინის, Z = პირაზინამიდის კომბინაციით დაინიშნოს. აქედან პირველი ორი თვის განმავლობაში ოთხივე ეს მედიკამენტი ერთად ინიშნება, შემდეგ კი ორი თვის განმავლობაში მკურნალობა იზონიაზიდის, რიფაპენტინის და მოქსიფლოქსაცინის კომბინაციით გრძელდება. სულ მკურნალობა 4 თვის განმავლობაში მედიკამენტების ყოველდღიურ რეჟიმში მიღებით ტარდება. ამ რეჟიმის დასაინიშნად საჭიროა რიფაპენტინის და მოქსიფლოქსაცინის ხელმისაწვდომობა.

4 თვიანი 2HPMZ/2HPM რეჟიმის გამოყენების პირობითი რეკომენდაცია რანდომიზებულ, მულტი-ნაციონალურ, ღია, კონტროლირებად, 3 ფაზიან კვლევას ეყრდნობა, სადაც ორი,

ოთხთვიანი, რიფაპენტიინზე დაფუძნებული სამკურნალო რეჟიმი სტანდარტულ ექვსთვიან საკონტროლო რეჟიმს შედარდა. კვლევაში  $\geq 12$  წლის, ჯანმო-ს მიერ რეკომენდებული ტესტებით ფილტვის ტუბერკულოზით ახლად დიაგნოსტირებული, იზონიაზიდის, რიფამპიცილის და ფთორქინოლონებისადმი სენსიტიური პაციენტები იყვნენ ჩართულნი. პირველადი ეფექტურობის შეფასების კრიტერიუმს რანდომიზაციიდან 12 თვის თავზე დაავადებისაგან თავისუფალი გამოსავალი წარმოადგენდა. კვლევის შედეგად გამოვლინდა, რომ ფილტვის სენსიტიური ტუბერკულოზის სამკურნალოდ 4 თვიანი, რიფაპენტიინზე დაფუძნებული, მოქსიფლოქსაცილის შემცველი სამკურნალო რეჟიმის ეფექტურობა არანაკლებია სტანდარტული 6 თვიანი რეჟიმის ეფექტურობასთან შედარებით, მკურნალობისადმი ამტანობა კი იგივეა. ასევე შეფასდა 4 თვიანი, რიფაპენტიინზე დაფუძნებული, იზონიაზიდის, ეტამბუტოლის და პირაზინამიდის შემცველი სამკურნალო რეჟიმი, მაგრამ ამ რეჟიმმა სტანდარტულ 6 თვიან რეჟიმთან შედარებით არანაკლები ეფექტურობა ვერ აჩვენა, ამიტომ ჯანმო-ს განხილვის საგანი მხოლოდ 4 თვიანი, რიფაპენტიინზე დაფუძნებული, მოქსიფლოქსაცილის შემცველი სამკურნალო 2HPZM/2HPM რეჟიმი გახდა.

განხილვის შედეგად ჯანმო-ს ჯგუფი მივიდა დასკვნამდე, რომ დღეს არსებულ მტკიცებულებებზე დაყრდნობით ფილტვის სენსიტიური ტუბერკულოზის სამკურნალოდ 4 თვიანი, რიფაპენტიინზე დაფუძნებული, მოქსიფლოქსაცილის შემცველი სამკურნალო 2HPZM/2HPM რეჟიმი შესაძლებელია 6 თვიანი 2HRZE/4HR რეჟიმის ალტერნატივად იყოს გამოყენებული. თუმცა 2HPZM/2HPM რეჟიმის იმპლემენტაციისათვის საჭიროა რიფაპენტიინის ხელმისაწვდომობის გაზრდა და მკაცრი ანტიბაქტერიული მართვა, იმის გათვალისწინებით რომ სამკურნალო რეჟიმში რეზისტენტული ტუბერკულოზის სამკურნალო მოქსიფლოქსაცილია ჩართული.

4 თვიანი, რიფაპენტიინზე დაფუძნებული, მოქსიფლოქსაცილის შემცველი სამკურნალო 2HPZM/2HPM რეჟიმი  $>12$  წლის ასაკობრივ ჯგუფში,  $>40$  კგ წონის ფილტვის სენსიტიური ტუბერკულოზით დაავადებულ დაავადებულ პაციენტებთან შეიძლება დაინიშნოს.

2HPZM/2HPM რეჟიმის დანიშვნის წინ აუცილებლად უნდა განისაზღვროს რიფამპიცილის, იზონიაზიდის და ფთორქინოლონებისადმი მგრძობელობა. ხოლო ეკვ, ღვიძლის ფუნქციური ტესტები და სხვა შესაძლო ლაბორატორიული კვლევები კლინიკური საჭიროების მიხედვით უნდა ჩატარდეს.

სენსიტიური ტუბერკულოზის მკურნალობა ნებისმიერი (2HRZE/4HR, 2HRZE/2HR, ან 2HPZM/2HPM) რეჟიმით მედიკამენტების ყოველდღიური მიღებით ტარდება და მეტად რეკომენდებულია ფიქსირებულდოზიანი კომბინაციების დანიშვნა, ვიდრე ცალ-ცალკე აბების.

თუ სენსიტიური ტუბერკულოზით დაავადებული პაციენტი ინტენსიური ფაზის ბოლოს ნახველის ნაცხით დადებითი რჩება, ინტენსიური ფაზის გახანგრძლივება რეკომენდებული არ არის. ასეთ შემთხვევაში სჭიროა მედიკამენტებისადმი მგრძობელობის განმეორებით ტესტირება და სამკურნალო რეჟიმის კორექტირება.

### **ფილტვგარეთა სენსიტიური ტუბერკულოზის მკურნალობა**

მკურნალობის რეჟიმი ფილტვისა და ფილტვგარეთა სენსიტიური ტუბერკულოზის უმეტესი ფორმებისთვის მედიკამენტების კომბინაციის და მკურნალობის ხანგრძლივობის მიხედვით იდენტურია. სენსიტიური ტუბერკულოზის ფილტვგარეთა ფორმების სამკურნალოდ უპირატესად 6 თვიანი 2HRZE/4HR რეჟიმია რეკომენდებული, თუმცა მკურნალობის ჯამური ხანგრძლივობა **ტუბერკულოზური მენინგიტის** სენსიტიური ფორმების უმეტესობისთვის 12 თვეა და მნიშვნელოვანია, რომ მკურნალობაზე პასუხი



აუცილებლად გათვალისწინებული უნდა იყოს. ძვალ-სახსრის ტუბერკულოზის სამკურნალოდ უპირატესობა 9 თვიან რეჟიმს ენიჭება, თუმცა იმის გათვალისწინებით, რომ მკურნალობაზე პასუხის შეფასება და განკურნების განსაზღვრა რთულია, მკურნალობა შეიძლება დადებითი რადიოლოგიური და კლინიკური დინამიკის მიღწევამდე გახანგრძლივდეს. მუცლის ღრუს ლიმფური კვანძების, ინტერსტინალური, შარდ-სასქესო სისტემის ტუბერკულოზის, ან გართულებული ტუბერკულოზური ლიმფადენიტის დროს რეკომენდებულია 6-9 თვიანი რეჟიმით მკურნალობა (პროცესის გავრცობის გათვალისწინებით).

ტუბერკულოზური მენინგიტისა და პერიკარდიტის სამკურნალოდ რეკომენდებულია კორტიკოსტეროიდების დამხმარე კურსი. ტუბერკულოზური მენინგიტით დაავადებულ პაციენტებთან მკურნალობის საწყის ეტაპზე, 6-8 კვირის განმავლობაში დექსამეტაზონი, ან პრედნიზოლონი უნდა დაინიშნოს. ტუბსაწინააღმდეგო მკურნალობის საწყის ეტაპზე კორტიკოსტეროიდული მკურნალობა ასევე შეიძლება დაინიშნოს ტუბერკულოზური პერიკარდიტით დაავადებულ პაციენტებთან.

**ცხრილი სენსიტიური ტუბერკულოზის სამკურნალო მედიკამენტების დოზები წონის მიხედვით**

მედიკამენტი	დოზა წონის მიხედვით	ფორმულაცია (მგ)	ფორმულაციის ტიპი	25-<30 კგ	30-<35 კგ	35-<50 კგ	50-<65 კგ	65 + კგ
				აბი	აბი	აბი	აბი	აბი
<b>FDC (HR)</b>		75/150	FDC	2	3	4	4	5
<b>FDC (HRE)</b>		75/150/ 275	FDC	2	3	4	4	5
<b>FDC (HRZE)</b>		75/150/ 400/275	FDC	2	3	4	4	5
<b>იზონიაზიდი (H)</b>	4-6 მგ/კგ	300	ფხვიერი	0.5	1	1	1	1.25
<b>რიფამპიცინი (R)</b>	8-12 მგ/კგ	300	ფხვიერი	1	1.5	2	2	2.5
<b>ეტამბუტოლი (E)</b>	15-25 მგ/კგ	400	ფხვიერი	1.5	2	3	3	4
<b>პირაზინამიდი (Z)</b>	20-30 მგ/კგ	400	ფხვიერი	2	3	4	4	5
<b>პირაზინამიდი (Z)</b>	20-30 მგ/კგ	500	ფხვიერი	1.5	2.5	3	3	4
<b>რიფაპენტინი (P)</b>	ფიქსირებული	150	ფხვიერი	-	-	8	8	8
<b>რიფაპენტინი (P)</b>	ფიქსირებული	300	ფხვიერი	-	-	4	4	4
<b>მოქსიფლოქსაცინი (M)</b>	ფიქსირებული	400	ფხვიერი	-	-	1	1	1

**სენსიტიური ტუბერკულოზის მკურნალობის მონიტორინგი**

ჩატარებული მკურნალობის ეფექტურობისა და სასურველი შედეგის მისაღებად მნიშვნელოვანის მონიტორინგის წარმოება:

- სიმპტომების შეფასება: ტუბერკულოზის სიმპტომების, ტუბსაწინააღმდეგო მედიკამენტებით გამოწვეული არასასურველი მოვლენების სიმპტომების და სხვა სიმპტომების შეფასება;
- მკურნალობისადმი დამყოლობის შეფასება: დოზების მიღების შეფასება და დოზების გამოტოვების შემთხვევაში მშობელთან ან მომვლელთან მიზეზების განხილვა და მხარდაჭერა დამყოლობის გასაუმჯობესებლად;
- პაციენტის წონის განსაზღვრა: წონა უნდა გაკონტროლდეს და წონის მატების შემთხვევაში დოზები შესაბამისად უნდა დაკორექტირდეს;

- ნახველის მიკროსკოპია;
- კულტურალური კვლევა;
- გულმკერდის რენტგენოგრაფია;
- საჭიროების შემთხვევაში სხვა ლაბორატორიული კვლევები, მაგ. ღვიძლის ფუნქციური სინჯები.

მონიტორინგი შემდეგი სიხშირით უნდა განხორციელდეს:

- სიმპტომები და წონაში მატება მკურნალობის დაწყებიდან 2 და 4 კვირის თავზე, ინტენსიური ფაზის ბოლოს (მკურნალობის მეორე თვის ბოლოს) და შემდეგ მკურნალობის ყოველი მომდევნო 2 თვის ბოლოს - 4 თვიანი მკურნალობის შემთხვევაში მკურნალობის დასრულებისას მეოთხე თვის ბოლოს; 6 თვიანი მკურნალობის შემთხვევაში მეოთხე თვის ბოლოს და მკურნალობის დასრულებისას მეექვსე თვის ბოლოს უნდა შეფასდეს;
- მკურნალობისადმი დამყოლობა მკურნალობის დაწყებიდან 2 და 4 კვირის თავზე და მთელი მკურნალობის მანძილზე ყოველი შემდეგი თვის ბოლოს უნდა შეფასდეს;
- ფილტვის სენსიტიური ტუბერკულოზით დაავადებული პაციენტების მონიტორინგისათვის ბაქტერიოსკოპია 4 თვიანი მკურნალობის შემთხვევაში ყოველთვიურად უნდა ჩატარდეს; 6 თვიანი მკურნალობის შემთხვევაში კი პირველ, მეორე, მეხუთე და მეექვსე თვეზე უნდა ჩატარდეს;
- ფილტვის სენსიტიური ტუბერკულოზით დაავადებული პაციენტების მონიტორინგისათვის კულტურალური კვლევა 4 თვიანი მკურნალობის შემთხვევაში **მეორე, მესამე და მეოთხე** თვეზე უნდა ჩატარდეს; 6 თვიანი მკურნალობის შემთხვევაში კი მეორე, მეხუთე და მეექვსე თვეზე უნდა ჩატარდეს;
- როგორც 4, ისე 6 თვიანი რეჟიმის შემთხვევაში თუ მკურნალობის ორი თვის შემდეგ ბაქტერიოსკოპია და/ან კულტურა დადებითია, ბაქტერიოლოგიური მონიტორინგის ყველა ეტაპზე FL-LPA უნდა ჩატარდეს. შემდგომი ტესტირება RR(+) ან RR(-) შედეგის მიხედვით, ლაბორატორიული დიაგნოსტიკის ალგორითმის შესაბამისად უნდა ჩატარდეს. მკურნალობა მიღებული მგრძობელობის მიხედვით უნდა გაგრძელდეს;
- გულმკერდის რენტგენოგრაფია მკურნალობის ინტენსიური ფაზის ბოლოს და მკურნალობის დასრულებისას უნდა ჩატარდეს;
- სხვა ლაბორატორიული კვლევები, მაგ. ღვიძლის ფუნქციური სინჯები საჭიროების შემთხვევაში ტარდება;

**ცხრილი სენსიტიური ტუბერკულოზის მკურნალობის მონიტორინგი**

შეფასება	საწყისი	2 კვირა	1 თვე	2 თვე	3 თვე	4 თვე	5 თვე	6 თვე	მკურნალობის შემდგომი მიდევნება**
<b>4 თვიანი მკურნალობა</b>									
სიმპტომები	X	X	X	X		X			X
დამყოლობა		X	X	X	X	X			
წონა	X	X	X	X		X			X
მიკროსკოპია	X		X	X*	X*	X*			
კულტურა	X			X*	X*	X*			
X-ray	X					X			X
<b>სხვა ლაბორატორიული კვლევები, მაგ. ღვიძლის ფუნქციური სინჯები***</b>									

<b>6 თვიანი მკურნალობა</b>									
სიმპტომები	X	X	X	X		X		X	X
დამყოლობა		X	X	X	X	X	X	X	
წონა	X	X	X	X		X		X	X
მიკროსკოპია	X		X	X*			X*	X*	
კულტურა	X			X*			X*	X*	
X-ray	X							X	X
<b>სხვა ლაბორატორიული კვლევები, მაგ. ღვიძლის ფუნქციური სინჯები***</b>									
<p>* თუ ბაქტერიოსკოპია და/ან კულტურა დადებითია, FL-LPA უნდა ჩატარდეს. შემდგომი ტესტირება RR(+) ან RR(-) შედეგის მიხედვით, ლაბორატორიული დიაგნოსტიკის ალგორითმის შესაბამისად უნდა გაგრძელდეს (იხ. სქემა 8.1);</p> <p>**სენსიტიური ტუბერკულოზის მკურნალობის შემდგომი მიდევნება მკურნალობის დასრულებიდან შემდეგი 2 წლის განმავლობაში, ყოველ 6 თვეში ერთხელ უნდა განხორციელდეს.</p> <p>***სხვა ლაბორატორიული კვლევები, მაგ. ღვიძლის ფუნქციური სინჯები საჭიროების შემთხვევაში ტარდება</p>									

**სენსიტიური ტუბერკულოზის მკურნალობის მონიტორინგის რეკომენდაციები**

R1.	ფილტვის სენსიტიური ტუბერკულოზით დაავადებული პაციენტების მონიტორინგისათვის ბაქტერიოსკოპია 4 თვიანი მკურნალობის შემთხვევაში ყოველთვიურად; 6 თვიანი მკურნალობის შემთხვევაში პირველ, მეორე, მეხუთე და მეექვსე თვეზე უნდა ჩატარდეს.
R2.	ფილტვის სენსიტიური ტუბერკულოზით დაავადებული პაციენტების მონიტორინგისათვის კულტურალური კვლევა 4 თვიანი მკურნალობის შემთხვევაში მეორე, მესამე და მეოთხე თვეზე; 6 თვიანი მკურნალობის შემთხვევაში მეორე, მეხუთე და მეექვსე თვეზე უნდა ჩატარდეს.
R3.	ნებისმიერი რეჟიმის შემთხვევაში თუ მკურნალობის ორი თვის შემდეგ ბაქტერიოსკოპია და/ან კულტურა დადებითია, ბაქტერიოლოგიური მონიტორინგის ყველა ეტაპზე FL-LPA უნდა ჩატარდეს. შემდგომი ტესტირება RR(+) ან RR(-) შედეგის მიხედვით, ლაბორატორიული დიაგნოსტიკის ალგორითმის შესაბამისად უნდა ჩატარდეს. მკურნალობა მიღებული მგრძნობელობის მიხედვით უნდა გაგრძელდეს.
R4.	სენსიტიური ტუბერკულოზით დაავადებულ პაციენტებთან მონიტორინგისათვის რენტგენოლოგიური კვლევა ინტენსიური ფაზის ბოლოს და მკურნალობის დასრულებისას უნდა ჩატარდეს.

**სენსიტიური ტუბერკულოზის სამკურნალო მედიკამენტებით გამოწვეული არასასურველი მოვლენების მართვა**

სენსიტიური ტუბერკულოზით დაავადებულ პაციენტთა უმეტესობა მკურნალობას მედიკამენტებზე მნიშვნელოვანი არასასურველი მოვლენების გარეშე ასრულებს, თუმცა მცირე ნაწილს შესაძლოა მაინც აღენიშნებოდეს არასასურველი მოვლენები. სენსიტიური ტუბერკულოზის მკურნალობის მონიტორინგის ერთ-ერთი მიზანი რეზისტენტობის გამოვლენასთან ერთად არასასურველი მოვლენების დროული გამოვლენა და მათი განვითარების პრევენციაა.

სამედიცინო პერსონალმა მედიკამენტებზე არასასურველი მოვლენების მონიტორინგი უნდა განახორციელოს პაციენტის განსწავლით, აუხსნას მას, როგორ ამოიცნოს არასასურველი მოვლენებისთვის დამახასიათებელი სიმპტომები, სთხოვოს პაციენტს,

შეატყობინოს მათ მსგავსი სიმპტომების შესახებ, ან მონიტორინგის მიზნით ჩატარებული ვიზიტის დროს სამედიცინო პერსონალმა პაციენტი მედიკამენტებზე არასასურველი მოვლენების სიმპტომების თაობაზე გამოკითხოს. მედიკამენტებზე არასასურველი მოვლენების შესახებ ინფორმაცია შეტანილ უნდა იქნეს პაციენტის სამედიცინო ბარათში. პაციენტმა, რომელსაც არასასურველი მოვლენები ზომიერად ან მსუბუქად აქვს გამოხატული, უნდა განაგრძოს მკურნალობის კურსი და პარალელურად ჩაიტაროს სიმპტომური მკურნალობა. თუ პაციენტს აღენიშნება მძიმე არასასურველი მოვლენები, მედიკამენტი, რომელიც ამგვარ შედეგს განაპირობებს, უნდა შეჩერდეს და პაციენტი დაუყოვნებლივ უნდა გაიგზავნოს სამედიცინო დაწესებულებაში, სადაც მოხდება მისი მდგომარეობის შემდგომი შეფასება და მკურნალობა. მძიმე არასასურველი მოვლენების მქონე პაციენტების მართვა უნდა განხორციელდეს სტაციონარში.

მაგალითისათვის, თუ პაციენტს განუვითარდა ქავილი გამონაყარის გარეშე და არ არსებობს მისი გამომწვევი სხვა ამკარა მიზეზი, რეკომენდებულია სიმპტომური მკურნალობის ჩატარება ანტიჰისტამინური ჯგუფის მედიკამენტებით, კანის დამატენიანებლებით და ტუბერკულოზის მკურნალობის კურსის გაგრძელება მეთვალყურეობით. გამონაყარის გამოვლენის შემთხვევაში უნდა შეწყდეს ყველა ტუბსაწინააღმდეგო მედიკამენტის გამოყენება. მდგომარეობის გაუმჯობესების შემდეგ პაციენტმა სათითაოდ უნდა განაახლოს ტუბსაწინააღმდეგო მედიკამენტების მიღება. თავდაპირველად მას უნდა მიეცეს ისეთი მედიკამენტი, რომელიც, სავარაუდოდ, ყველაზე ნაკლებად განაპირობებს არასასურველი მოვლენის წარმოშობას (რიფამპიცინი ან იზონიაზიდი). გამოყენებულ უნდა იქნეს მცირე დოზები, მაგალითად, 50 მგ იზონიაზიდი. დოზა ეტაპობრივად უნდა გაიზარდოს 3 დღის განმავლობაში. შემდგომ, იმავე წესით, ვამატებთ კიდევ ერთ მედიკამენტს. თუ რომელიმე მედიკამენტის დამატებისას ზემოთ აღწერილი მოვლენები განვითარდა, ეს ნიშნავს, რომ სწორედ ეს მედიკამენტი იწვევს არასასურველ მოვლენებს.

ცნობილია, რომ იზონიაზიდით გამოწვეული ერთ-ერთი ხშირი არასასურველი მოვლენაა პერიფერიული ნეიროპათია, რომლის განვითარების პრევენციისთვის იზონიაზიდს შემცველ რეჟიმზე მყოფ ყველა პაციენტს ტუბსაწინააღმდეგო მკურნალობასთან ერთად უნდა ჩაუტარდეთ პრევენციული მკურნალობა B6 ვიტამინით (პირიდოქსინით) - 10-25 მგ დღეში.

გვერდითი მოვლენების მართვა და მკურნალობის მონიტორინგი იქნება ხელისშემწყობი ფაქტორი მკურნალობის პერიოდში განვითარებული რეზისტენტობის და ტუბსაწინააღმდეგო მედიკამენტებით გამოწვეული არასასურველი მოვლენების დროული გამოვლენისა; ხოლო 4 თვიანი 2HPMZ/2HPM და 4 თვიანი 2HRZE/2HR რეჟიმი - ახალი ერა ტუბერკულოზის მკურნალობაში.

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**MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) ASSOCIATED WITH COVID-19: A CASE SERIES EXPERIENCE IN M.IASHVILI CHILDREN'S CENTRAL HOSPITAL, GEORGIA**

*Ana maghradze<sup>1</sup>, Ivane Ckhaidze<sup>2</sup>, Nani kavlashvili<sup>3</sup>*

*<sup>1,2,3</sup> Tbilisi State Medical University, International Faculty of Medicine and Stomatology, Pediatric Department, Tbilisi, Georgia*

*ORCID ID: 0000-0002-4952-3510*

**ABSTRACT**

During pandemic COVID-19 in majority of children presented less severe phenotype, multisystem inflammatory syndrome in children (MIS-C) associated with SARS-CoV-2 subsequently evolved as a post-infectious inflammatory condition associated with severe clinical deterioration and multi organ involvement.

Aim of the study was to assess the clinical and lab characteristics and outcomes of MIS-C in Georgia. The study comprised 89 children with MIS-C admitted to Iashvili children's central hospital from December 2020 to October 2022. Data were obtained from medical record retrospectively.

58 (54.2%) of patients were male. Median age of patients was 8.5 (1-17) years. The most common presenting symptoms were - fever (100%), gastrointestinal (GI) (8%), rash (48.1%) and vomiting (46%) were. Average fever duration was 9 (4 -12) days. Shock and/or hypotension were common in patients with MIS-C (24%). In total, 38.7% of the patients admitted to pediatric intensive care unit and 19.3% received vasopressor support. 20% of patient had depressed left ventricular ejection fraction. Cardiac symptoms (69%) predominated over respiratory (40%) and neurological (32%) symptoms. Admission lab findings - elevated CRP -99.8%, procalcitonine-97.1%, erythrocyte sedimentation rate-98%, D-dimer-98.8% and ferritin-78%; Lymphopenia-98.9%, neutrophilia - 96% and hypoalbuminemia 40.3%. 38% received IV Intravenous immunoglobulin, 98.2% - corticosteroids; Anakinra was not used in our clinic. Median duration of hospital length of stay was 14.5 days. Comorbidities were present in 1.1% of the patients. No mortality was recorded.

While being rare MIS-C has very severe presentation that need early recognition and aggressive treatment. The increasing number of MIS-C cases shows that this phenomenon is more common than was thought at the beginning of pandemic. Here is not enough evidence about the long-term consequences yet and we conduct monitoring and evaluation of patients in dynamics.

**Keywords:** COVID-19; SARS-CoV2; children; multisystem inflammatory syndrome in children (MIS-C).

**STUDY OF GUT MICROBIOTA IN HEMODIALYSIS PATIENTS**

*A. Shamanadze; T. Kandashvili;*

*Tbilisi State Medical University, Tbilisi, Georgia.*

**ABSTRACT**

Chronic Kidney Disease (CKD) is the global problem. Evidence showed that chronic inflammation is a risk factor for increased cardiovascular mortality in the population with Kidney Failure (KF) remaining on Kidney Replacement Therapy (KRT). The gastrointestinal tract is one of the important sources of inflammation in HD patients. Notable disruptions to the intestinal barrier take place in HD patients because of the uremic environment and the process of HD itself. Uremic gut microbiome may have serious effects on patients' quality of life (QoL) and, especially, on their psychological, social, and economic prosperity.

**Aim:** to consider changes of QoL in HD patients by the correction of intestinal microflora.

**Methodology :** study includes 272 (112 female, 160 male; age -18-75) hemodialysis patients with the special questionnaire that we have developed for this study to reveal gastro-intestinal complaints; and by quality of life questionnaire – “Missoula VITAS Quality of life index MVQOLI”. Patients received hemodialysis therapy for 4h, three times weekly using cellulose triacetate dialyzers. The Kt/V was  $1.5\pm 0.3$ , reflecting adequacy of the dialysis regimen. Fecal samples were analyzed before and after treatment with probiotics using microbiological methods of plating, enumeration, and counting colonies on specific growth media.

**results:** It was revealed significant alteration of the colonic bacterial flora in hemodialysis patients, with the excess of the uremic toxin producing bacteria. There was correlation between gut dysbiosis and HD patient's quality of life.

**Conclusions:** Our study reveals relationships between QoL and gut dysbiosis in HD patients. Correction of intestinal flora with probiotics-containing *L. acidophilus*, *B. longum*, and *S. Thermophilus*, improves the quality of HD patients' lives.

**Keywords:** Chronic Kidney Disease, hemodialysis, quality of life, gut microbiota, probiotics.



**ISOLATION OF INDUCIBLE CLINDAMYCIN AND METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* STRAIN IN PATIENT WITH COMMUNITY-ACQUIRED PNEUMONIA: CASE REPORT**

***Giorgi Mgeladze***

*Medical Company Test-IMP”, Tbilisi, Georgia;*

*Richard Lugar Center for Public Health Research, Tbilisi, Georgia.*

***Shorena Khetsuriani***

*Microbiology Department, Tbilisi State Medical University, Tbilisi, Georgia.*

**ABSTRACT**

The occurrence and distribution of multidrug-resistant *S. aureus*, especially methicillin-resistant *Staphylococcus aureus* (MRSA), has become a global problem and one of the major causes of infections. MRSA antimicrobial resistance has become an important threat to global health. *S. aureus* has an uncommon ability to acquire new antimicrobial resistance genes. Many factors cause *S. aureus* to become resistant to antibiotics, but one of the factors is the inappropriate and frequent use of antibiotics. Clindamycin is a broadly used antibiotic for the treatment of various staphylococcal infections, but induced resistance to clindamycin (ICR) is becoming increasingly common. Clindamycin has a predominantly bacteriostatic effect. It inhibits ribosomal translocation in a similar way to the macrolides. It does this by reversibly binding to the rRNA of the bacterial 50S subunit of the ribosome, overriding the macrolide binding sites.

The current study demonstrates a case of community-acquired pneumonia caused by MRSA ICR in a 59-year-old previously healthy patient. Routine clinical and laboratory methods included physical examination, chest radiograph, sputum, and blood culture tests. The isolated strain had typical morphological, tinctorial, and biochemical features.

Our case shows an example of an isolated MRSA ICR in a patient with community-acquired pneumonia. The isolation of MRSA ICR highlights the importance of improving public health practices and establishing new strategies to control MRSA infections. Although community-acquired pneumonia caused by MRSA ICR is infrequent, the number of new cases has recently increased. As *S. aureus* is part of the human microbiome, taking antibiotics is pointless and often leads to the establishment of resistance. Taking antibiotics without a doctor's recommendation is completely inappropriate and raises the risk of developing resistant microorganisms.

**Keywords:** *Staphylococcus aureus*, inducible clindamycin resistance, MRSA, community-acquired pneumonia

**INVESTIGATIONS OF VIBRATIONAL PROPERTIES OF PATHOGENIC ORGANISMS BY COMPUTING METHODS**

*Paata J. Kervalishvili, Nino Gordeladze*

*Grigol Robakidze University Medical School, Tbilisi, Georgia*

**ABSTRACT**

Diseases caused by pathogenic infections are one of the biggest problems of modern biomedicine and as methods involved in diagnostics are getting faster and more efficient, methods of their therapy are still need to be stronger. This retrospective study aimed to explore nano bio spectroscopy research and technology in the field of virology in order to provide a theoretical and computer modeling support for the techniques used, and to suggest the applying tools that have not been used previously. The interdisciplinary collaboration for development of nanobiomedicine is an engine of strengthen the abilities of researchers in development of new biophysical and biomedical methods and tools. These works which are based on novel achievements in optical spectrometry, laser and molecular physics as well as information technologies and systems are critically important for study of common properties of nano-scale virus-like particles, and elaboration of basic concepts and new method for estimation unique vibration/oscillation properties, determine the unique “fingerprints” of pathogenic micro-organisms, especially viruses.

**Keywords:** pathogenic organisms, vibrational spectroscopy, computer modeling, radiation resonance therapy

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**IMPACT OF DIABETES ON CHRONIC RENAL FAILURE**

*Lika Bedinasvhili*

*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

*Student Scientific-Research Organization "ENDEAVOR" of TSMU, Tbilisi, Georgia*

**ABSTRACT**

Diabetes prevalence worldwide has increased dramatically in the last few decades due to an increase in obesity. Diabetes is one of the major complications of type 1 and type 2 diabetes and Diabetic nephropathy is the leading cause of end-stage kidney disease worldwide but current treatments remain suboptimal. This review examines the evidence for inflammation in the development and progression of diabetic nephropathy. Several pathways have been identified in diabetic nephropathy that indicate abnormal intracellular metabolism: (I) the activation of polyol and PKC (protein kinase C) pathways, (II) the formation of advanced glycation end-products, and (III) intraglomerular hypertension caused by glomerular hyperfiltration. Upstream of these three major pathways, hyperglycaemia is the major driving force of the progression to ESRD from diabetic nephropathy. Microinflammation and subsequent extracellular matrix expansion are also common progression pathways in diabetic nephropathy. In oxidative stress have been shown to contribute to the development and progression of diabetic nephropathy, the mechanisms by which this occurs are still being investigated. However, there is increasing evidence supporting a role for inflammation in type 1 and type 2 diabetes. Cytokines, profibrotic growth factors, and inflammation include transforming growth factor, monocyte chemoattractant protein-1 (MCP-1), connective tissue growth factor, tumor necrosis factor, interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-18 (IL-18), and cell adhesion molecules. Diabetes-related nephropathy has been associated with increased vascular inflammation and fibrosis, among others. The stimulus for the increase in inflammation in diabetes is still under investigation; however, reactive oxygen species are a primary candidate. Thus, targeting oxidative stress-inflammatory cytokine signaling could improve therapeutic options for diabetic nephropathy. Specifically, the current review will focus on understanding the relationship between oxidative stress and inflammatory cytokines in diabetic nephropathy to help determine which comes first in diabetic nephropathy progression: inflammation or oxidative stress.

**COVID 19 AND PARKINSON'S DISEASE: OLFACTORY SYSTEM IMPAIRMENTS**

*Nino Akhuashvili, Elene kurdgelashvili*

*Tbilisi State Medical University, Tbilisi, Georgia*

**ABSTRACT**

Anosmia, also known as smell blindness, is a neuropathogenic disorder characterized by loss of smell. Anosmia is a significant pathogenic feature of the present Covid-19 pandemic caused by SARS-CoV-2 and a common early non-motor hallmark in Parkinson's disease. It is predicted that SARS-CoV-2 infection will be a risk factor for acquiring Parkinson related symptoms since SARS-CoV-2 seems to affect the dopamine system and cause the loss of dopaminergic neurons. Lewy bodies (abnormal deposits of a protein alpha-synuclein) in the substantia nigra are a hallmark of Parkinson's disease. Although the exact mechanism is unknown, one widely held theory in Parkinson's disease is that the Lewy pathology begins in the olfactory bulb and dorsal motor nucleus of the vagus and then reaches the substantia nigra. Loss of dopaminergic neurons lead to motor symptoms in PD. ACE2(Angiotensin-converting enzyme 2) is considered to be the main target receptor of covid-19, that is believed to be one of the mechanisms of olfactory impairment. This receptor has been found in various organs, including the olfactory cleft region where ACE2 receptors are presented in high intensity. Recent data shows that ACE2 and dopa decarboxylase are the key enzymes for the synthesis of dopamine in non-neuronal cells. SARS-CoV infection inhibits the expression of ACE2, which may contribute to the impairment of dopamine biosynthesis. Moreover, SARS-CoV-2 infection seems to cause accumulation of alpha-synuclein deposits.

Anosmia is a common symptom of both Covid-19 and Parkinson's disease. As far as the olfactory bulb is involved in the pathogenesis of both diseases, Covid-19 may increase the risk of PD through different mechanisms.

**Key words:** Covid 19, Parkinson's disease, Anosmia, Dopamine system.

**MATURATION AND CIRCUIT INTEGRATION OF TRANSPLANTED HUMAN CORTICAL ORGANOIDS INFLUENCING ANIMALS' BEHAVIOR**

*<sup>1,2</sup>Mariam Mikuchadze*

*<sup>1</sup>Faculty of Medicine, Tbilisi State Medical University, Tbilisi, Georgia*

*<sup>2</sup>Student Scientific-Research Organization "ENDEAVOR" of TSMU, Tbilisi, Georgia*

Brain organoids — lab-grown, self-organizing structures made of stem cells — are used in research to better understand brain development and disease progress. However, these structures lack connections seen in real brains, limiting their usefulness and making integration with other circuits that control behaviour impossible. To overcome this, human organoids has now been transplanted into the somatosensory cortex of newborn athymic rats, they develop mature cell types that integrate into sensory and motivation-related circuits. MRI reveals post-transplantation organoid development across multiple stem cell line, whilst single-nucleus profiling shows progression of corticogenesis and the unfolding of activity-dependent transcriptional programs. In fact, transplanted cortical neurons display more complex morphological, synaptic and intrinsic membrane features than their in vitro analogue, which enables the discovery of defects in neurons derived from individuals with Timothy syndrome. Anatomical and functional findings show that transplanted organoids receive thalamocortical and corticocortical signals, and in vivo recordings of neural activity demonstrate that these signals can produce sensory responses in human cells. Finally, cortical organoids extend axons throughout the rat brain and their optogenetic activation can stimulate reward-seeking behaviour. Research is showing that these implanted organoids respond to stimuli and could influence the animals' behaviour, by engaging to hosts circuits that control behaviour. It is awaited that this perspective will be useful for detecting circuit-level phenotypes in patient-derived cells that cannot otherwise be revealed.

**Key Words:** Cortical Organoids, Brain Development and Disease Progression, Detecting Circuit-Level Phenotypes, Behaviour, Transplantation

**APPROACHES AND CHALLENGES IN THE MANAGEMENT OF ADDISON'S DISEASE**

*Keso Khachidze*

*Tbilisi state medical university, faculty of medicine, Tbilisi, Georgia*

**ABSTRACT**

Primary adrenal insufficiency (PAI), or Addison's disease, is a rare, potentially deadly, but treatable disease. is defined as the clinical manifestation of chronic glucocorticoid- and/or mineralocorticoid deficiency due to failure of the adrenal cortex which may result in an adrenal crisis with potentially life-threatening consequences. Based on statistical data, patients with PAI are at higher risk of developing other autoimmune diseases. Addison's disease is a possible diagnosis in any patient who presents with weakness, weight loss, hyperpigmentation, hyponatremia, and hypotension. Laboratory findings, including depressed levels of cortisol and aldosterone, help to confirm the diagnosis. The diagnosis of PAI is often delayed by many months, and most patients present with symptoms of acute adrenal insufficiency. Because PAI is rare, even medical specialists in this therapeutic area rarely manage more than a few patients. Currently, the procedures for diagnosis, treatment and follow-up of this rare disease vary greatly within Europe. The common autoimmune form of PAI is characterized by the presence of 21-hydroxylase autoantibodies; other causes should be sought if no autoantibodies are detected. The clinical picture is caused by deficiency of cortisol and aldosterone. These deficiencies are accompanied by adrenal androgen depletion of yet unknown significance. The current therapy is the replacement of glucocorticoids and mineralocorticoids, but the available drugs do not restore the normal diurnal variations in serum hormone levels. The clinical consequences of the grossly unphysiological replacement therapy are largely unknown. Many patients with Addison's disease on standard replacement therapy complain of fatigue, weariness, and reduced stress tolerance. One particular concern has been negative effects on both bone metabolism due to over-replacement of glucocorticoids and androgen depletion. Acute adrenal crisis is a life-threatening condition that requires immediate treatment. Annual follow-up by an endocrinologist is recommended with the focus on optimization of replacement therapy and detection of new autoimmune diseases.

**Key words:** 21-hydroxylase; Addison's disease; adrenal crisis; autoimmune polyendocrine syndrome; cortisol.

**SCHIZOPHRENIA AND MODERN APPROACHES TO ITS TREATMENT**

*Liana Jalagania<sup>1,2</sup>; Nino Kikvadze<sup>1,2</sup>; Gigi Gorgadze<sup>1,2</sup>*

*<sup>1</sup>Faculty of Medicine of Tbilisi State Medical University, Georgia;*

*<sup>2</sup>Student Scientific-Research Club "ENDEAVOR" of Scientific Research-Skills Center of TSMU, Georgia.*

**ABSTRACT**

Schizophrenia is a common, severe mental illness that most clinicians will encounter regularly during their practice. This report provides an overview of the clinical characteristics, epidemiology, genetics, neuroscience, and psychopharmacology of schizophrenia to provide a basis to understand the disorder and its treatment.

Schizophrenia, characterised by psychotic symptoms and in many cases social and occupational decline, remains an aetiological and therapeutic challenge. Contrary to popular belief, the disorder is modestly more common in men than in women. Nor is the outcome uniformly poor. A division of symptoms into positive, negative, and disorganisation syndromes is supported by factor analysis. Catatonic symptoms are not specific to schizophrenia and so-called first rank symptoms are no longer considered diagnostically important. Cognitive impairment is now recognised as a further clinical feature of the disorder.

Roughly half of schizophrenia patients recovered or significantly improved over the long term, suggesting that functional remission is possible. Several factors predict the course of schizophrenia, including demographic, clinical, and treatment characteristics, as well as socioeconomic variables. Antipsychotics are a fundamental element of schizophrenia treatment, although the available antipsychotics have significant limitations. In this context, psychosocial interventions are supported by substantial evidence of efficacy in many outcome measures and rehabilitation interventions should be considered as an evidence-based practice and need to become a part of the standard treatment of schizophrenia.

Schizophrenia has a complex presentation with a multifactorial cause. Nevertheless, advances in neuroscience have identified roles for key circuits, particularly involving frontal, temporal, and mesostriatal brain regions, in the development of positive, negative, and cognitive symptoms.

As recovery is a multidimensional concept, some authors suggested that at least two areas should be taken into account: clinical remission and social functioning. Functional outcome should be a priority target for therapeutic interventions in schizophrenia and in this perspective measuring treatment response, remission and functional recovery is essential. Only an integrated and multifaceted approach involving pharmacotherapy, psychosocial interventions, and attention to environmental circumstances can improve outcome in schizophrenia.

**Key words:** Schizophrenia, treatment, functions, perspective, symptoms

**TRANSPOSITION OF THE GREAT ARTERIES**

*Nini Mikadze, Nini kikvadze*

*Tbilisi State Medical University, Tbilisi, Georgia*

**ABSTRACT**

Transpositional of the great arteries (TGA), is a congenital cardiac malformation characterized by atrioventricular concordance and ventriculoarterial (VA) discordance. The incidence is estimated at 1 in 3 500- 5 000 live births. In 50% of cases, the ventriculoarterial discordance is an isolated finding and other 10% of cases is associated with noncardiac malformation. The onset and severity depend on functional and anatomical variants, that influence the degree of mixing between the two circulations. If no obstructive lesions are present, cyanosis may go undetected and only be perceived during episodes of crying or agitation. In these cases, signs of congestive heart failure prevail. The exact etiological factor is unknown, however, taking anti-epileptic drugs during pregnancy, the influence of herbicides and other chemical agents on the mother are factors that increase the risk. Mutations in growth differentiation factor-1 gene, the thyroid hormone receptor-associated protein-2 gene and the gene encoding the cryptic protein have been shown implicated in discordant VA connections, but they explain only a small minority of TGA cases. Timely detection of the disease is very important, so early diagnosis is made by echocardiogram, which also provides morphological details necessary for surgical intervention.

Over time, most patients develop systemic heart failure, even in the absence of associated lesions. Even in the case of an asymptomatic state, the pathology is fully detected visually and surgical intervention is planned if necessary. In cases with normal ventricular function and mild tricuspid failure, it seems unreasonable to intervene surgically. In patients with significant associated lesions, surgery is indicated. In the long term, the traditional approach may not help tricuspid regurgitation and systemic ventricular failure. Anatomical correction is the proposed alternative to ease the right ventricular overload and restore the systemic left ventricular function. However, this is a prolonged operation and not without risks and long-term complications.



**SACUBITRIL/VALSARTAN TO TREAT HEART FAILURE**

*Elmir Aivazov*

*Tbilisi State Medical University, Faculty of medicine, Tbilisi, Georgia.*

**ABSTRACT**

Sacubitril/valsartan (Entresto) is the first drug to be approved by FDA (Jul 7, 2015) in a new class of drugs called angiotensin receptor neprilysin inhibitor (ARNI). This agent can be used to treat the patients with chronic heart failure (NYHA Class II-IV) with reduced ejection fraction (HFrEF). Sacubitril is a neprilysin inhibitor, which turns into LBQ657 after administration. LBQ657 inhibits the neprilysin and thus increases BNP and NT-pro BNP levels. These agents increase natriuresis, vasodilation and anti-proliferation. Valsartan, on the other hand, blocks the angiotensin II receptors and thus decreases vasoconstriction effect of angiotensin II and aldosterone synthesis. All these mechanisms ensure a reduction in the load on the heart. Patients must be able to tolerate ACE inhibitors or ARB before being started on sacubitril/valsartan because sacubitril increases bradykinin level, like ACE inhibitors do and can potentially cause angioedema. Therefore combination of sacubitril/valsartan with ACE inhibitors is contraindicated. The results of the PARADIGM-HF clinical trial (head-to-head study) involving 8442 patients with chronic heart failure and systolic dysfunction shows that sacubitril plus valsartan combination is more effective compared to enalapril alone. Additionally, patients with chemotherapy-related acute cardiac dysfunction (CTRCD) with severely reduced ejection fraction were successfully treated with sacubitril/valsartan. Despite of the efficacy of these drug, more patients experienced angioedema in the sacubitril/valsartan arm than in the enalapril; however, this outcome was not statistically significant. Sacubitril/valsartan combination should be discontinued when pregnancy is detected because of the fetal harm. Also, The safety and efficacy of sacubitril plus valsartan have not been established in pediatric patients.

**Keywords:** Heart failure, sacubitril/valsartan, neprilysin

**FLUORESCENCE SPECTROPHOTOMETRY AND ITS USE IN MODERN MEDICINE**

*Nia Gogokhia*

*Tbilisi State Medical University, Medicine faculty, Biology department, Tbilisi, Georgia*

*Nino khvitia*

*Tbilisi State Medical University, Medicine faculty, Biology department, Tbilisi, Georgia*

**ABSTRACT**

Fluorescence spectrophotometry is a class of techniques that assay the state of biological system by studying its interactions with fluorescent probe molecules. Fluorescence and phosphorescence are photon emission processes that occur during molecular relaxation from electronic excited states. The use of fluorescence in biology and medicine is ubiquitous. Infectious diseases, caused by microorganisms are major killer around the world. These deaths have been increased since 2002. Malaria is an acute febrile parasitic disease with major lethality. One of the target protein in human serum is albumin. It undergoes proteolysis, suggesting that the parasite has the ability to take up human serum albumin which is important for intraerythrocytic growth and differentiation. In recent years, quantification of absolute protein numbers in cellular structures using fluorescence microscopy has become a reality. When the molecular species is fluorescent, its concentration can be determined directly from the intensity of fluorescence. The plasma of a malaria patient is flooded with the fluorescent decay products of RBC. These will be clinically viable new simple technique for differential noninvasive low-cost diagnosis of malaria. There are many limitations or inconveniences and drawbacks associated with other various diagnostic techniques. They are time consuming and require many reagents. At the moment, fluorescence spectroscopy seems to be a promising emerging diagnostic technique. This excellent research tool filled with high sensitivity and specificity. Introduction of fluorescence spectroscopy methods in our department give students possibility to introduce scientific-research methods of molecular biology into clinical practice. An important advantage of spectroscopy is the absence of the need for constant purchase of materials and reagents and maximum reduction of additive equipment. Over the past few years, it is observed that the fluorescence spectroscopy technique applications have been continuously growing. Initially used as an analytical tool in order to determine the presence of specific molecules in solutions, but now used in various applications like biochemistry and biophysics for studying molecular interactions. The global market is segmented into pharmaceutical industries, clinical laboratories, academic and research institutes and others.

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**BREASTFEEDING PRACTICE IN GEORGIA, NIGERIA, BRAZIL AND THE UK -META ANALYSIS**

*Aleksandre Machitadze<sup>1</sup>*

*<sup>1</sup>Tbilisi State Medical University, Public Health and Management, Georgia.*

*Sophio Malakmadze<sup>2</sup>*

*Tbilisi State Medical University, Public Health and Management, Georgia.*

*lali Begadze*

*Tbilisi State Medical University, Public Health and Management, Georgia..*

*supervisor: Ana Botchorishvili*

*invited lecturer, Tsmu, department: nutrition, aging medicine, environmental and occupational health;*

**ABSTRACT**

It is a well-known fact that breastfeeding has advantages for physical and nutritional health. It can be vital for both the mother and the child. Breast milk offers all the essential nutrients in the right amounts, all the energy and liquids a baby needs for growing and development in the first six months. It is easily absorbed and it has been internationally acclaimed that it affects children's IQ. The **purpose** of the study is to evaluate the health benefits (physical, mental) of breastfeeding based on 4 countries surveys including: Georgia, England, Brazil and Nigeria also the reasons of their statistical differences related to breastfeeding. For **methodology** we have used meta-analyses: identified 19 articles from PUBMED, Google Scholar and HINARY databases. **Conclusions:** The rate of breastfeeding is the lowest in the UK due to the cultural barriers, inadequate support, lack of information, or just the choices made not to breastfeed. Breastfeeding is far more prevalent in Brazil than it is in the United States, possibly as a result of the country's vigorous breastfeeding promotion. According to the Ministry of Health, more than 50% of Brazilian mothers exclusively breastfeed their infants up to the age of six months, compared to 16% of American mothers. Nigeria has one of the highest rate of children malnutrition in the world due to the lowest incidence of exclusive breastfeeding. Numerous factors, including : emotional, cultural, economical, and health considerations may have an impact on breastfeeding pattern. In Georgia, 2018, breastfeeding statistics have shown that 33% of newborns were breastfed for the first time during the first one hour within birth. Moreover, based on the statistics women who gave birth by caesarean section, are less likely to give newborns breast milk earlier than the women who gave birth naturally and 1 in 5 babies aged 0-5 months are only on breastfeeding. Discussing regarding the above implementation of measures which support breastfeeding is utterly needed.

**Keywords:** breastfeeding pattern, malnutrition, exclusive breastfeeding

**THE MAIN TRENDS IN THE ORGANIZATION OF LEUKEMIA TREATMENT MEASURES IN THE CHILDREN'S CONTINGENT**

*Ekaterine Mirvelashvili*

*Associate Professor, Department of Public Health, Management, Economics and politics.*

*Akaki Robakidze*

**ABSTRACT**

Leukemia is an oncological disease in which bone marrow cells mutate, normal mature leukocytes do not develop and they are transformed into cancer cells. It is the most common cancer among children, and more than a third of childhood cancers are caused by leukemia. The incidence and general epidemiological characteristics of childhood leukemias in Georgia at the level of the entire country practically do not differ from the similar characteristics of internationally developed countries. Depending on the course, leukemia is divided into two main forms: acute and chronic forms. Acute leukemia (acute leukemia) is divided into acute myeloblastic leukemia (acute myeloblastic leukemia, acute myeloleukosis, acute myeloblastosis) and acute lymphoblastic leukemia. These forms, in turn, have separate subtypes. Chronic myeloblastic leukemia became the first type of blood cancer, a targeted treatment complex was developed for its therapy, thanks to which in most cases it is possible to achieve remission and control of leukemia.

Leukemia can be caused by genetic factors, exposure to radiation and chemicals, and exposure to chemotherapy and radiation used to treat other cancers.

Leukemia symptoms are varied and usually appear in the acute form of leukemia. Chronic leukemia can last for years without symptoms and can be diagnosed only on the basis of a routine blood test. In acute leukemia, symptoms most often appear due to the failure of blood cells, the breakdown of leukemic cells or the disruption of the function of human organs caused by leukemic cells. Severe forms of leukemia develop very quickly, which forces the patient to consult a doctor. The disease is diagnosed by conducting laboratory studies as a result of determination of blood content. Often, chronic leukemia is detected by chance in a routine blood test, which allows determining the number of leukocytes in long-term dynamics. Leukemia is treated under the supervision of a hematologist. Standard treatment for leukemia involves treatment with various chemotherapy drugs, sometimes with antibodies that recognize cancer cells.

The fact that research has revealed the facts about the spatial temporal clustering of childhood leukemias in Georgia and the distinct temporal interval of specific clustering for Georgia (about 40-50% of the incidence is recorded in the range of 1-2 year old children) presents important prospects for identifying specific risk factors for Georgia and developing appropriate preventive measures. In connection with cancer treatment in Georgia, they talk about the following problems: the availability of funds, the equipment of clinics and the lack of qualifications and services of doctors. The main goal of the health care system of Georgia is the availability of the fundamental right to health to quality health care services, the aspects of which are many.

**Key Words:** Leukemia, Children Population, Healthcare, Problems, Treatment

**HOW ORAL CONTRAVEPTIVE USE CAN LEAD TO LIVER CANCER**

*Tsisana Uguvala*

*Scientific supervisor: David Tsxomelidze*

*Tbilisi state medical university.*

**ABSTRACT**

It is a fact that women who intake oral contraceptives have a higher risk of getting liver cancer, but the reason behind it is unclear. Females who have above hormone level is in danger of getting liver cancer too, for example, skirts from Asia have fewer cases of cancer than sisters from Europe (the first ones get diagnosed 3 times rarer). Some scientists consider estrogen as a problem, having the theory that estrogen could have a toxic effect on hepatocytes, but for me, progesterone is one to blame (In the study "Progesterone and related compounds in hepatocellular carcinoma: Basic and clinical aspects" researchers proved that higher level of hormone can cause breast hepatocellular carcinoma and other forms of cancer). Progesterone is a precursor of androgen, which is stimulated by, LH and decreased by FSH, ladies who took pills have a lower level of FSH, cause their ovaries don't need to get stimulated, and they don't produce anything. Which leads to more androgen being produced (at least it lever couldn't get controlled by our regulation systems). As we know, the liver excreting androgens from the body. It leads to the destruction and poisoning of its cells. Also, it's clear, the liver can not neutrilise and excrete a colossal amount of androgens. It became even more clear when dames with normal liver function still have hirsutism signs. For overcompensating for greater levels of androgens, the liver could also produce more of its cells (we all know more cells, greater chances for a mistake), which could be adaptive and get compensated. So you will never see until it progressed to ginormous cancer. hormonal pills aren't as adaptive and avant-garde to fit the body. In a standard of personalised medicine. That can also lead to patients who get a dose above recommended for them, it could easily affect the liver as the main filter of our body.

**Keywords:** liver cancer, cancer,oral contraceptives, progesterone, androgen.

**IMPORTANCE OF DEEP BRAIN STIMULATION IN TREATING GILLES DE LA TOURETTE SYNDROME AND CRITERIA USED IN SELECTION OF PATIENTS FOR THE PROCEDURE**

*Anzori Kvirikashvili*

*Tbilisi state medical university, Medicine, Georgia.*

**ABSTRACT**

Tourette syndrome (TS) is a complex neuropsychiatric disorder often starting in childhood and characterized by the presence of multiple motor and vocal tics and psychiatric comorbidities. Patients with TS usually respond to medical treatment, and the condition often improves during adolescence; however, procedure called deep brain stimulation has been considered a possible approach for the subset of patients with ongoing medically refractory disease. selection of patients with TS for deep brain stimulation (DBS) rests on 5 fundamental criteria. High tic severity and tic-related impact on quality of life (first 2 criteria) require confirmation from objective, validated measures. Failure of behavioral and pharmacologic therapies (third criteria) should be assessed taking into account refractoriness through objective and subjective measures supporting lack of efficacy of all interventions of proven efficacy, as well as true lack of tolerability, adherence, or access. Educational interventions and use of remote delivery formats (for behavioral therapies) play a role in preventing misjudgment of treatment failure. Stability of comorbid psychiatric disorders for 6 months (fourth criteria) is needed to confirm the predominant impact of tics on quality of life, to prevent pseudo-refractoriness, and to maximize the future DBS response. The 18-year age limit (fifth criteria) is currently under reappraisal, considering the potential impact of severe tics in adolescence and the predictive effect of tic severity in childhood on tic severity when transitioning into adulthood. Here is described 3 patients with TS who underwent DBS targeting the bilateral thalamic centromedian/parafascicular complex (CM/Pf) with an excellent clinical outcome. At 1-year follow-up, the mean reduction in the total Yale Global Tic Severity Scale score in the 3 patients was 70% (range, 60%-80%). This study further supports the role of the CM/Pf DBS target in medically intractable TS.

**Keywords:** Deep brain stimulation, Tourette syndrome, criteria for deep brain stimulation.

**USE OF STEM CELLS IN PATIENTS WITH LEFT HEART HYPOPLASTIC SYNDROME**

*Tchankvetadze Otari*

*Tbilisi state medical university Faculty of Medicine, Tbilisi Georgia*

**ABSTRACT**

Hypoplastic left heart syndrome is one of the most severe congenital heart defects characterized by underdevelopment of the left ventricle, outflow tract, and aorta. Without aggressive palliative surgery, the outcome is usually fatal. Hypoplastic left heart syndrome surgery stages are the Norwood, Glenn and Fontan procedures. Despite complete 3-stage surgical palliation, right ventricular failure progresses and this continues to aggravate the patient's condition. That is why there has been interest in a new approach to the management of right ventricular failure in patients with hypoplastic left heart syndrome. The use of stem cells could be an innovative approach in the treatment of right ventricular failure. The field has identified numerous stem cell populations from different tissues (cardiac or bone marrow or umbilical cord blood), different age groups (adult versus neonate-derived), and different donors (autologous versus allogeneic), with preclinical and clinical experience demonstrating the potential utility of each cell type. Animal studies have shown the mechanisms of how stem cells affect the damaged myocardium. Recent studies have comprehensively evaluated the individual components of the stem cells' secretomes, shedding new light on the intracellular and extracellular pathways at the center of their therapeutic effects. The results of these studies created the basis for their use in clinical practice. Today, stem cells already exist in the pediatric population. This article reviews the many stem cell types applied to congenital heart disease, their preclinical investigation and the mechanisms by which they might affect right ventricular dysfunction in patients with hypoplastic left heart syndrome, and finally, the completed and ongoing clinical trials of stem cell therapy in patients with congenital heart disease.

**Keywords:** cell transplantation, hypoplastic left heart syndrome, stem cells, heart failure.

**ADVANCEMENT OF SKIN GRAFTING INTO 21<sup>ST</sup> CENTURY**

***Proma Ajoy Shil***

*Tbilisi state medical university, Faculty of Medicine, Tbilisi, Georgia*

***Varsha Wadhe***

*Tbilisi state medical university, Faculty of Medicine, Tbilisi, Georgia*

***Naga Harika Korrapati***

*Tbilisi state medical university, Faculty of Medicine, Tbilisi, Georgia*

***Luiza Gabunia***

*Tbilisi state medical university, Faculty of Medicine, Tbilisi, Georgia*

**ABSTRACT**

Aim of skin grafting is to restore cosmetic damage and improve quality of life. Autologous skin grafting has opened a wider approach for treatment. Today, old, and new technologies allow us new treatment concepts that led to a greater reconstructive clockwork for reconstructive surgery of 21<sup>st</sup> century. We aimed to understand the history and wide use of skin grafting in medicine through literature review. We learnt that Autologous split thickness skin grafting was developed more than 3500 years ago. Skin grafting is a closure technique used in dermatology to close wounds. Specialized treatments for grafting called – Full thickness and split thickness grafting have helped provide a safer and effective way of wound closure. Grafts are generally used in variety of clinical situations such as traumatic conditions, burn reconstruction, vitiligo and neurosurgery. Today, skin grafting is considered as the gold standard for the treatment of major traumatic loss of skin. FDA approved a new treatment option called RECELL autologous cell harvesting device that collect s a small sample from patient and immerses it in an enzyme solution with cells that have wound healing properties. This tissue replacement can be used for reconstruction of skin defects due to diabetes. Urologists may encounter patients with diseases that lead to severe tissue loss that need complex closures. The constant improvement of innovative methods of skin replacement has led to a better survival rate and quality of life has increased tremendously.



**December 09-11, 2022 / Tbilisi, Georgia**

**ASSOCIATION BETWEEN SARS-COV-2 AND PSORIASIS**

***Divya SunilKumar***

*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

***Ranasinghe Arachchige Dona Kashmira Nawodi Weerasekara***

*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

***Naga Harika Korrapati***

*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

***Luiza Gabunia***

*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

**ABSTRACT**

Since the beginning of the pandemic in 2020, there has been growing concern among healthcare professionals about the risk of association between the infection caused by the novel Coronavirus and autoimmune diseases, in particular Psoriasis. Psoriasis is frequently associated with other autoimmune disorders such as Systemic Lupus Erythematosus, Chron's Disease, etc., and an increased risk for comorbidities such as diabetes, obesity, increased cardiovascular risk, and metabolic syndrome. The aim is to study the association between SARS-COV-2 virus and Psoriasis in Covid infected patients. We did an extensive search of two databases such as PubMed and Google Scholar. The search strategy involved using combinations of the terms Psoriasis, Covid 19, pandemic, dermatology & autoimmune diseases. Psoriasis flareup have recently appeared in the setting of COVID-19 due to adverse effects of medications or increased immune response. Psoriasis is distinguished by chronic inflammation that is driven by a T-cell-mediated autoimmune response and characterized by high levels of interleukin (IL)-23, IL-17, and TNF-a. Psoriasis flare-ups following COVID infection can also be attributed due to the administration of anti-malarial medications such as Hydroxychloroquine (HCQ) early in the pandemic. The underlying mechanism contributing to this condition is HCQ's inhibitory effect on epidermal transglutaminase, which leads to epidermal cell collection, and its promotion effects on interleukin17 (IL17) production, which leads to keratinocyte overgrowth. Given the crucial role of inflammation in the pathogenesis of psoriasis, it can be suggested that hyperinflammation status caused by COVID-19 may also alter the course of psoriasis.

**IRRATIONAL USE OF ANTIBIOTICS AND ANTIBIOTIC RESISTANCE IN GEORGIA**

***Bukhrashvili Tinatin<sup>1</sup>,***

*<sup>1</sup>Student of Tbilisi State Medical University, Faculty of Medicine*

***Vardosanidze Nino<sup>2</sup>***

*<sup>2</sup>Student of Tbilisi State Medical University, Faculty of Medicine*

**ABSTRACT**

The irrational use of antibiotics and associated growth of antibiotic resistance is a widely acknowledged threat to global health.

It is beyond doubt, that the underlying cause of antibiotic resistance is the overall volume of the antibiotic use. Irrational use of antibiotics includes self-medication, treatment of non-bacterial illness and sometimes even the prescription of incorrect doses.

The irrational use of antibiotics is associated with poor health outcomes, longer hospitalization and increased costs to both, patient and government.

The aim of our study is to present the frequency of antibiotic use, its main drivers and to describe the ratio of irrational use of antibiotics with associated risks.

In this paper we tried to compare our results with surveys conducted in Europe.

For our survey we made two questionnaires, one was filled by randomly chosen citizens of Tbilisi and the second one was filled by georgian doctors and residents. First questionnaire, which was adressed to non-medical representatives, was filled by 600 people. The second one, on the other hand, was filled by 48 people from the medical field.

The results showed, that the unnecessary antibiotic use in Georgia is significantly higher, compared to Europe.

We have also performed a broad search of the current literature in databases such as Pubmed and Google Scholar.

**Keywords:** Antibiotics; Antibiotic Resistance; Irrational Use; Europe; Georgia .

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**AN EXPERIMENTAL CLINICAL THERAPY WITH A NOVEL BACTERIOPHAGE**

*Swarali Chodnekar*

<sup>1</sup>*Teaching University Geomedi LLC, Faculty of Medicine, Tbilisi, Georgia.*

<sup>1</sup>*ORCID ID: <https://orcid.org/0000-0002-5176-7311>*

**ABSTRACT**

Antibiotic resistance has become increasingly relevant problem over the past decades. Due to stagnation in the development of novel antibiotic drugs, resistance to antimicrobials poses an increasingly severe threat to the health of the general population. The bacteria that pose the greatest threat to human health because of their growing resistance to antibiotics are the members of the Enterobacteriaceae family, particularly *Klebsiella* species. The understanding of the epidemiology of these strains and their mechanisms of resistance are key components in the fight against these infections. One alternative/complement to antibiotic therapy is the use of bacteriophages. Bacteriophage / phage therapy harvests naturally occurring lytic bacteriophages, which can be isolated from regular environmental reservoirs, to target and destroy pathogenic bacteria in a human host. Bacteriophages are known for being highly specific, infecting only a narrow range of targeted bacterial strains.

This paper briefly outlines the methodologies for identifying of bacteria and their resistance against antibiotics. The paper provides real-life clinical applications of bacteriophage therapy, while enlisting economic methods to test for phage susceptibility. The paper describes methodologies to isolate a novel phage cocktail for a multi-phage resistant bacterium, means of administration of bacteriophages and the challenges involved therein.

The paper aims to publish the results of the ‘original experimental clinical therapy’ carried out by the author for a patient with Pan-Drug resistant *Klebsiella Pneumoniae*. The patient being a man with a bilateral lung transplant recipient that had developed a hospital acquired chronic *K. pneumoniae* infection in the pleural cavity. The treatment is further complicated due to a resolving pleuro-cutaneous fistula.

**Keywords:** Pan-Drug Resistance, Bacteriophage therapy, Challenges, Experimental Clinical Therapy.

**CLINICAL CASES OF BORRELIOSIS IN GEORGIA**

*Malvina Javakhadze<sup>1</sup>*

<sup>1</sup>*Tbilisi State Medical University, Infectious Disease Department, Tbilisi, Georgia*

<sup>1</sup>*ORCID ID: 0000-0002-1090-8106*

*Nasim Muhammed Asraf<sup>2</sup>*

<sup>2</sup>*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

<sup>2</sup>*ORCID ID: 0000-0003-1113-4269*

*Shifna Latheef<sup>3</sup>*

<sup>3</sup>*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

<sup>3</sup>*ORCID ID: 0000-0003-4533-0452*

*Ziya Sherin<sup>4</sup>*

<sup>4</sup>*Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

<sup>4</sup>*ORCID ID: 0000-0002-8542-6216*

**ABSTRACT**

**Introduction:** Borreliosis (Lyme disease) is a multisystem disorder affecting populations on three continents. The disease is expanding throughout Europe, with over 200,000 cases per year. With a bimodal age distribution in incidence, the disease has become Europe's most common tick-borne disease.

**Purpose of the study:** To review the medical history of hospitalized and ambulatory patients diagnosed with borreliosis in the pediatric department of Acad.Vakhtang Bochorishvili Clinic, and to characterize the features of the disease course in the population of Georgia.

**Research material and method:** Retrospective research was conducted. We studied the medical history of 9 hospitalized patients and 15 outpatients who were diagnosed with borreliosis in 2017. We analyzed the clinical symptoms according to the age structure and severity of the patients.

**Analysis of the obtained results:** According to the data of the National Center for Disease Control (NCDC), confirmed cases of borreliosis among children in Georgia since 2011 (till 2020) is approximately 135 cases. Out of 9 hospitalized patients, the initial diagnosis in all cases was fever of unknown etiology. Among them, 7 patients had creeping erythema (78%) and 2 had a disseminated form without erythema. All of them had fever, which was the reason for hospitalization. Only 3 patients (33%) reported tick bites. In all other cases, tick bites were not reported. Out of 15 outpatients, only 4 had a one-time increase in temperature, and 5 reported subfebrility for 2-3 days. The reason for consulting the doctor was a rash, which was initially classified as erythema crawler, and all of them were treated according to the protocol. Diagnosis and monitoring of the disease were carried out by serological tests on Borrelia. At the beginning, antiBorrelia burgdorferi IgM and IgG were evaluated. Further confirmation was done by immunoblotting method. Treatment with amoxicillin+clavulanic acid or doxycycline for 21 days, depending on age. We also observed a severe form of hepatitis development in a 2-year-old girl, who recovered shortly.

**Conclusion:** Thus, borreliosis has become a rare case in children in Georgia and is mostly mild, in the form of skin manifestation.

**Keywords:** Borreliosis, Lyme, Retrospective, Georgia

**CLINICAL MANIFESTATIONS AND ETIOLOGY OF ENTEROVIRAL INFECTIONS IN GEORGIA: A CASE SERIES AND REVIEW**

*<sup>1</sup>Malvina Javakhadze*

*<sup>1</sup>Tbilisi State Medical University, Faculty of Medicine, Infectious Diseases, Tbilisi, Georgia*

*<sup>1</sup><https://orcid.org/0000-0002-1090-8106>*

*<sup>2</sup>Alexis Tressa Babu*

*<sup>2</sup>Tbilisi State Medical University, Department of Medicine, European MD, Tbilisi, Georgia*

*<sup>2</sup><https://orcid.org/0000-0001-7132-4449>*

*<sup>3</sup>Asiya Fatima*

*<sup>3</sup>Tbilisi State Medical University, Department of Medicine, European MD, Tbilisi, Georgia*

*<sup>3</sup><https://orcid.org/0000-0002-4111-8676>*

*<sup>4</sup>Sreelakshmi Kathiru*

*<sup>4</sup>Tbilisi State Medical University, Department of Medicine, European MD, Tbilisi, Georgia*

*<sup>4</sup><https://orcid.org/0000-0001-9874-8137>*

**ABSTRACT**

**Introduction:**

Enteroviruses are the most common and significant causes of infectious illness in infants and children. They are associated with a broad spectrum of clinical syndromes, including Hand, Foot, and Mouth disease, Herpangina, Acute hemorrhagic conjunctivitis, Pleurodynia, Aseptic meningitis, Myopericarditis, and Encephalitis. The coxsackie virus is a common cause of enteroviral infections in Georgia during the fall and summer seasons.

**Purpose of study:**

The objective of the study was to comprehend the progression of enteroviral infection in infected patients who were hospitalized, taking into account their age, clinical history and severity.

**Methods:**

Clinical histories were obtained and studied of 85 patients diagnosed with enteroviral gastroenteritis in the pediatric department of Acad. Vakhtang Bochorishvili Clinic for this retrospective method study.

**Results:**

The most frequent clinical form was hand, foot, and mouth disease (HFMD), detected in 81% of patients. The leading cause of the disease in most cases was Group A coxsackievirus or enterovirus 71. In some cases, other strains were noted. 90% of patients were admitted to the clinic on the second day after the disease onset. Following a 3-5 day incubation period, the disease developed to an acute phase marked by rash and fever that persisted for 2-3 days in a majority of individuals without sequelae. The rash appeared papular-vesicular on the background of intact skin. The disease was of moderate severity with no severe complications and a 3-5 days recovery time. Herpangina came in second in terms of frequency and was associated with a benign course mainly seen in patients aged 3-7 years.

**Conclusion:**

Therefore, care needs to be taken to avoid misdiagnosis of the etiological agent which is not necessarily an enterovirus, hence a patient with diarrhea need not always be tested for this group of viruses. The enteroviral form often follows its course with skin lesions of vesicular-papular nature, this manifestation often helps with the differential diagnosis

**Keywords:** Enterovirus; HFMD; Children; Coxsackievirus; Herpangia; Rash

**ANALYZING NEUROLOGICAL AND PSYCHIATRIC DISORDERS USING CONNECTOMES**

***Maduri Balasubramanian<sup>1</sup>***

*<sup>1</sup>Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

*<sup>1</sup>Orcid Id:<https://orcid.org/0000-0002-5634-6057>*

***Adithya Lal<sup>2</sup>***

*<sup>2</sup>Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

***Naga Harika Korrapati .<sup>3</sup>***

*<sup>3</sup>Tbilisi State Medical University, Faculty of Medicine Tbilisi, Georgia*

***Luiza Gabunia***

*Tbilisi State Medical University, Tbilisi, Georgia*

**ABSTRACT**

To understand the functioning of a network, one must know the main elements and their connections. Connectomes are the map of neural connections across the brain. With many neurologic and psychiatric symptoms corresponding more closely to networks of connected regions, the use of connectome to understand lesions in different locations that cause the same symptoms can be linked to common networks.

We aim to understand the similarities between neurological and psychiatric conditions using lesion analysis. This is a literature review conducted using articles from Google Scholar, PubMed, and NEJM. Articles published in the last five years (2018-2022) were taken for review.

Using improved methods for data acquisition, analysis, and sharing, a single hierarchical map of the neural connection ranging from single neurons to populations of neurons to larger systems like cortical areas.

Although connections between neurons were unchangeable once established only individual synapses could be altered, recent evidence suggests that connectivity is subjected to change, termed neuroplasticity. There are two ways that the brain can rewire: the formation and removal of synapses in an established connection or the formation/removal of entire connections between neurons.

Using this research can be applied to various neurological conditions to help us to understand their pathogenesis.

One example is Huntington's disease where there is an overall reduction of stimulation of the connectomic pathway, which ultimately affects the connection between various brain structures.

Human connectomes have opened up a whole new avenue for studying disease mechanisms. By comparing diseased and healthy connectomes, we can gain insight into certain psychopathologies, such as neuropathic pain, and potential therapies for these disorders.

**Keywords:** connectome, neurology, psychiatry, neural connection, lesion analysis

**December 09-11, 2022 / Tbilisi, Georgia**

**BIOMEDICAL RESEARCH- OPPURTUNITIES AND ETHICAL CHALLENGES**

*Ria Pillai*

*TSMU, Faculty of Medicine, Tbilisi, Georgia*

*Syed Mukarram*

*TSMU, Faculty of Medicine, Tbilisi, Georgia*

**ABSTRACT**

**Purpose:** In order to improve compliance with ethical standards in the context of continuously expanding and growing research, such as to ensure satisfying and better patient care and lower the risk of research, failing to observe moral code and all patient rights, the primary goal of this paper is to analyze the key opportunities and challenges in biomedical research. **Background:** Since antiquity, discovering effective ways to care for people has been both an opportunity and a struggle, which has manifested itself in the ongoing self- and experimentation of caretakers. Medical research, whether basic or applied, is not only vital to the advancement of medicine but also a means of improving people's quality of lives. **Content:** Starting with historical experience and literature study, the paper analyzes the primary ethical standards regulating any type of medical research. **Discussion:** Over the past several years, there has been a significant increase in the number of individuals involved in medical research, making bioethics a more practical science capable of creating guidelines to guarantee the moral growth and upliftment of the medical industry. **Conclusions:** The reality of medical practice and scientific research have become continually more strongly entwined with bioethics in recent years, which has helped to advance multidisciplinary bioethics study as well as the incorporation of moral considerations into medical practice. The transformation from research conducted only for the goal of publication and professional promotion to research conducted out of compassion and the desire to improve patient wellbeing must be associated with bioethics, and more specifically, bioethical education.

**Keywords:** bioethics, medical research, patient rights

**ULTRASTRUCTURAL CHARACTERISTICS OF STRUCTURAL ELEMENTS OF GASTRIC MUCOSA IN OBESITY**

***Eldar Gasimov<sup>1</sup>***

<sup>1</sup>*Azerbaijan Medical University, Department Cytology, embryology and histology. Baku, Azerbaijan*

<sup>1</sup>*ORCID ID: 0000-00025104-4260*

***Taryel Omerov<sup>2</sup>***

<sup>2</sup>*Azerbaijan Medical University, Department of Surgical Diseases I, Baku, Azerbaijan*

<sup>2</sup>*ORCID ID: 0000-0002-7216-7980*

***Rashad Abizade.<sup>3</sup>***

<sup>3</sup>*Azerbaijan Medical University, I General Medicine Faculty, Baku, Azerbaijan*

<sup>3</sup>*ORCID ID: 0000-0003-3632-8385*

***Fuad Rzayev<sup>4</sup>***

<sup>4</sup>*Azerbaijan Medical University, Laboratory of Electron Microscopy, Baku, Azerbaijan*

<sup>4</sup>*ORCID ID: 0000-0002-8128-1101*

**ABSTRACT**

**Background.** Obesity plays a major role in the development of hypertension, type II diabetes, cardiovascular diseases, osteoarthritis, and cancer types. The research aimed to ultrastructural characteristics of structural elements of gastric mucosa in obesity.

**Method.** The samples were fixated which was obtained by biopsy from 20 patients (male =8, female=12) in a solution containing 2% Paraformaldehyde, 2% Glutaraldehyde, and 0.1% Picric acid prepared in Phosphate buffer (pH 7.4). After the Araldite-Epon blocks were prepared according to general methods accepted in electron microscopy. Semithin sections (1-2µm) were obtained with the aid of Leica EMUC7 ultra-microtome for further investigation by light microscope Primo Star (Zeiss) Stained ultrathin sections (50-60 nm) were examined under the Transmission Electron Microscope JEM-1400 at 80 kV.

**Result.** A study of specimens taken showed that in 6 patients, in the lamina propria of the gastric mucosa observed beside with significant increase in a number of plasmatic cells, no detectable neutrophils, that shown obesity following with chronic inactive gastritis. In 3 patients, the detection of lymphocytoneutrophil infiltration within lamina propria of the gastric mucosa suggests that they have an active form of chronic gastritis. According to the result, in obesity patient parietal cell height is  $21,19 \pm 3,57 \mu\text{m}$ , 86.9 % of total area is cytoplasm. Mitochondria account for 80-90% of the ultrastructural visible organelles in the cytoplasm.

**Conclusion.** A more than 2-fold increase in the height of parietal cells against the background of chronic inactive gastritis during obesity (compared to literature data) and a sharp increase in mitochondria in the cytoplasm suggest an increase in the synthesis of HCL acid in these patients.

**Keywords:** gastric mucosa, gastritis, parietal cell, obesity, transmission electron microscope.



**December 09-11, 2022 / Tbilisi, Georgia**

**PECULIARITIES OF SEVERE RESPIRATORY DISTRESS SYNDROME CAUSED BY NOVEL CORONAVIRUS (COVID 19) AND OTHER RESPIRATORY PATHOGENS IN PATIENTS WITH HYPERFERRITINEMIA TAKING ACE INHIBITORS**

***Magda Rurua***

*doctor reanimatologist, doctoral student at Tbilisi State Medical University.*

***Levan Ratiani-MD,PhD***

*Head of department of anesthesia-reanimatology at Tbilisi State Medical University. General director at "The First University Clinic".*

***Qetevan Matchavarian***

*Associate professor of anesthesia-reanimatology at Tbilisi State Medical University.*

***Elene Patchkoria***

*MD. Assistant-professor at infectious diseases department at Tbilisi State Medical University*

***Tamar sanikidze***

*MD,PHD of Department of Biophysics at Tbilisi State Medical University.*

**Background:** The disease caused by the novel coronavirus (SARS-COV -2) Covid 19, as it is already known, is characterized by heterogeneous clinical picture, difficult pathophysiology and wide spectrum of the disease. The main complication is acute respiratory distress syndrome (ARDS) and subsequent hypoperfusion syndrome. Big importance is given to the effective summation of visual check and results of clinical tests of disease's specific parameters.

**Methods and Materials :** During 2020-2021years we studied 212 hospitalized patients in the Department of Critical Medicine of the First University Clinic. The aim of our study is to reveal peculiarities of Acute Respiratory Distress Syndrome ( ARDS) caused by COVID 19 and other Respiratory pathogens in case of Hyperferritinemia in Patients who did or did not take ACE inhibitors. Patients were divided in different groups. Patients with COVID 19 who were taking ACE inhibitors. Non COVID 19 patients who were not taking ACE Inhibitors. Patients with Covid 19 and non Covid 19 who were not taking ACE inhibitors. Data were analyzed by SPSS statistical software version 20.

**Results:** Among 212 hospitalized patients in the Department of Critical Medicine 134 were male (63.3 %) and 78 were females ( 36.7 %); The average age of the patient is 40-70 years. We studied Angiotensin II; Interleukin 6; C reactive protein, Leukocytes, Procalcitonin, coagulation factors. PCO<sub>2</sub>; Change sin P<sub>O2</sub>; ejection fraction and pulmonary arterial pressure

initial level of Angiotensin in patients with COVID 19 was higher then in non COVID 19 patients in case when the level of ferritin does not exceed 1500 (P < 0.01). In condition of Hyperferritinemia (>1500) there is no difference ; PCO<sub>2</sub> decreases in case of taking ACE inhibitors in patients with Covid 19 when the level of Ferritin more then 1500 . Changes regarding P<sub>O2</sub> were not statistically reliable ( P>0.05). ACE inhibitors reduce the level of IL 6; CRP; WBC, D Dimer ( P <0.01) in every group patients were the level of ferritin was less then 1500.) ; ACE inhibitors increase Pulmonary pressure in Covid 19 patients ( P<0.01).

**Conclusion :** According to our study ACE inhibitors can reduce the expression of pro inflammatory cytokines and chemokines induced by Angiotensin II, modulate the cytokine response and the formation of inflammatory markers. Furthermore, Hyperferritinemia (Ferritin >1500 ng/ml )in covid patients is associated with a higher risk of mortality and can be considered as an indicator of disease severity.

**Key words:** ARDS, ACE inhibitors , Ferritin.

**December 09-11, 2022 / Tbilisi, Georgia**

**THE EFFECT OF STEROID, SILICONE, SILOXANE AND HEPARIN-CONTAINING DRUGS ON THE DEVELOPMENT OF POSTOPERATIVE SCARS**

***Nino Kuridze<sup>1</sup>***

*Plastic-reconstructive Surgeon, Georgia*

***Luiza Gabunia<sup>2</sup>***

*Associate Professor of Medical Pharmacology Department of Tbilisi State Medical University (TSMU), Georgia*

*ORCID ID: 0000-0003-0856-2684*

***Ketevan Ghambashidze<sup>3</sup>***

*Associate Professor of Pathophysiology Department, TSMU, Georgia*

*ORCID ID: 0000-0002-3845-9306*

***Nana Chelidze<sup>4</sup>***

*Assistant Professor of Pathophysiology Department, TSMU*

***Davit Delibashvili<sup>5</sup>***

*Associate Professor of Pathophysiology Department, TSMU*

**ABSTRACT**

Pathology of skin scars and the number of patients suffering with dermatogenic problems developed due to various injuries, wounds, surgical interventions, burns etc., increases every day all over the world. Scars often cause functional, cosmetic and mental problems. The patient suffers from continuous itching, pain, redness, tightness, restriction of movement in the area of damage and has a certain degree of psychological discomfort. Pharmaceutical market offers wide specter of anti-scar remedies and methods of treatment (surgical intervention, cryo-, laser-, hormone therapy, peeling, mesotherapy, dermabrasion etc.). However, the desired results have not yet been achieved, since the complications of existing treatments (frequent recurrences, accumulation of toxic radicals and tissue damage products, inflammation, swelling etc.) limit their widespread use and reduce the effectiveness of anti-scar treatment. At present, for anti-scar treatment the great attention has been paid on steroid, silicone, siloxane and heparin-containing drugs - Contractubex, Epicin, Dermatix ultra and Diprosan. They manifest good therapeutic effects in mono- and complex therapy leading to quick healing of wounds without pathological scarring. Diprosan reduces collagen synthesis by inhibiting fibroblast division and increasing the concentration of collagenase. It has an anti-inflammatory and anti-allergy effect. Contractubex has keratolytic, fibrinolytic, anti-microbial and anti-inflammatory effects, stimulates cell regeneration without hyperplasia, inhibit proliferation of keloid fibroblasts. Epicin is characterized by anti-inflammatory, antimicrobial and rapid regenerative action. Dermatix Ultra exhibits scar preventive and scar modeling action, promotes rapid regeneration of the skin. Based on all of the above-mentioned, it is very interesting to study the comparative effectiveness of the mentioned drugs against scars and reveal the main link of the pathogenesis of their action that will enable practicing doctors to obtain the best results in the treatment of postoperative skin scars in mono or complex therapy in combination with instrumental treatment.

**Key words:** Postoperative scar, Silicone, Siloxane, Heparin.

**Introduction**

Pathology of skin scars and the number of patients suffering with dermatogenic problems developed due to various injuries, wounds, surgical interventions, burns etc., increases every day all over the world.

Scars often cause functional, cosmetic and mental problems. The patient suffers from continuous itching, pain, redness, tightness, restriction of movement in the area of damage and has a certain degree of psychological discomfort.

There are different types of scars (normotrophic, atrophic, hypertrophic, keloid), which differ from each other in structure, architecture and functional state. Therefore, treatment requires an individual approach of treatment [Neodyne, 2022].

The wound healing and scar formation is a complex process influenced by genetic factors (eg, collagen metabolism), as well as age, gender, ethnicity, hormonal levels (pregnancy, puberty), and environmental factors. In case of complex treatment, it is very important to take into account the characteristic features of the scar, its external color, localization, depth, area, functional state, etc. [Ogawa R, et al. 2019].

The most common hypertrophic scars that create aesthetic and functional problems often lead to the development of contractures, syndactyly, which, in turn, can be exposed to ulceration and even malignancy. Keloid scars are benign growths of fibrous tissue. As a result of histological studies, it has been established that keloids are large collagen fibers [Glass, D., 2017]. Characteristic symptoms are cosmetic problems, pain, erythema, itching, paresthesias and functional disorders.

Numerous treatments have been used for keloid and hypertrophic scars, which include conventional therapies such as occlusive dressings, compression therapy, and steroids; surgical therapies such as excision and cryosurgery; and adjuvant and emerging therapies including radiation therapy, interferon, 5-fluorouracil, imiquimod, tacrolimus, sirolimus, bleomycin, doxorubicin, transforming growth factor-beta, epidermal growth factor, verapamil, retinoic acid, tamoxifen, botulinum toxin A, onion extract, silicone-based camouflage, hydrogel scaffold, and skin tension offloading device [Berman B. 2017].

The use of surgical methods of treatment is effective for keloid and hypertrophic scars, or when conservative treatment is ineffective. It is used to remove relatively less thick and limited scar tissue, the edges of which are mobile. Method of cryodestruction, or cryotherapy, is used as an alternative surgical method for the treatment of hypertrophic and keloid scars [Salem S, Abdel, 2021; Samar A., 2021]. Liquid nitrogen freezes scar tissue. In the area of the scar, it causes cell damage by forming intracellular crystals. According to the indications, a combined method of treatment, for example, cryotherapy with corticosteroids, is preferable. Radiation therapy is used primarily for keloid scars, although its effectiveness is still controversial [Maliha Z., 2022]. Laser therapy is often used in combination with the other methods [Nathaniel M., 2021; Shikunova, I. 2018]. Owing to the local exposure, it is possible to control the depth of exposure and spare the healthy tissues.

The most popular cosmetic procedures for aesthetic correction are peeling, mesotherapy, dermabrasion, etc [King M., 2018]. The use of these methods is more suitable for the correction of small scars. The most high-tech is the use of biological dressings - xenocan, cultured human cells, wound dressings, etc. [Rees R., 2001].

Compression therapy (constant compression of 20-40 mmHg) counteracts the growth of scar tissue, mechanically holds it in a limited space. By pressing on the blood vessels of the scar, it inhibits the nutrition of the scar, which leads to the cessation of its growth and partial regression [Kerckhove E, Anthonissen M. 2020].

Silicone preparations, plates, and silicone gel dressings are used to treat hypertrophic scars, keloids, and contractures. Compression reduces the volume of the extracellular matrix. The therapeutic effect of silicone gel is associated with its occlusive properties and a decrease in water evaporation from the epidermis [Oliveira G., 2001].

Hormone therapy is used for treatment of keloid scars in combination with other methods (surgical operations, silicone sheets, etc.), as well as for symptomatic treatment [YatingYang et al., 2022].

Injections of enzyme preparations (hyaluronidase, longidase, lidase, etc.) are widely used. The specific substrate of hyaluronidase is hyaluronic acid, which is a mucopolysaccharide. It contains acetylglucosamine and glucuronic acid (intermediate "cementing" of the connective tissue). Hyaluronidase causes splitting of one of the pathological components of the extracellular matrix, the connective tissue binder - hyaluronic acid to glucosamine and glucuronic acid. Accordingly, it increases

the permeability of tissues and blood vessels, facilitates the movement of interstitial fluid in interstitial spaces, reduces tissue swelling and prevents scar formation. The action of hyaluronidase is reversible - a decrease in concentration restores the adhesiveness of hyaluronic acid. Longidase with immunomodulatory properties is used to prevent scarring. Lidaza is used for joint contractures, ankylosing spondylitis, hematomas, long-term non-healing ulcers, and scleroderma.

Cellular technologies have been actively used in recent years to improve the aesthetics of scars. Cellular compositions have a significant bioenergetic potential. Growth factors, cytokines, nitric oxide, etc., act on fibroblasts. It is known that after skin damage by laser, needle and other instruments, the skin is supplied with new stem precursors of fibroblasts from the bone marrow, adipose tissue and capillary pericytes, which contributes to the rejuvenation of its own stem. They actively trigger the synthesis of collagen, elastin, enzymes, glycosaminoglycans, growth factors and other biologically active molecules, which leads to hydration and vascularization of the dermis, and its strengthening. Currently, neofibrolifting is used to reconstruct the microstructure of the dermis in superficial, photoaging and other cases [Tsepikolenko A. et al., 2019].

Although pharmaceutical market offers wide specter of anti-scar remedies and methods (surgical intervention, cryo-, laser-, hormone therapy, peeling, mesotherapy, dermabrasion etc.), the desired results have not yet been achieved, since the complications of existing treatments (frequent recurrences, accumulation of toxic radicals and tissue damage products, inflammation, swelling etc.) limit their widespread use and reduce the effectiveness of anti-scar treatment.

At surgical removal of keloid scars the relapses develops in 70-90% of cases. Cryotherapy is a painful and traumatic procedure that often causes depigmentation of the skin. After cryodestruction, the inflammatory process lasts 3 or more weeks. The problem of depth control and local impact has not been solved to date. After cryodestruction, tissue decay products accumulate in the wound, hypoxia begins and free radicals are produced as a result of oxidative stress, i.e., conditions are again created for the formation of pathological scars. Thus, cryotherapy is a rather controversial method of treating even small hypertrophic scars. The use of steroids causes side effects such as hypopigmentation, skin atrophy and prolonged wound healing. Radiation therapy causes swelling of the connective tissue and rupture of fibroblasts, collagen fibers. It is not used for localization of scars in the head, face, chest. Due to its carcinogenic effect, its use is strictly limited and is used only in severe cases. The recurrence rate for laser therapy is 60-75% for hypertrophic scars and 80-90% for keloid scars. Contraindications to cosmetic procedures: peeling, mesotherapy, dermabrasion, autoimmune diseases, immunopathies, etc., requires an individual comprehensive approach. Silicone patches must be worn for a long time, which causes maceration and inflammation of the skin. Silicone plates cannot be fixed on mobile and open areas of the body (folds, neck, etc.). Complications of hormonal therapy are atrophy and pigmentation disorders.

At present, for anti-scar treatment the great attention has been paid on steroid, silicone, siloxane and heparin-containing drugs such as: Contractubex, Epicin, Dermatix ultra and Diprosan. They manifest good therapeutic effects in mono- and complex therapy leading to quick healing of wounds without pathological scarring [Neerja Puri, 2009; Mustafa T Sahin, et al. 2012]. Diprosan reduces collagen synthesis by inhibiting fibroblast division and increasing the concentration of collagenase. It has an anti-inflammatory and anti-allergy effect [Xiao-E Chen, 2017]. Contractubex has keratolytic, fibrinolytic, anti-microbial and anti-inflammatory effects, stimulates cell regeneration without hyperplasia, inhibit proliferation of keloid fibroblasts [Ayengin K., Kılıç N., 2019]. Epicin is characterized by anti-inflammatory, antimicrobial and rapid regenerative action. Dermatix ultra exhibits scar preventive and scar modeling action, promotes rapid regeneration of the skin.

### **Conclusion:**

Based on all of the above-mentioned, could be said that it is very interesting to study the comparative effectiveness of the mentioned drugs against scars and reveal the main link of the pathogenesis of their action that will enable practicing doctors to obtain the best results in the treatment of postoperative skin scars in mono-, or complex therapy in combination with instrumental treatment.

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**PREVALENT MULTIDRUG RESISTANT BACTERIAL ISOLATES FROM A PAEDIATRIC CLINIC ARE HIGHLY SUSCEPTIBLE TO BACTERIOPHAGES**

*Sopio Tsertsvadze<sup>1</sup>*

*TSSMU Tbilisi, Georgia.*

<sup>1</sup>ORCID ID: 0000-0000-0000-0000

*Chkaidze Ivane<sup>2</sup>*

<sup>2</sup>TSMU Tbilisi Georgia.

<sup>2</sup>ORCID ID: 0000-0000-0000-0000

**ABSTRACT**

Gram negative bacilli (GNB), primarily *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and Enterobacteriaceae species in addition to *Staphylococcus aureus* and coagulase-negative (CoN) staphylococci are important health care associated pathogens worldwide with high potential for horizontal spread. Bacteriophages are considered as effective and safe tool for control of multidrug resistant bacterial infections.

Study identified prevalent bacterial flora in the respiratory department with ICU of a large children's hospital, and to analyze antibiotic and phage susceptibility profiles of obtained isolates. More than 300 various samples from patients with respiratory disorders and from fomites were collected during 6 sampling series, 28 months in total. The collected isolates (540 strains) were identified by biochemical profiling and using API systems (API20E, API20NE, ApiStaph, ApiStrep)

Among GNB isolates collected at the children's hospital (from both – patients and fomites) *P. aeruginosa* was most frequently isolated (about 40%) followed by *Serratia marcescens* (9%), *K. pneumoniae* and *A. baumannii* (6% each). Among gram-positive bacteria *S. aureus* and CoN staphylococci remained dominant (25.5 and 27% correspondingly) followed by *Sterpotococcus spp.* (11.5%). Majority of clinical isolates of *P. aeruginosa* and *A. baumannii*, also *K. pneumoniae* were shown to be multidrug resistant, frequently resistant to carbapenems. Only few antibiotics - mainly colistin, ciprofloxacin, Gentamicin and tobramycin were still but not always active. *S. aureus* strains showed variable profiles of antibiotic susceptibility with obvious resistance to Beta-lactams, also some strains revealed warning signs of vancomycin resistance.

The isolates of prevalent clinical pathogens were screened against commercial phage preparations "Pyophage", "Intestiphage" and "Staph Phage" and individual phages from Eliava collection - 32 phages of *P. aeruginosa*, 16 - *A. baumannii* and 8 - of *S. aureus* and CoN staphylococci. Up to 90% of *S. aureus* strains were also lysed by Sau phages. The high cumulative lytic activity of phages was demonstrated towards multidrug resistant clinical isolates of *P. aeruginosa*, *A. baumannii* and *K. pneumoniae*. Based on the obtained results 4 individual phages *P. aeruginosa* with broad host range, also 4 phages of *A. baumannii* and 5 - of *S. aureus* were selected as candidate phages for further development of phage preparations for infection control in paediatric hospitals.

**RESTORATION OF VOICE THROUGH ELECTROPHONOPATHIC LARYNGEAL STIMULATION IN PATIENTS WITH LARYNGEAL PARESIS AND PARALYSIS**

*I. Katsarava<sup>1</sup>, N. Gamkrelidze<sup>2</sup>, N. Pavliashvili<sup>2</sup>, L. Kvatchadze<sup>2</sup>*

*<sup>1</sup> PhD Candidate of Tbilisi State Medical University*

*Otorinolaringologist, phoniatriation of National Center of Audiology*

*Djafaridze-Kevanishvili clinic*

*<sup>2</sup> Department of Pathophysiology, Tbilisi State Medical University*

The aim of the research was to study the effects/prospects of neuromuscular electrophonopedic stimulation (NME) in patients diagnosed with laryngeal paresis and paralysis.

**Materials and methods.** Study was conducted on 25 patients (22 women and 3 men) with bilateral and unilateral laryngeal paresis or paralysis aged 9 to 62 years. The condition was caused by any of them: thyroidectomy, stress, cardiac surgery, viral infection.

Before treatment, patients reported the following complaints: hoarseness, voice fatigue after vocal exertion, cough, shortness of breath during speech and physical exertion.

To clarify the diagnosis, the following were used: anamnesis, clinical picture of the larynx - indirect laryngoscopy, optical stroboscopy - using an electronic stroboscope. In addition, optical endoscopy was performed using an ATMOS 90° endoscope with video recording of the inspiratory phase and phonation phase. The degree of damage of the innervation of the laryngeal muscular apparatus was determined using the vocaSTIM-Master device. At the same time, the patient performed the phonopedic exercises recorded on the CD disc, while the laryngeal muscles were electrically stimulated.

**Research Results.** It was revealed that by the 10th day of treatment, 23 patients declared significant positive dynamics of the subjective symptoms of the disease. If before the treatment the average total, subjective assessment of vocal damage was 8.7 points, after the treatment this indicator decreased to 2.6 points.

According to the GRBAS (An auditory-perceptual evaluation method for hoarseness) scale, the voice was evaluated with an average of 8.9 points before treatment, and after treatment this figure was 4.1 points. Positive dynamics were also noted when analyzing the acoustic parameters of the sound. IMF (intrinsic mode function) before treatment was  $6.1 \pm 2.6$  seconds, after treatment -  $11.1 \pm 4.9$  seconds. A significant increase in sound power was observed. If the maximum sound power before treatment was  $74.0 \pm 6.5$  dB, after treatment this indicator increased by almost 10 dB and amounted to  $85.8 \pm 6.9$  dB.

**Conclusions:**

1. The coefficient of accommodation is an objective indicator of degree of vocal damage.
  2. The laryngeal neuromuscular electrophonopedic stimulation technique allows not only to reliably determine the degree of impairment of the accommodation ability of the laryngeal muscular apparatus, but also to reveal the dynamics of its recovery during treatment.
  3. The use of the vocaSTIM device ensures rapid voice recovery in laryngeal paresis due to a combination of neuromuscular electrical stimulation and phonopedic exercises, which are individually selected for each patient.
- The visual analogue scale (VAS)
  - Range of motion (ROM)
  - Disabilities of the arm, shoulder and hand (DASH)
  - Shoulder and Hand scores
  - The American Shoulder and Elbow Surgeons Scores (ASES)



- Radiographic parameters.
- The visual analogue scale (VAS)
- Range of motion (ROM)
- Disabilities of the arm, shoulder and hand (DASH)
- Shoulder and Hand scores
- The American Shoulder and Elbow Surgeons Scores(ASES)
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- Shoulder and Hand scores
- The American Shoulder and Elbow Surgeons Scores(ASES)
- Radiographic parameters.

**A COMPARATIVE ANALYSIS OF THE SURGICAL TREATMENT OF FRACTURES OF THE PROXIMAL END OF THE HUMERUS**

*Davit Subeliani*

*Tbilisi State Medical University, Faculty of Medicine, Department of Orthopedics and Traumatology, Tbilisi, Georgia.*

*ORCID ID: 0000-0002-3475-3604*

*Levan Cikvatia*

*Tbilisi State Medical University, Faculty of Medicine, Department of Orthopedics and Traumatology, Tbilisi, Georgia.*

**ABSTRACT**

A proximal end fracture of the shoulder bone is one of the often common fractures and ranks third in terms of frequency (after a fracture of the hip and forearm) . Due to the fact that the shoulder joint is one of the complex joints in the human body, the incorrectly selected method of treating an intraarticular multifragment fracture of the shoulder joint leads to unsatisfactory consequences in the postoperative period and a high degree of disability. As with other types of surgical interventions, osteosynthesis and arthroplasty of a multifractional fracture at the proximal end of the shoulder bone are associated with a high degree of disability. The most common problem of them is the unsatisfactory function of the limb in the postoperative period, which leads to a deplorable consequence – a solid decrease in disability. Today there is no uniform rule that allows both the pros and cons of any treatment method to be determined during the operational period .The most effective methods in terms of results among the operational methods available today are osteosynthesis with a metal plate and screw, although today the trend in developed countries around the world is the tendency to arthroplasty of the upper end of the shoulder joint in the acute period of multifractional fracture, which ensures the activation of the disease in the early stages of surgery and the relieve of pain syndrome.

Patients to be examined are divided into two groups: in each group there are patients with a multifragment fracture at the proximal end of the shoulder bone. The number of patients is between 40 and 40 patients in each group. One group of patients participating in the study is undergoing shoulder fracture osteosynthesis with metal construction, and patients from the second group undergo shoulder joint arthroplasty.

To evaluate postoperative results, research methods are used:

1. The visual analogu scale(VAS),
2. Range of motion(ROM),
3. Disabilities of the arm,shoulder and hand(DASH),
4. Houlder and Hand score,
5. The American shoulder and Elbow Surgeons score(ASES),
6. Radiographic parameters.

main goal of our research is to provide a clear answer to the question: Is the upper end of the shoulder at the upper end of the joint a multifractional fracture During osteosynthesis more effective compared to arthroplasty or vice versa? The purpose of the study is to evaluate the results of these two surgical treatment methods and develop appropriate guidelines that reduce the likelihood of disability in the postoperative period, which will ensure that cost reductions and cash optimization are optimised.

**TREATMENT OF TRAUMATIC SOFT TISSUE INJURIES OF THE SHOULDER WITH THE COMBINATION OF INTERFERENTIAL CURRENT AND LASER THERAPY**

***Vasil Potskhveria***

*Tbilisi State Medical University, Department of Physical Medicine, PhD Student, Tbilisi, Georgia,*

***Valeri Akhalkatsi***

*Tbilisi State Medical University, Faculty of Physical Medicine and Rehabilitation, Department of Physical Medicine, Clinical Center of Sports Medicine and Rehabilitation, Tbilisi, Georgia*

***Lela Maskhulia***

*Tbilisi State Medical University, Faculty of Physical Medicine and Rehabilitation, Department of Physical Medicine, Clinical Center of Sports Medicine and Rehabilitation, Tbilisi, Georgia*

*ORCID ID: 000-0002-8893-374X*

***Marine Matiashvili***

*Tbilisi State Medical University, Faculty of Physical Medicine and Rehabilitation, Department of Physical Medicine, Clinical Center of Sports Medicine and Rehabilitation, Tbilisi, Georgia*

***Natalia Pavliashvili***

*Tbilisi State Medical University, Faculty of Medicine, Department of Pathophysiology, Tbilisi, Georgia*

**ABSTRACT**

Soft tissue injuries of shoulder is a common cause of shoulder pain and functional limitation in athletes in many kind of sports, regardless of their qualifications. These injuries have a significant impact on their career development and limit their ability to participate in competitive sports. 52 young athletes, aged 18-30 years old, were selected for study. The aim of the study was to evaluate the effectiveness of interferential current therapy and laser therapy in the treatment of traumatic soft tissue injuries in athletes, compared independently using of interferential current therapy. Patients were randomly divided into three groups and appropriate rehabilitative interventions were performed. Athlete's shoulder function and the results of medical rehabilitation measures were assessed before and after treatment using Penn Shoulder Score (PSS), Western Ontario Rotator Cuff Score (WORC), Kerlan-Jobe Orthopedic Clinical shoulder and elbow score (KJOC) scales. The fragment of the present study includes the evaluation of patients in the first and second groups with combination of laser therapy and interferential current therapy (group 1) and mono-therapy (group 2) with interferential current, the evaluation was done by PSS scale. In the treatment of traumatic injuries of soft tissues of the athlete's shoulder. The positive effect obtained in the study, pain inhibition at the spinal level is associated with interference therapy, and endogenous pain inhibition - with low-intensity laser therapy. Also, the stimulating effect of anti-inflammatory and reparative processes of laser therapy, in combination with interference therapy, reliably improves the patient's condition and increases the range of motion in the joint. Based on the results obtained in the study, combination of interferential current therapy and laser therapy helps to restore traumatic injuries of soft tissues, probable reduce of rehabilitation period and optimize the return to sport activity.

**Key words:** injuries of shoulder, shoulder function, combined physiotherapy

**December 09-11, 2022 / Tbilisi, Georgia**

**THE CAUSE OF MALOCCLUSION**

*Avtandil Bakradze, M.D., Ph.D*

*Tbilisi State Medical University, Dentistry, Orthodontics, Tbilisi, Georgia.*

**ABSTRACT**

A main factor for crooked teeth is related to the size of jaws. In order the jaws to develop properly, they should provide enough room for all of the thirty-two teeth that grow in the mouth. Over time, our teeth have grown crooked, but our jaws have grown smaller. The dominant explanation for this trend is mainly genetic influence and some well-known syndromes. William R. Proffit in his book -''Contemporary Orthodontics'' claims, that 60% of reasons causing the malocclusion is still unknown. That's why the further research is necessary to provide specific answers on that topic. The epidemic's roots lie in cultural shifts in important daily actions we seldom think about; things like chewing, breathing, or the position of our jaws at rest, and these changes have in turn been brought about by much bigger sociohistorical developments—namely, industrialization. Its most obvious symptoms are oral and facial: crooked teeth receding jaws, a smile that shows lots of gums, mouth breathing, and interrupted breathing during sleep. That the diseases just noted are related to modern civilization is strongly indicated by the near absence of their symptoms in the evolutionary and historical records. Contrary to what has often been assumed, our article indicates that environmental factors are causing way more damage, than the genetic factors do. With a proper attention to diet, eating habits, breathing patterns, and overall oral posture (static position of the jaws and the tongue), many aspects of this epidemic, like molar impaction, could be ameliorated or avoided entirely. Jaws could return to their normal patterns of growth.

**Keywords:** Oral posture, enviromental factors, crooked teeth, industrialization.

**SPONTANEOUS PERINEPHRIC SUBCAPSULAR HEMATOMA IN A CASE OF AIDS**

*Kvloria Kakhaberi*<sup>1</sup> *Kochiashvili Giorgi*;<sup>2</sup> *Kochiashvili Davit*;<sup>3</sup>

<sup>1</sup>*Tbilisi State Medical University The First University Clinic – urologist*

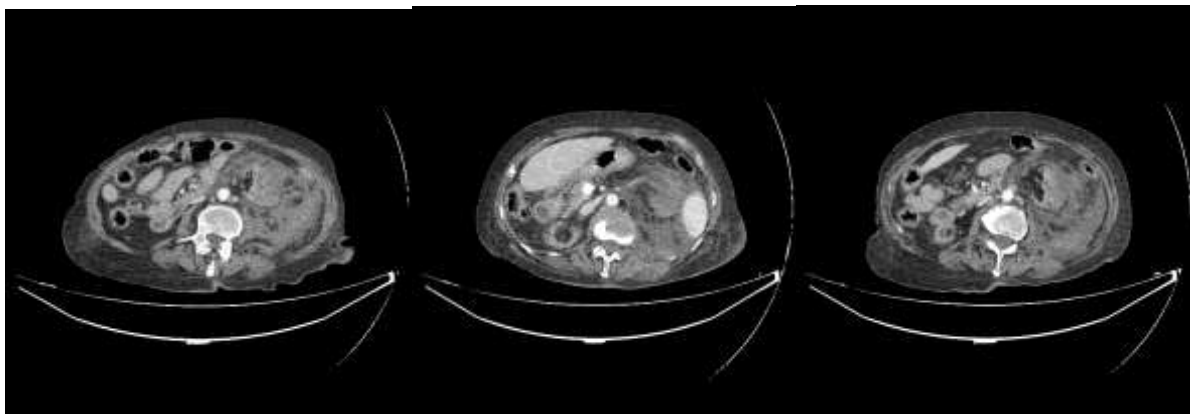
<sup>2</sup>*TSMU, Faculty of Medicine, Tbilisi, Georgia*

<sup>3</sup>*TSMU, Faculty of Medicine, Tbilisi, Georgia*

**ABSTRACT**

**Purpose:** Getting information about wary rare decease, patient history, clinics, labs. Treatment and outcome. **Background:** Spontaneous perirenal hematoma in HIV is an exceedingly rare occurrence: has been hypothesized to be related to the development of a necrotic vasculitis involving small vessels. **Content:** We report a case of spontaneous perinephric subcapsular hematoma. A 21-year-old woman with HIV was admitted with following complains: Pain in the lumbar region left side, irradiation in abdomen left side, nausea, vomiting, strong overall weakness. temperature 39-40 °C. Symptoms started with strong pain, attached high temperature and pain patient applied to clinic. PR 110/min, BP was 110-70 mm Hg, The pelvic shake syndrome was positive, urination free, urine clear. CBC WBC - 20.11 \* 10<sup>9</sup>/L , hgb 9.5 g/dl. CRP 188 mg/L, CREA 87.20 μmol/L, contras ct left kidney showed a subcapsular hematoma, and relatively new inhomogeneous hemorrhagic masses, In the middle of hematoma there was extravasation of a contrast. On the same side, the parenchyma was thin, Treatment: Nephrectomy was performed, after dissection of Gerota's fascia there was 500 ml blood with clots. Destructive kidney was identified, nephrectomy was performed, complete hemostasis, silicon drainage was infected in retroperitoneum. Wound was closed layer by layer. During the operation cryoplasma transfusion and hemotransfusion was performed. 3 hours after operation, patient was fully recovered from anesthesia, she was hemodynamic stable. On 3-d day patient was fully active already, Patient discharged on eighth day without drainage. After 2 weeks the wound was completely healed, Hystomorfolological conclusion: lymphoplasmocistal infiltration – renal acute infection damage. **Conclusions:** In our opinion this case is interesting because that spontaneous perinephric subcapsular hematoma is very rare in patients with hiv. In patients with perinephric haematoma HIV infection should be excluded, and treatment must be individually choosed.

**Key words:** Spontaneous perirenal hematoma, HIV.



**FOOD PROTEIN-INDUCED ALLERGIC PROCTOCOLITIS IN THREE MONTH OLD INFANT: CASE REPORT**

*Ekaterine Uberi*<sup>1</sup>

<sup>1</sup> *Givi Zhvania Academic Clinic of Pediatrics, Tbilisi State Medical University, Department of Pediatrics, Tbilisi, Georgia.*

*Ekaterine Nakhutrishvili*<sup>2</sup>

<sup>2</sup> *Givi Zhvania Academic Clinic of Pediatrics, Tbilisi State Medical University, Department of Pediatrics, Tbilisi, Georgia.*

*Peter Samuel*<sup>3</sup>

<sup>3</sup> *Tbilisi State Medical University, International Faculty of Medicine, Tbilisi, Georgia.*

*Naser Izziddin Abdel Hadi Rawashdeh*<sup>4</sup>

<sup>4</sup> *Tbilisi State Medical University, International Faculty of Medicine, Tbilisi, Georgia.*

**ABSTRACT**

Cystic fibrosis (CF) is a chronic, progressive, and often fatal genetic disease, also being the most common genetic disease to be identified among the Caucasians population. Food protein-induced allergic proctocolitis (FPIAP) is a type of delayed inflammatory non-IgE mediated gut food allergy that is prevalent among the pediatric age groups. This is the case report of a 3-month-old female infant presenting with symptoms of FPIAP with underlying cystic fibrosis. The manifestation of symptoms started after switching dietary nutrition from breast feeding to cow's milk, the main accompanying symptoms in the patient were feeding intolerance, vomiting, skin rashes, peripheral edema and signs that indicated failure to thrive due to insufficient weight gain. Following careful clinical examination and identification of FPIAP, dietary substitution was prescribed, however this did not yield satisfactory results which consequently raised suspicion towards an additional associated pathology which was later confirmed as CF through genetic testing. Eventually the patient was treated with pancreatic enzyme replacement therapy (PERT) in addition to the dietary changes, which resulted in the improvement of the clinical picture. Our case report highlights the rarity of both diseases being concurrently present in one individual and the importance of combined medical treatment for positive clinical outcomes. By discussing the complexity and challenges corresponding to the diagnosis of FPIAP & CF, this case report should serve as encouragement for early screening of CF in the pediatric population and help pediatricians to recognize, diagnose and treat the sequelae of symptoms associated with these diseases.

**Keywords:** Food protein-induced allergic proctocolitis (FPIAP); Cystic Fibrosis (CF); Pediatric; Screening

**December 09-11, 2022 / Tbilisi, Georgia**

**A CASE REPORT: ACUTE MYOCARDIAL INFRACTION AND DEATH IN ASYSTOLE AFTER PRIMARY CORONARY ANGIOPLASTY**

*Temur Kopadze<sup>1,2</sup>; Anzor gogiberidze<sup>3</sup>*

*<sup>1</sup>Faculty of Medicine of Tbilisi State Medical University, Georgia;*

*<sup>2</sup>Student Scientific-Research Club "ENDEAVOR" of Scientific Research-Skills Center of TSMU, Georgia;*

*<sup>3</sup>Department of Normal Anatomy of TSMU, Georgia*

**ABSTRACT**

**Introduction:** Acute myocardial infarction is myocardial necrosis resulting from acute obstruction of a coronary artery. In this report, we review a case of a 66 years old male patient with acute myocardial infarction.

**Method:** Case report

**Case :** Without any prior symptom, he started to have severe chest pain and sought emergency medical care after about 24 hours, due to pain persistence. The patient was aware of being hypertensive and was a smoker. At physical examination he had a heart rate of 90 bpm and blood pressure of 110/70 mmHg. Lung examination showed no alterations. Heart assessment showed a systolic murmur in the lower left sternal border and mitral area.

**Result:** The patient underwent coronary angiography, which disclosed proximal occlusion of the left anterior descending artery with images suggesting the presence of thrombi. He was submitted to balloon-angioplasty in the affected segment without restoration of distal coronary flow (unsuccessful procedure) and the patient developed irreversible cardiac arrest and died.

**Discussion:** The autopsy confirmed acute myocardial infarction, which was very extensive, affecting the left ventricular anteroseptal wall and the right ventricular anterior wall. It is noteworthy the fact that the detailed examination of the ventricular septum showed the presence of two previous microinfarctions, an old (healed) one and an ongoing one. The presence of atherosclerosis of the coronary arteries was identified, with massive plaques in the proximal segment of the left anterior descending artery, which resulted in chronic obstruction of 80% of the lumen. It is known that acute coronary occlusions with luminal thrombosis are usually associated with large lipid-core plaques, which undergo rupture due to the instability of their thin fibrous cap, as observed in this case. Aside from the great extent of the infarcted area, the patient developed an important mechanical complication of acute myocardial infarction, the occurrence of ventricular septal rupture with the establishment of VSD - which certainly aggravated his hemodynamic condition, progressing to cardiogenic shock -, acute pulmonary edema and death. It should be emphasized that the patient had two classic risk factors for atherosclerosis and myocardial infarction: systemic hypertension and chronic smoking.

**A CASE REPORT: CLARITHROMYCIN-NIFEDIPINE INTERACTION AS POSSIBLE CAUSE OF VASODILATORY SHOCK**

***Vakhtang Mazanashvili<sup>1,3</sup>***

*<sup>1</sup>Faculty of Medicine of Tbilisi State Medical University, Georgia;*

*<sup>3</sup>Students' Scientific Society of Tbilisi State Medical University, Georgia:*

***Mariam Kipshidze<sup>1,2,3</sup>***

*<sup>1</sup>Faculty of Medicine of Tbilisi State Medical University, Georgia;*

*<sup>2</sup>Student Scientific-Research Club "ENDEAVOR" of Scientific Research-Skills Center of TSMU, Georgia;*

*<sup>3</sup>Students' Scientific Society of Tbilisi State Medical University, Georgia*

***Luiza Gabunia<sup>4</sup>***

*<sup>4</sup>Director of Scientific Research-Skills Center, Associate Professor of Medical Pharmacology Department of Tbilisi State Medical University*

**ABSTRACT**

**Objective:** To characterize the risk of acute adverse events following coprescription of clarithromycin compared with azithromycin or nifedipine in older adults taking a calcium-channel blocker.

**Case:** A 77-year-old male with uncontrollable hypertension developed shock, heart block, and multiorgan failure 2 days after clarithromycin was added to his antihypertensive treatment (nifedipine, captopril, doxazosin). Invasive monitoring revealed hyperdynamic shock with decreased systemic vascular resistances.

**Results:** This life-threatening clinical picture, including shock and heart block, was possibly the result of a pharmacokinetic interaction between clarithromycin and nifedipine.

**Discussion:** Nifedipine is metabolized by isoenzyme CYP3A4. This metabolic pathway is inhibited by clarithromycin, thus potentially increasing the plasma Nifedipine concentration, which may lead to excessive calcium-channel blocker effects. Clinical manifestations of excessive calcium-channel blockade comprise hypotension or vasodilatory shock and heart block, as in our case. An objective causality assessment revealed that this drug interaction was the possible cause of these adverse effects. Because of an initial diagnosis of septic shock, suspicion of this entity was delayed and specific diagnostic and treatment were not possible.

**Keywords:** Clarithromycin-Nifedipine interaction; calcium-channel blocker; hypertension; shock.



**MULTIPLE LOCATED INDEPENDENT MALIGNANT TUMORS – MALIGNANT MIXED MULLERIAN TUMOR, INVASIVE DUCTAL CARCINOMA WITH MTS IN AXILLARY LYMPH NODES AND RIGHT LUNG - A CASE REPORT**

***Boris Bendeliani***<sup>1</sup>

<sup>1</sup>*Faculty of Medicine of Tbilisi State Medical University, Georgia;*

<sup>1</sup>*Student Scientific-Research club “ENDEAVOR” of Scientific Research-Skills Center TSMU, Georgia.*

<sup>1</sup>*ORCID ID: 0000-0002-7432-4062*

***Nino Kikvadze***<sup>2</sup>

<sup>2</sup>*Faculty of Medicine of Tbilisi State Medical University, Georgia;*

<sup>2</sup>*Student Scientific-Research club “ENDEAVOR” of Scientific Research-Skills Center TSMU, Georgia.*

<sup>2</sup>*ORCID ID: 0000-0001-6033-270X*

***Gigi Gorgadze***<sup>3</sup>

<sup>2</sup>*Faculty of Medicine of Tbilisi State Medical University, Georgia;*

<sup>2</sup>*Student Scientific-Research club “ENDEAVOR” of Scientific Research-Skills Center TSMU, Georgia.*

<sup>3</sup>*ORCID ID: 0000-0002-7885-639X*

***Nana Chikhladze***<sup>4</sup>

<sup>4</sup>*Caraps Medline Tbilisi, Georgia*

***Margalita gogoladze***<sup>5</sup>

<sup>5</sup>*General Surgery Department of Tbilisi State Medical University, Georgia.*

<sup>5</sup>*ORCID ID: 0000-0002-3881-1672*

**ABSTRACT**

In this paper will be reviewed one of the rarest clinical cases. Generally, it is called multiple independent malignant tumors. In this case, diagnosis includes Malignant mixed mullerian tumor (MMMT), which is a particularly rare type of cancer that mostly occurs in postmenopausal women, and Invasive ductal carcinoma (IDC) with MTS in the left lymphatic nodes and right lung, which is the most common type of breast cancer spread in globe.

**Case report:** A 73-year-old postmenopausal woman presented with a history of lower abdominal pain and weight loss. Transvaginal ultrasound revealed an enlarged uterus with cystic mass. A total radical hysterectomy was done. In the same year, new kinds of symptoms developed, although they were not related to Uterus cancer and surgical procedure. The patient noticed the right breast dimpling with the thickening of the nipple. The thoracic CT scan revealed the unknown origin breast cancer, with contralateral MTS in the right axillary lymphatic nodes and right lung. Depending on the results of the histomorphology/immunohistochemistry tests that were performed on the tissue taken from the right breast biopsy, chemo-target therapeutic treatment was selected.

**Conclusion:** the diagnosis of MMMT with the other independent IDC and MTS in lung and axillary lymph nodes is a particularly rare clinical case, depending on the difficulties of emotional and psychological factors. The management of treatment is complicated. This case report grips the mechanism of developing those two multiple located independent malignant tumors, surgical-therapeutic treatment and prognosis.

**Key words:** Malignant mixed mullerian tumor, Invasive ductal carcinoma, MTS, uterus, breast.

**PIG-TO-HUMAN HEART TRANSPLANTATION – CHALLENGES AND OUTCOMES**

*Ana Bitskinshvili*

*Faculty of Medicine of Tbilisi State Medical University, Georgia.*

*Student Scientific-Research Club “ENDEAVOR” of Scientific Research-Skills Center of TSMU, Georgia.*

**ABSTRACT**

Scarcity of hearts from human donors is the major factor constraining expanded application of cardiac transplantation. Each year >7% of the ≈4000 patients on the United Network for Organ Sharing waiting list die resulting from the unavailability of a suitable human donor heart. The use of pigs as a source of hearts for use as “xenografts” in humans (cardiac xenotransplantation) could potentially address the current donor heart shortfall. If predictably healthy organs were dependably available when needed, many patients who are currently not offered heart transplantation or whose condition deteriorates while waiting might also benefit.

Why pig?- The rapid development of genetic engineering techniques enables genome modifications in pigs that reduce the cross-species immune barrier. Triple-knockout (TKO) pigs (in which expression of the 3 known pig carbohydrate xenoantigens has been deleted) are an optimal source of organs for transplantation into human recipients, many of whom do not have natural antibodies against TKO pig cells.

Are pig and human hearts identical?-There are minor differences, for example -The porcine organ has a classic ‘Valentine heart’ shape-unguligrade stance. The human heart, in contrast, is trapezoidal in silhouette, reflecting man's -orthograde posture. The morphologically right atrium of the pig was characterised by the tubular shape of its appendage (a feature observed on the left in the human heart). The porcine superior and inferior caval veins opened into the atrium at right angles to one another, whereas in man the orifices are directly in line. Transplantation is accompanied by many risks. One of the most important and dangerous are the human immune response and cytomegalovirus (PCMV).

The operation which was held on January 7th January of 2022 proved that the transplantation of a pig's heart to human is not just a hypothesis. 57-year-old man with nonischemic cardiomyopathy who was dependent on venoarterial extracorporeal membrane oxygenation (ECMO) and was not a candidate for standard therapeutics, including a traditional allograft, received a heart from a genetically modified pig.

**Conclusion:** The recent groundbreaking clinical results showing the feasibility of transplanting transgenic pig organs into humans raise hopes that xenotransplantation can help solve the critical shortage of human donor organs.

**Keywords:** transplantation, xenotransplantation, heart transplantation, pig's heart.

**A CASE REPORT: COVID-19 VACCINATION ON ASTHMATIC INDIVIDUALS**

**Mariam Kipshidze**<sup>1,2,3</sup>

<sup>1</sup> Faculty of Medicine of Tbilisi State Medical University, Georgia;

<sup>2</sup> Student Scientific-Research Club "ENDEAVOR" of Scientific Research-Skills Center of TSMU, Georgia;

<sup>3</sup> Students' Scientific Society of Tbilisi State Medical University, Georgia; 1

**Giorgi Choladze**<sup>4,5,6</sup>

<sup>4</sup> doctor cardiologist

<sup>5</sup> invited lecturer at Tbilisi State Medical University

<sup>6</sup> holder of doctoral incentive project and Phd research grant

**Nino Didbaridze**<sup>7</sup>

<sup>7</sup> Assistant professor of Immunology Department

**ABSTRACT**

**Objective:** to report the case of COVID-19 vaccination on asthmatic female.

**Methods:** Case report

**Introduction:** Asthma is a disease of diffuse airway inflammation. Symptoms and signs include dyspnea, chest tightness, cough, and wheezing. The diagnosis is based on history, physical examination, and pulmonary function tests. Treatment involves controlling triggering factors and drug therapy, most commonly with inhaled beta-2 agonists and inhaled corticosteroids. There is ongoing debate regarding the role of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection in asthma exacerbation, and its long-term impact on the lung function of individuals with asthma. In contrast, the potential impact of coronavirus disease 2019 (COVID-19) vaccination on asthma is entirely unexplored.

**Case study:** This study examined a challenging case of severe asthma exacerbation in a 28-year-old female following two doses of the mRNA-based vaccine BNT162b2 (Pfizer-BioNTech) at IRCCS Policlinico San Matteo in Pavia, Italy. The patient, a fourth-year resident at the hospital, was vaccinated in early 2021. She was an occasional smoker with a 10-year history of asthma and seasonal allergic rhinitis. She tested negative for SARS-CoV-2 on several molecular swabs and serology tests.

**Results:** After receiving the second dose of vaccine, the patient started to experience worsening of respiratory symptoms. Following several episodes and a severe asthma attack, the patient required treatment with mepolizumab, a biologic drug (interleukin-5) antagonist monoclonal antibody.

**Conclusion:** This single case study is insufficient to draw conclusions about the association between asthma exacerbation and the COVID-19 vaccine. While the cause-effect link between vaccination against SARS-CoV-2 and worsening of asthmatic disease might only be suggested at present, this case is a valuable prompt for further investigation. This is particularly true from the perspective of mass vaccination of adolescents and children currently underway across the globe. Many studies have shown that mRNA vaccines are likely to induce production of interferon I (IFN-1) and it is known that the bronchial epithelium of asthmatics produces less IFN-I in response to a viral infection.

**Keywords:** COVID-19 vaccination; Mass vaccination; Asthma; SARS-CoV-2.

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**A CASE REPORT : MEDIAN ARCUATE LIGAMENT SYNDROME**

***Mariam Gigiadze<sup>1,2</sup>; Mariam Beriashvili<sup>1,2</sup>***

*<sup>1</sup>Faculty of Medicine of Tbilisi State Medical University, Georgia;*

*<sup>2</sup>Student Scientific-Research Club "ENDEAVOR" of Scientific Research-Skills Center of TSMU, Georgia.*

***Erekle Gigiadze<sup>3</sup>***

*<sup>3</sup>k. Eristavi National Center Of Experimental And Clinical Surgery, Department Of Radiology*

**ABSTRACT**

**Objective:** to report the clinical cases of Median arcuate ligament syndrome

**Methods:** case report

**Case 1 :**A 55-year-old woman presented with abdominal pain and nausea. She had a 3-year history of chronic and recurrent postprandial abdominal pain and weight loss. Established right breast cancer 1 month ago. The patient is undergoing neoadjuvant chemotherapy.

**Results:** An ultrasound and X-ray examination of the abdomen relieved excessive fluid content in the stomach and bowel. Computed Tomography Angiography (CTA) showed the narrowing and compression of celiac artery by median arcuate ligament.

**Case 2:** A 44-year-old woman presented for medical check-up with a history of the radical hysterectomy of the uterus, related to oncology. A CT examination was performed.

**Results:** CT with contrast determined MALS.

**Discussion:** Median arcuate ligament syndrome – celiac artery compression – Dunbar syndrome is a rare, but clinically significant condition that should be considered in patients with chronic abdominal pain, weight loss and gastrointestinal complaints. The disease is caused by the compression of the celiac artery by an abnormally low lying ligament which results into postprandial abdominal pain, weight loss, bruit. However, 10 to 24% of population may not have any symptoms of disease. Once suspected, patients should undergo mesenteric duplex ultrasound. CTA shows typical "J-hook" conformation of the celiac artery. Treatment for MALS is surgical.

**Key words:** Median arcuate ligament syndrome; celiac artery compression; CTA;

**CUSHING'S SYNDROME OR COMMON ACUTE CARDIOLOGIC PATIENT? – A CASE REPORT**

*Giorgi Zhorzholiani<sup>1</sup>, Gigi Gorgadze<sup>1</sup>, Ia avaliani<sup>2</sup>, Marina Kuparadze<sup>2</sup>, Khatuna Jalabadze<sup>3</sup>*

*<sup>1</sup>Faculty of Medicine of Tbilisi State Medical University, Tbilisi, Georgia*

*<sup>2</sup>Department of Propedeutics of Internal Diseases of TSMU, Tbilisi, Georgia*

*<sup>3</sup>Clinic Guli, Tbilisi, Georgia*

**Introduction:** The diagnosis of Cushing's syndrome is challenging to endocrinologists as patients often present with an insidious history, together with subtle external clinical features. Moreover, complications of endogenous hypercortisolism, such as visceral obesity, diabetes, hypertension and osteoporosis, are conditions commonly found in the population, and discerning whether these are truly a consequence of hypercortisolism is not straightforward. To avoid misdiagnosis, a careful investigative approach is essential.

**Case report:** A 60-year-old patient with heart failure and arterial hypertension entered the clinic. Face - red in color, with slightly pronounced hirsutism. Abdominal and neck fat, thin limbs, single subcutaneous bruise on the forearm. The patient underwent coronary angiography, which revealed diffuse damage to the coronary arteries, without hemodynamically significant stenosis, and drug therapy was recommended. Echographically, moderate fibrosis of the left atrium, significant fibrosis of the aortic annulus and cusps of the right cavities was noted. Fibrosis of the mitral annulus and chambers. Contractile function is impaired mainly at the expense of the septal and apical segments. Doppler: first-degree aortic insufficiency, third-fourth degree severe mitral and tricuspid regurgitation. Tricuspid valve rigid, significant pulmonary hypertension. No fluid in the pleural cavity. Intracardiac shunt not revealed by contrast examination. To summarize, the patient had bilateral heart failure, mitral and tricuspid valve insufficiency, and arterial hypertension. The diagnosis reached a dead end - it became important to differentiate whether it was a common cardiology case, or the symptoms caused by Cushing's syndrome, which was suspected based on the patient's physiognomy, or carcinoid syndrome, based on intense fibrosis of the valve. For differentiation, 24-hour analyzes of adrenocorticotrophic hormone and cortisol in urine were prescribed to the patient. Both indicators were within the normal range.

**Conclusion:** The case is particularly interesting because all parameters indicated Cushing's syndrome, although each was accompanied by an exclusion circumstance. It is worth noting that there exists Cyclic Cushing's syndrome (also known as intermittent or periodic) - a disease characterized by periods of transient hypercortisolemia shifting into periods of normo- and/or hypocortisolemia. Diagnosis of cyclic Cushing's syndrome is based on at least three periods of confirmed hypercortisolemia interspersed by two periods of normocortisolemia. Cyclic Cushing's syndrome is one of the greatest challenges in modern endocrinology due to its diverse clinical picture, unpredictable duration and frequency of phases, and various etiologies. Thus, Patient needs Frequent measuring of urinary cortisol or salivary cortisol levels.

**THROMBOTIC MICROANGIOPATHY DUE TO SOLITARY LYMPHOMA OF SPLEEN**

*Nithesh Hariharan*

*Tbilisi State Medical University, USMD program*

**ABSTRACT**

Thrombotic microangiopathy is a cluster of clinical syndromes including the formation of micro vascular thrombus, microangiopathic haemolytic anemia and end organ damage, usually the kidneys, heart, brain or GI system. Classical causes are TTP, Shiga toxin induced HUS or complement over activation in atypical HUS. However, metastatic cancers, especially to the bone marrow can also result in thrombotic microangiopathy. This is because of abnormal angiogenesis in the marrow with aggressive growth of tumours and secondary myelofibrosis may injure the endothelial cell lining of the marrow vasculature by direct invasion. Damage on endothelium results in release of vWF which causes platelet clumping and formation of clots in small vessels. As RBC goes through clots, it results in haemolysis and formation of schistocytes. This is the case of a 58-year-old man who had splenomegaly due to solitary lymphoma in his spleen and was admitted to the hospital for splenectomy. His total and direct bilirubin were high, thrombocytopenic and had normocytic anemia (Hb- 8). However, splenectomy couldn't be done cause his platelet count was even after 5 days after admission and there was a risk of increased bleeding. He was discharged and 3 days later, re admitted to the hospital cause of diffuse abdominal pain, fever (38.9), chills. Lab reports showed high creatinine (206), anion gap metabolic acidosis, increased lactate, elevated LFT, normocytic anemia with severe thrombocytopenia, increased procalcitonin. CT scan showed massive splenomegaly and colon ischemia. The patient had thrombus formation in renal arteries and mesenteric vessels, resulting in splenic flexure necrosis and sepsis.

**Keywords:** Thrombotic microangiopathy, Lymphoma of the spleen, TTP, atypical HUS, chemo induced thrombotic microangiopathy.

**TACROLIMUS INDUCED SUBCONJUNCTIVAL HEMORRHAGE: CASE REPORT**

*Nino Karanadze*<sup>1</sup>

<sup>1</sup> *Tbilisi State Medical University, Department of Ophthalmology – Lions Eye Diabet Clinic, Tbilisi, Georgia.*

*Peter Samuel*<sup>2</sup>

<sup>2</sup> *Tbilisi State Medical University, International Faculty of Medicine, Tbilisi, Georgia.*

*Salah Rabea Salah Al-Tamary*<sup>3</sup>

<sup>3</sup> *Tbilisi State Medical University, International Faculty of Medicine, Tbilisi, Georgia.*

*Mohammed Fathi Farhan Alrawashdeh*<sup>4</sup>

<sup>4</sup> *Tbilisi State Medical University, International Faculty of Medicine, Tbilisi, Georgia*

**ABSTRACT**

Subconjunctival hemorrhage (SCH) is the bleeding from small blood vessels that occurs between the conjunctiva and the episcleral. This ocular condition is relatively common in ophthalmological practice. The cause of SCH is simply classified as traumatic and spontaneous. Traumatic SCH is by far the most prevalent and it is relatively common amongst contact lens users due to the relative friction between the lens and the conjunctiva. Ocular surgery is the second leading cause of traumatic SCH. Spontaneous SCH is more complex in presentation as it has a wide array of causes ranging from elevated venous pressure and strenuous exercise to causes such as adverse reaction to pharmacological drugs. This case report is based on a 55 year-old female presenting with spontaneous SCH. The patient had recently undergone a recent kidney transplantation surgery months ago and is currently on immunosuppressive therapy using **tacrolimus** (FK506). Tacrolimus is a potent immunosuppressor alongside other drugs such as cyclosporine, tacrolimus acts as a calcineurin phosphatase inhibitor thereby inhibiting T cell development. The use of tacrolimus is associated with optic neuropathy such as Central retinal vein occlusion and subconjunctival hemorrhage causing blurry vision in patients that are on this drug regimen. The patient has a long history of hypertension and this was supportive towards the diagnosis of SCH as hypertension proves to be one of the most common risk factors towards spontaneous SCH. The patient has had three episodes of SCH and had consulted the ophthalmologist following the third episode. Standard visual examination was followed, the red eye due to SCH was confirmed using a slit lamp and the logMAR visual acuity was recorded to be low on both eyes however the correction with +1.50 spherical lens for right and +1.25 spherical lens for left yielded perfect 1.0 acuity. Tonometry and other tests were within normal range. Ophthalmoscopy reveals retinal vessel narrowing. This case report highlights the importance of correlating the association between spontaneous SCH and the use of tacrolimus. In patients that rely on immunosuppression through tacrolimus usage, additional risk factors for possible ocular manifestations should be considered and addressed.

**Keywords:** Subconjunctival Hemorrhage (SCH) ; Tacrolimus; Hypertension

**A CHALLENGING CASE OF PTEN HAMARTOMA TUMOR SYNDROME IN A JUVENILE MALE WITH CONGENITAL MACROCEPHALY: A CASE REPORT**

***Sheeda Jabeen<sup>1</sup>***

*<sup>1</sup>Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

*<sup>1</sup>ORCID ID: 0000-0003-3039-463X*

***Shifa Mohamed Rafi<sup>1</sup>***

*<sup>1</sup>Tbilisi State Medical University, Faculty of Medicine, Tbilisi, Georgia*

*<sup>1</sup>ORCID ID: 0000-0003-3959-3395*

***Kakha Bregvadze<sup>2</sup>***

*<sup>2</sup>Tbilisi State Medical University, Department of Molecular and Medical Genetics, Tbilisi, Georgia*

*<sup>2</sup>ORCID ID: 0000-0002-6506-0632*

***Tinatn Tkemaladze<sup>2</sup>***

*<sup>2</sup>Tbilisi State Medical University, Department of Molecular and Medical Genetics, Tbilisi, Georgia*

*<sup>2</sup>ORCID ID: 0000-0003-1924-6695*

**Introduction:**

*PTEN* is a tumor suppressor gene that regulates cellular growth, migration, and apoptosis via the P13K/AKT/mTOR signaling pathway. PTEN hamartoma tumor syndrome (PHTS) is caused by heterozygous pathogenic variants in the *PTEN* gene and includes several related syndromes such as Cowden syndrome (CS), Bannayan-Riley-Ruvalcaba syndrome (BRRS), PTEN-related Proteus syndrome (PS), and Proteus-like syndrome (PLS). Patients with PHTS have an increased lifetime risk of developing thyroid, breast, endometrial, and other cancers.

**Case Description:**

We present a case of a 12-year-old male with congenital compensated macrocephaly evident on prenatal ultrasound. He had delayed speech and was diagnosed with autism spectrum disorder (ASD) since early childhood. Currently he has mild intellectual disability and learning difficulties at school. From 5 years he developed progressive hypertrophy of the left arm and at 7 years surgery was performed to remove masses in left ulnar vicinity. However, tissue growth progressed and at 10 years biopsy from the lesion revealed hamartoma with vascular and myxoid lipomatous elements. Currently hypertrophy is slowly progressive limiting elbow, wrist, and finger extension. At 11 years palpable nodules in the neck area became apparent. Ultrasound examination revealed thyroid hypertrophy with multiple small nodules and the biopsy confirmed follicular neoplasia. Upon genital examination multiple 0.2-1 cm penile freckles were evident. At the age of 12 whole exome sequencing (WES) was performed, which revealed heterozygous pathogenic variant in the *PTEN* gene: c.388C>T (p.Arg130\*). Parental segregation analysis confirmed *de novo* status. Based on the diagnosis corresponding multidisciplinary health surveillance plan was planned.

**Discussion:**

Presented case highlights that PHTS should be suspected in any individual with isolated or combined findings of macrocephaly, hemihypertrophy, ASD and multiple cancers. WES provides high diagnostic yield in patients with unexplained progressive multiorgan involvements. Early diagnosis of PHTS is of particular importance to warrant appropriate surveillance to detect any tumors at the earliest stage.

**Keywords:** PTEN, PHTS, macrocephaly, cancer, penile freckles



**DIGITAL TRANSFORMATION AND CHALLENGES IN THE SUPPLY CHAIN**

*Lily Petriashvili<sup>1</sup>*

*<sup>1</sup>Georgian technical University, Faculty of Informatik and Control Systems, Department of Program Engeneering, Tbilisi, Georgia.*

*<sup>1</sup>ORCID ID: 0000-0003-3593-4877*

*Tamar Lominadze<sup>2</sup>*

*<sup>2</sup>Georgian technical University, Faculty of Informatik and Control Systems, Department of Information Technology, Tbilisi, Georgia.*

**ABSTRACT**

Digital transformation of the world economy and the dynamics of the colossal growth in terms of information flows have made relevant adoption of innovative technologies in the processes of business management. Data analysis, risk assessment technologies and decision support systems enable companies to adapt to modern challenges. In the current conditions of globalization, the consumer has the priority due to which quality of service and timely delivery of the required products determine the competition and trends among large corporations.

One of the key areas of an enterprise facility is supply, which consists of a chain of operations determining not only the efficiency of the product distribution, but also the quality of the product delivered to customers. A supply chain represents well-defined and efficiently managed organizational processes creating all the conditions for customers to receive high quality product and service.

A technical progress has brought new challenges to the people as to how healthy the products we daily eat are, because the amount of hazardous products has already reached the apogee.

Nowadays, the economic potential of many countries depends almost entirely on exports. In such countries, most people focus on purchasing cheap products giving a good chance to dishonest local entrepreneurs and exporters to add hazardous substances to the content of products that reduce the operating expenses tied to the production of goods and are much cheaper, but significantly damage human health and cause various diseases. Such types of products are mainly foodstuffs, building materials, clothing, toys, etc.

The purpose of our research is to use artificial intelligence carry out an analysis of the product identification information and to identify hazardous products at the customs checkpoints and the locations the vendible items are delivered to customers from. Through this experimental research, we have highlighted several commodity groups and substances that are potentially harmful and dangerous to human health.

**Keywords:** Digital transformation, SCM, Human health, AI (Artificial intelligence).

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**MARKETING PLAN OF DIFLUCAN**

*Nana Dugashvili*

*TSMU, Social and klinikal farmasi, Department of Social and Clinical Pharmacy, Tbilisi, Georgia,*

*Ketevan Kakabadze*

*Ltd. "IP Group", Tbilisi, Georgia*

*Nino Ghvedashvili*

*Ltd. "IP Group", Tbilisi, Georgia*

*Natia Kvizhinadze*

*TSMU, Social and klinikal farmasi, Department of Social and Clinical Pharmacy, Tbilisi, Georgia*

*Ana Tughushi*

*"PSP" Pharma, Tbilisi, Georgia*

*Tbilisi State Medical University, Tbilisi, Georgia*

**Relevance of the topic**

There are two main criteria for determining the relevance of a topic: the product selected and the local marketing landscape.

Diflucan (Fluconazole 150mg Caps. # 1 - Original Product, Pfizer) is a systemic antifungal and has a 5% market share in the local market, while being much more affordable than market leaders and "followers". It has much more affordable price compared to "followers". The local market is saturated with generic fluconazole's and in the current context it's important to identify those "gaps" and devise elimination strategies to achieve a better marketing position.

**Reason of research**

Based on the knowledge gained from the master's program and the available reliable sources, a marketing plan for Diflucan (Fluconazole 150 mg. Caps. # 1) is developed according to the standard classic structure.

**Research tasks**

The main task of the community is to find specific solutions for the set goals in the same market conditions.

**Subject of the topic**

The subject of the topic is to create a marketing plan for the product - Diflucan (150 mg Caps. # 1) by generating profitable actions, using the available resources properly and fully adhering to the structural components.

**Results**

According to the results, Diflucan's marketing goal for 2022 will be to reach 8% of the market share and 7% of the total (40% total increase). Diflucan (150 mg caps.) Core marketing strategy for the next year is to increase the market share by planning consistent marketing activities, actively using the price advantage and expanding the reach of the target audience by increasing the number of medical representatives.

**Keywords:** Diflucan (Fluconazole 150 mg), Marketing Plan, resources, marketing activities.

**MEDICAL PRE-CLINICAL LABORATORY SCIENCES**

***Kristine Museliani<sup>1</sup>***

*Agricultural University of Georgia,  
Faculty of Agricultural Science, Tbilisi, Georgia*

***Tamriko khobelia<sup>2</sup>***

*Georgian Technical University,  
Faculty of Chemical Technology and Metallurgy, Tbilisi, Georgia.*

***Edisher kvesitadze<sup>3</sup>***

*Georgian Technical University,  
Faculty of Agricultural Sciences and Biosystems Engineering, Tbilisi, Georgia.*

**ABSTRACT**

Physiological changes in the body depend on biologically active substances, with the help of which biochemical processes are carried out. These include vitamins, enzymes, certain products obtained with the help of microorganisms, antibiotics, etc. An excess or deficiency of their quantity causes diseases, and laboratory detection of diseases caused by such substances and proper treatment of the patient is of great importance for human health. Laboratory medicine is an integral component of patient care. Approximately 60% to 70% of medical decisions are based on laboratory results. Physicians in specialties that order the tests are teaching medical students laboratory medicine and test use with minimal input from laboratory scientists who implement and maintain the quality control for those tests. Based on that, the development of laboratory skills is of great importance for medical students. Developing laboratory skills begins with disciplinary fields such as biochemistry, immunology, microbiology, and others. Today, in these fields of medical direction, for various reasons, less time is devoted to laboratory methods, which can negatively affect the development of a student as a professional. To solve this problem, our scientific team has developed pre-clinical laboratory kits, which allow the practical component to be carried out in the relevant field. kits are tailored to the student, academic time, and the learning provided by the program. They contain all the consumables that the student needs to conduct the pre-clinical lab test, it is designed for the student's individual work, in which they are helped by specially created instructions, where each stage is written and easy to understand, that ensure maximum involvement of students and the development of independent work skills. Kits contribute to the formation of laboratory skills, increasing competence in each field mentioned above and acquiring prior knowledge for clinical practice.

**Keywords:** Laboratory medicine, laboratory kits, test, practice, health.

**THE NEED TO MAINTAIN A HEALTHY WAY OF LIFE TO ENSURE THE PHYSICAL AND MENTAL HEALTH OF THE POPULATION**

*Marina Shakarashvili, Manana Abuladze, Devi Tabidze, Levan Baramidze*

*Tbilisi State Medical University, Tbilisi, Georgia*

**ABSTRACT**

According to the data of the World Health Organization "WHO", human health is determined: 50-55% by following a healthy way of life, 25% by environmental conditions, 15% by genetic factors and 5% by the activity of the healthcare system. A healthy lifestyle is a way of promoting a person's life, which aims to promote health. It is also considered as the basis of disease, mortality prevention and life expectancy increase. A healthy lifestyle includes all those elements of behavior aimed at improving individual and public health. The research shows that promotion of a healthy lifestyle in Georgia should be strengthened as the primary value of health, prevention of bad habits and unhealthy behavioral attitudes. At present, a large part of the population is unaware of the positive and negative effects of a healthy lifestyle and bad habits. Based on the relevance of the problem, the aim of the work and the task of the research is the physical and mental health of a person, which is an integral part of health. As it is known from the definition of health - health is complete physical, mental and social well-being. It is important to correctly analyze the state of health, which unconditionally reflects the ability of the body to adapt to the living environment. During physical and mental health of a person, there are no violations of structural, functional and adaptive mechanisms. . Studies have established that during the onset of the disease, there is a decrease in the functional states of the organism, exhaustion, which has a direct impact on the physical and mental state of a person. Jano defined the criteria of adequacy of physical and mental health: adequate perception of a person, presence of adequate reactions to environmental factors, adequacy of actions committed by a person and the ability to adequately manage actions (response and reaction). Within the framework of the sociological research conducted by us, the following were clearly identified: 1. 723 citizens were interviewed through the social network during the research process. 2. The age distribution is: 1st group - 19-35 years, 2nd group - 55-65 years and the third group is people over 65 with chronic pathologies and under the supervision of a doctor. 3. Only 42% of the surveyed population is interested in and follows a healthy lifestyle. 4. 62% of the population suffers from various types of physical and mental disorders. 5. There is a real need to fill the lack of information in the population. 6. Unhealthy habits of life - tobacco of harmful habits are revealed. Alcohol, drugs, unhealthy diet, unsportsmanlike lifestyle and high percentage of other factors. 7. Avoidance of active involvement of governmental and non-governmental sectors in solving the problem. 8. Activation of information media in promotion of a healthy way of life. All this will actually reduce the statistical data of physical and mental health disorders in the population.

*Physical and mental health It is an integral part of health*

**THE SIGNIFICANCE OF POST-OPERATIVE BRACING IN PREVENTING KNEE ARTHROFIBROSIS AFTER ACL RECONSTRUCTION**

**Valeri Akhalkatsi<sup>1</sup>**

*<sup>1</sup>Tbilisi State Medical University (TSMU), Faculty of Physical Medicine and Rehabilitation, Department of Physical Medicine, Clinical Center of Sports Medicine and Rehabilitation, Georgia.*

**Marine Matiashvili<sup>2</sup>**

*<sup>2</sup>TSMU, Faculty of Physical Medicine and Rehabilitation, Department of Physical Medicine, Clinical Center of Sports Medicine and Rehabilitation, Georgia*

**Lela Maskhulia<sup>3</sup>**

*<sup>3</sup>TSMU, Faculty of Physical Medicine and Rehabilitation, Department of Physical Medicine, Clinical Center of Sports Medicine and Rehabilitation, Georgia*

*ORCID ID: 0000-0002-8893-374X*

**ABSTRACT**

High-energy injuries of the knee joint can cause ligament damage which may have complications in 4-6% of all cases in the form of movement limitation and arthrofibrosis. There are several intra- and extraarticular factors that could be closely connected with formation of arthrofibrosis. One of the most important factor is the utilization of knee brace as the means of immobilization during the post-operative period. There are various opinions on the matter of using a knee brace after an anterior cruciate ligament (ACL) reconstruction surgery. For instance, 85% members of the American Orthopedic Society for Sports Medicine (AOSSM) support and utilize this method. Despite the fact that movement limitations in the affected joint are rare after the aforementioned surgical procedure, the issue of preventing and eliminating knee extension deficit during the post-operative period is still relevant. The following research is based on the evaluation of the findings in 22 patients with extension deficits 2 weeks after arthroscopic ACL reconstruction surgery and it studies the effectiveness of knee brace in eliminating extension limitation during a 3-week rehabilitation period. After implementation of 5-week rehabilitation program, function of quadriceps muscle was equally improved in all patients, and at the same time, undesired effect of utilization of the knee brace during 3 weeks on the functional status of the quadriceps muscle was modest and didn't exceed 6.4%.

The results of the above mentioned research showed that utilization of knee brace in the rehabilitation process during 3 weeks is significantly effective method ( $P < 0.008$ ) for eliminating knee extension deficit in a way that the negative influence on the function of the quadriceps muscle of the affected limb stays negligible.

**Key words:** knee injury, arthrofibrosis, knee brace

**MEDICAL TOURISM AS A BRANDED PRODUCT IN THE EUROPEAN MEDICAL MARKET**

*Devi Tabidze, Ekaterine Mirvelashvili, Nino Khachapuridze, Marina Kajrishvili*

*Tbilisi State Medical University, Tbilisi, Georgia*

**ABSTRACT**

Today, medical tourism is one of the most competitive players in the country's economy. Tourism is not a new product for Georgia, while medical tourism has been developing since 2000. By 2019, 14% of the total income from tourism in the country belongs to medical tourism. According to Saxstat data, by 2022 it is expected to increase to 30%. Due to the natural and climatic diversity and territorial location of Georgia, it is possible to develop it as a branded product with high tourist potential. In the Caucasus region and beyond, there are mountain and sea resort zones in one "space", which .In general, they represent the best infrastructural environment for carrying out treatment and rehabilitation measures. To date, Georgia has registered about 200 resort zones, about 100 for medical purposes - specific air, waters, sands, mud, medicinal plants. According to WHO definition, medical tourism is the purposeful migration of those who want to receive recreation and treatment, complex high-tech services. Balneological-resort direction has one of the oldest and historical potentials in Georgia. It originated at the turn of the 19th century. Tbilisi, Borjomi, Sairme, Tskaltubo, Nunis, Ureki, Grigoleti, Upsira, Tsaishi, Tsikhisdziri, Tsemi, Tsaghveri, Shovi, Java and many others are worth mentioning among the balneological resorts. In Georgia, there are about 2000 mineral springs, whose Among them, carbonated mineral waters are the most common. Factors hindering the development of medical tourism. In order to maximize the potential of medical tourism in Georgia, it is necessary to analyze the hindering factors that prevent its development. Development of medical tourism is hindered by: poor infrastructure. Problems in the transport system, unsatisfactory sanitary-hygienic conditions. Informative and insufficient advertising activities, inconsistency of the legal base with European standards, less activities of tourist agencies, and many other elements. Based on the retrospective analysis conducted by us, the need for the development of medical tourism was highlighted.

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**DIGITAL HEALTH, CONTEMPORARY CHALLENGES AND PERSPECTIVES**

***Irine Zarnadze***

*TSMU, Department of Public Health, Health care Management, Polity and Economy; Tbilisi, Georgia*

*ORCID ID: 0000-0001-5511-437X*

***Shalva Zarnadze***

*TSMU, Deapartement of Nutrition, Aging Medicine, environmental and occupational health; Tbilisi Georgia*

*ORCID ID: 0000-0002-6895-9205*

***Dali Kitovani***

*TSMU, Department of Public Health, Health care Management, Polity and Economy; Tbilisi, Georgia*

*ORCID ID: 0000-0003-3026-4667*

***Lili Lomtadze***

*TSMU, Department of Public Health, Health care Management, Polity and Economy; Tbilisi, Georgia*

*ORCID ID: 0000-0002-1504-7587*

**ABSTRACT**

**Introduction:** Digital healthcare provides and expands the possibilities of receiving quality medical care in modern medicine. The advantages of digital healthcare can be divided into two groups. The first is the regulation of payments and co-payments for medical services, which are very sensitive, and the second is the possibility of transforming health systems.

**The purpose of the research:** consisted of assessment of digital healthcare implementation and systemic transformation in healthcare systems of different countries.

**Research Methods:** Observational study, the study was retrospective, conducted over a period of 6 months. Papers published in English and Georgian from 2015 to September 2022, a total of 45 papers, were studied and evaluated.

**Results:** An analysis of various studies has shown that: Digital health systems enable in line with the principles of financial sustainability and caring for the disadvantaged, the insurance systems were merged and enlarged to become a social insurance system to cover everyone. To effectively promote various services, in addition to establishing specialized departments and offices for various services and policy promotions. The implementation of the “Family Doctor Integrated Care Program,” the “Patient-Centered Integrated Outpatient Care Program in Hospitals,” the “Integrated Home Health Care Program,” and various programs is aimed at improving medical accessibility and quality of patient-centered medical care system, by providing patients with safe, appropriate, and continuous integrated medical services according to their needs, and to reduce the waste of medical resources.

**Conclusion:** The implementation of digital health programs promotes efforts to safeguard the medical benefits and rights of the patients. Despite the rapid development of various medical technologies, medical expenses have also risen greatly, causing financial burdens on the. Digital health systems have the responsibility with the medical providers on good communication and focuses on seeking the balance between financial and clinical needs

**Keywords:** Digital Health, Challenges, Perspectives

**THE COMPOSITE MASSES ADHESION PECULIARITIES ON THE TOOTH ENAMEL-CEMENT CONNECTION (CEJ) STRIP <sup>1</sup>**

*Professor Marina Mamaladze <sup>1</sup>*

*<sup>1</sup> Tbilisi State Medical University, Department of Odontology, Tbilisi, Georgia*

*Dr., PhD candidate Ekaterine Zarkua <sup>2</sup>*

*<sup>2</sup> Tbilisi State Medical University, Tbilisi, Georgia*

*Assoc. Professor Lia Sanodze <sup>3</sup>*

*<sup>3</sup> Tbilisi State Medical University, Department of Odontology, Tbilisi, Georgia*

**ABSTRACT**

The success of tooth restoration with composite materials depends on many factors. The widespread introduction of new generation composites and adhesive systems significantly increased the long-term operation time of teeth, raised the aesthetic parameters of the restoration and ensured the restoration of not only the anatomical indicators of the tooth, but also its function.

Despite the above, with composites, which belong to the group of plastics, the dentist faces a constant challenge in the process of filling/restoring teeth. This is primarily determined by the eclecticism of the tooth structure and the "content" of the composite. In the later, dentin's water content and especially in cementum is high.

That is why, in the case of diseases and injuries in the area of the tooth neck (cervical), where the cement covering the root is exposed and the dentin uncovered by enamel is visible, the selection of adhesive systems is of crucial importance in the tooth restoration process.

During the research, the condition of 35 human teeth was evaluated. All teeth belonged to the group of lower premolars. In the area of 15 teeth neck, class V - medium caries was diagnosed, in 10 cases of recession and 10 of wedge defects.

In the restoration process, V generation adhesive system Ena bond (Micerium) (for 18 teeth) and VII generation adhesive Peak Universal (Ultradent.corp) (for 17 teeth) were used. The tooth restoration was performed using the composite Enamel+ to ensure the maximum visual identity of the restored tooth. After one year, the quality of the restorations and the areas of depressurization were evaluated using the caries detector Sable Seek (Ultradent). During the implementation of the mentioned method, the perimeter of the marginal connection remained colored, the intensity of which was further adjusted by a specially designed algorithm. During the dental treatment, the restoration protocol was followed: adequate anesthesia, sparing, minimally invasive preparation, isolation of the operative field, restoration and post-restoration treatment of the tooth.

The results of our study revealed the following: it was found that cases of dental feelings depressurization (discoloration, deformation, increased sensitivity, etc.) when using of the VII generation adhesive system were 1.25 times more frequent, than when restoring teeth with the V generation adhesive.

**Keywords:** Composites, adhesive systems, cervical lesion, restoration.



**TRIMETAZIDINE AS A MODIFIER OF AC-MODE OF CHEMOTHERAPY-DRIVEN HYPERDYSLIPIDEMIA**

*Avagimyan A. A.<sup>1,2</sup>*

*<sup>1</sup>MD, Pathological Anatomy and Clinical Morphology Department,  
Yerevan State Medical University after M. Heratsi, Yerevan, Armenia*

*<sup>2</sup>PhD student, A. P. Avtsyn Research Institute of Human  
Morphology of FSBI "NRCS Petrovsky", Moscow, Russia*

*ORCID ID: 0000-0002-5383-8355*

*Kakturskiy L.V.<sup>3</sup>*

*<sup>3</sup>MD, PhD, MsD, Acad., Scientific Director, A. P. Avtsyn Research Institute of Human  
Morphology of FSBI "NRCS Petrovsky", Moscow, Russia*

*ORCID ID: 0000-0001-7896-2080*

## **Introduction**

Cardio-oncology confers is a multidisciplinary crisis of contemporary medicine [1]. Doxorubicin+cyclophosphamide (AC) mode of chemotherapy serves as an effective strategy for breast cancer treatment. However, the development of widely variable cardiovascular complications, from sinus arrhythmia to decompensated heart failure, have been noted [2,3]. The latter is aggravated by the fact that, despite the time map of various multidisciplinary studies conducted within the recent 60 years, the scientific world hasn't reached a consensus on the question - How to protect the heart and vessels from chemotherapy-related failure without reducing the effectiveness of chemotherapy?

## **Purpose of the study**

The present research is aimed to assess the proatherogenic potential of the AC chemotherapy mode, with substantiation of trimetazidine (TMZ) intake.

## **Material and methods**

The fundamental, randomized, controlled, experimental *in vivo* study was conducted on 80 inbred, male Wistar rats who were randomly divided into four equal groups (1 - saline, 2 - AC, 3 - AC + TMZ, 4 - TMZ). The course dosages of doxorubicin, cyclophosphamide, and TMZ were administered at 15, 150, and 42 mg/kg, respectively. The experiment duration last was 14 days (chronic cardiotoxicity). TMZ was chosen as a probable stabilizer of cholesterol metabolism. The deviations of the following parameters were evaluated in the framework of this study: total cholesterol (TC), triglycerides (Tg), high-density lipoproteins (HDL), low-density lipoproteins (LDL), coronary risk index (CRI), and atherogenic coefficient (CA). The markers of cholesterol metabolism mentioned above were measured via certified test systems produced by Elabscience Biotechnology (China) using SpectraMax 250 rider (Molecular Devices, USA).

## **Results**

In group № 2, the concentration of TC is higher by 80.3 and 80.7%, Tg is higher by 80.5 and 88.0%, LDL is higher by 149.3 and 158.6%, HDL is lower by 46.8 and 43.5%, CA is higher by 187.4 and 172.8%, CRI is higher by 115.8 and 113.9% than in groups № 1 and 4, respectively. While the comparative groups № 3 and 2, it was noted that TMZ induces a decrease in the TC level by 26.6%, Tg by 46.4%, LDL by 38.2%, an increase in HDL by 18.2%, as well as a decrease in CA by 55.5% and CRI by 44.2% (Tukey's post-hoc test,  $p < 0.05$ , one-way ANOVA,  $p < 0.0001$ ).

**Conclusions**

AC mode of chemotherapy is an inducer of atherogenic hyperlipidemia. TMZ provides a slight but pathogenically important tendency to cholesterol-metabolism stabilization.

**Keywords:** cardiotoxicity, cardio-oncology, trimetazidine.

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**A CASE OF CERULEAN CATARACT**

***Nino Karanadze***<sup>1</sup>

<sup>1</sup> *Tbilisi State Medical University, Department of Ophthalmology – Lions Eye Diabet Clinic, Tbilisi, Georgia.*

***Peter Samuel***<sup>2</sup>

<sup>2</sup> *Tbilisi State Medical University, International Faculty of Medicine, Tbilisi, Georgia.*

***Syed Amaan Ali***<sup>3</sup>

<sup>3</sup> *Tbilisi State Medical University, International Faculty of Medicine, Tbilisi, Georgia.*

***Yusuf Hassoun***<sup>4</sup>

<sup>4</sup> *Tbilisi State Medical University, International Faculty of Medicine, Tbilisi, Georgia.*

**ABSTRACT**

Cerulean Cataracts are a form of congenital cataracts that are characterized by diffuse blue dotted opacifications across the nucleus and cortex of the lens. They Cerulean cataracts are inherited as an autosomal dominant trait. At least four loci for the cerulean cataract phenotype have been mapped – congenital cataract-1 (CCA1;17q24), CCA2 (22q11.2-q12.2), CCA3 (2q33-q35), and CC4 (16q22-q23). Multiple causative mutations have been identified, including mutations in the beta-B2-crystallin gene (CRYBB2), gamma-D-crystallin gene (CRYGD), V-MAF avian musculoaponeurotic fibrosarcoma oncogene homolog gene (MAF), and the major intrinsic protein of lens fiber gene (MIP). Patients with cerulean cataracts usually have preserved visual acuity and rarely need cataract extraction before adult age. Because many newborns are asymptomatic until 18-24 months of age, cerulean cataracts are considered to be a form of developmental cataract rather than a true congenital cataract. Progression of cerulean cataracts is slow and may not become significant until the third or fourth decade of life, when patients begin to notice a gradual decrease in vision in both eyes. However, children who develop signs of visually significant cataracts such as nystagmus and amblyopia may require cataract surgery earlier. This case report is about a woman who is 54 years old she was referred to ophthalmologist as she had changes in retina. She is Georgian and getting diagnosed with cerulean cataract in this country is very rare thus making this patient very important for this geographical region. She has no history of allergy, underwent cholecystectomy 15 years ago, she has over reactive bladder, she has been prescribed reading glasses (+2.5). Her far vision was good 0.8 and she does not need correction for the same. She was diagnosed under the slit lamp and her diagnosis was confirmed, her IOP remains within normal limits. She also had hair in her eyes so was suggested to cut hair. She is currently under further diagnosis and needs further OCT test for the same. Since this is a rare case this case needs further assistance and the reason for the retinal changes along with cataract is important to be known.

**Keywords:** cerulean cataract, autosomal dominant, lens, mutations

**INFLUENZA SEASONALITY IN THE DIFFERENT PARTS OF THE WORLD**

*Lela Tsakadze<sup>1</sup>*

*<sup>1</sup>Doctoral student, SMU, Tbilisi, Georgia*

*Ivane Chkaidze<sup>2</sup>*

*<sup>2</sup>Professor of Paediatrics, Head of the Paediatric Department, TSMU Georgia*

**ABSTRACT**

Influenza is responsible for more than 5 million severe cases and 290,000 to 650,000 deaths every year worldwide. Developing countries account for 99% of influenza deaths in children under 5 years of age. It is important to know country and regional specific seasonality's of different influenza viruses. From 2013 to 2019, influenza A(H1N1)pdm2009, A(H3N2), and A(H5N1) viruses, as well as influenza B Victoria and Yamagata lineages, circulated in African regions. Influenza A(H1N1)pdm2009 and A(H3N2) highly circulated in northern and southern Africa regions. Influenza activity followed annual and regional variations. In the tropical zone, influenza activities were marked by the predominance of influenza A subtypes despite the circulation of B lineages. One season was identified for both the southern and northern regions of Africa. In the eastern zone, four influenza seasons were differentiated, and three were differentiated in the western zone. The retrospective analysis of data collected from the 2000-2001 to 2015-2016 influenza seasons by the Czech Republic national influenza surveillance network showed, that Influenza A represented 78.6% of positive cases overall and accounted for more than 55.0% of all influenza cases in every season, except for 2005-2006 (6.0%). Both A/H1N1 and A/H3N2 were detected in most seasons, except for 2001-2002 and 2003-2004 (only A/H3N2), and 2007-2008 and 2009-2010 (only A/H1N1). Influenza B represented 21.4% of positive cases overall (range, 0.0-94.0% per season). Both influenza B lineages were detected in three seasons, a single B lineage in 11, and no B strain in two. For the 11 seasons where influenza B accounted for  $\geq 20\%$  of positive cases, the dominant lineage was Yamagata in six and Victoria in four. In the remaining season, the two lineages co-circulated. Influenza surveillance in nine consecutive seasons, 2003-2012 years in Turkey showed that (a) influenza season has extended in Turkey and it lasts through May; (b) influenza peaks in different age groups depending on the season; (c) every year a different influenza type and subtype dominates the season; (d) influenza B has been circulating with increasing rate especially in the past six seasons.

**Keywords:** Influenza virus, A/H1N1, A/H3N2

**HUMAN HEART TRANSPLANTATION – NEW CHALLENGES AND OUTCOMES**

*Ana Bitskinashvili*

*Faculty of Medicine of Tbilisi State Medical University, Georgia.*

*Student Scientific-Research Club “ENDEAVOR” of Scientific Research-Skills Center of TSMU, Georgia.*

**ABSTRACT**

Scarcity of hearts from human donors is the major factor constraining expanded application of cardiac transplantation. Each year >7% of the ≈4000 patients on the United Network for Organ Sharing waiting list die resulting from the unavailability of a suitable human donor heart. The use of pigs as a source of hearts for use as “xenografts” in humans (cardiac xenotransplantation) could potentially address the current donor heart shortfall. If predictably healthy organs were dependably available when needed, many patients who are currently not offered heart transplantation or whose condition deteriorates while waiting might also benefit.

Why pig?- The rapid development of genetic engineering techniques enables genome modifications in pigs that reduce the cross-species immune barrier. Triple-knockout (TKO) pigs (in which expression of the 3 known pig carbohydrate xenoantigens has been deleted) are an optimal source of organs for transplantation into human recipients, many of whom do not have natural antibodies against TKO pig cells.

Are pig and human hearts identical?-There are minor differences, for example -The porcine organ has a classic ‘Valentine heart’ shape-unguligrade stance. The porcine superior and inferior caval veins opened into the atrium at right angles to one another, whereas in man the orifices are directly in line.

Transplantation is accompanied by many risks. One of the most important and dangerous are the human immune response and cytomegalovirus (PCMV).

The operation which was held on January 7th January of 2022 proved that the transplantation of a pig's heart to human is not just a hypothesis. 57-year-old man with nonischemic cardiomyopathy who was dependent on venoarterial extracorporeal membrane oxygenation (ECMO) and was not a candidate for standard therapeutics, including a traditional allograft, received a heart from a genetically modified pig.

**Conclusion:** The recent groundbreaking clinical results showing the feasibility of transplanting transgenic pig organs into humans raise hopes that xenotransplantation can help solve the critical shortage of human donor organs.

**Keywords:** transplantation, xenotransplantation, heart transplantation, pig's heart.

**KIDNEY INJURY IN COVID-19 PATIENTS IN FIRST UNIVERSITY CLINIC OF TBILISI STATE MEDICAL UNIVERSITY**

***Sopiko Dvalishvili***

*TSMU, Faculty of medicine, Tbilisi, Georgia*

***Marina Noniashvili***

*TSMU, Science supervisor, Department of Internal Medicine Tbilisi, Georgia*

***Tamar Kandashvili***

*TSMU, Department of Internal Medicine,*

*Science supervisor, Tbilisi, Georgia*

Covid-19 mainly targets the respiratory and immune systems, but other organs might be infected, including the kidneys. Acute kidney injury is second among the most common extrapulmonary manifestations of Covid-19. The incidence of acute kidney injury in COVID-19 patients has been associated with worse prognosis. Acute kidney injury is the second leading cause of death after acute respiratory distress syndrome in covid patients.

**The purpose of the study:** In this study we aimed to investigate pathological changes in kidney function during the course of COVID-19 in patients who have never been diagnosed with kidney disease before and were hospitalized after at least 24 hours from the first symptoms of Covid-19.

**Methods:** In this retrospective study we collected and analyzed demographics, underlying diseases, signs, symptoms and laboratory data of 71 Covid-19 patients based on The First University Clinic data base. All of them were hospitalized after at least 24 hours from first symptoms of Covid-19. Kidney injury was evaluated by markers including estimated glomerular filtration rate(eGFR), serum creatinine and blood urea nitrogen.

**Results:** A total of 71 patients with 22 mild, 44 moderate and 5 severe COVID-19 were included in this study. Meanwhile hospitalization the level of creatinine was increased in 41% and blood urea nitrogen was increased in 15% of patients. Also, eGFR was decreased in 57% of patients. The average variable of eGFR was 46,7 mL/min. The kidney injury markers, included eGFR, serum creatinine and blood urea nitrogen all worsened with an increase in disease severity. Acute kidney injury was not demonstrated in neither of patients age groups.

**Conclusion:** The study results show that altered kidney function in COVID-19 patients is associated with SARS-CoV-2. It is necessary to determine new biomarkers of kidney injury in COVID-19 patients to establish optimal treatment strategy.

**Key words:** SARS-CoV-2, biomarkers, kidney injury

კორონავირუსით გამოწვეული ინფექციები (SARS-CoV-2) ფართოდ არის გავრცელებული მსოფლიოს მასშტაბით. მიუხედავად იმისა, რომ ვირუსის ძირითადი სამიზნე არის რესპირატორული და იმუნური სისტემა, თირკმლის მწვავე დაზიანება აღმოჩნდა ერთ-ერთი ხშირი გამოვლინება კოვიდით დაავადებულ პაციენტებში. თირკმლის დაზიანება და მისი შემდგომი კლინიკური გამოვლინებები, როგორცაა ჰემატურია და პროტეინურია გამოვლინდა კოვიდ პაციენტების დაახლოებით 40%-ში.<sup>1</sup> თირკმელების მწვავე დაზიანება წარმოადგენს სიკვდილიანობის ძირითად მიზეზს კოვიდინფიცირებულ პაციენტებში მწვავე რესპირატორული დისტრესის შემდეგ. თირკმლის მწვავე დაზიანება ხშირად ართულებს COVID-19-ის მიმდინარეობას ჰოსპიტალიზაციის პერიოდში და მკვეთრად

ზრდის დაავადების სიმძიმეს, იწვევს ჰოსპიტალიზაციის პერიოდის გახანგრძლივებას და არასასურველ გამოსავალს.<sup>2</sup>

COVID-19-ის დროს თირკმლის მწვავე დაზიანების პათოგენეზი არის მულტიფაქტორული და ჯერ კიდევ არ არის ბოლომდე შესწავლილი. კოვიდიან პაციენტებში თირკმლის დაზიანება შეიძლება იყოს გამოწვეული პირდაპირი და არაპირდაპირი მექანიზმებით. ორივე მათგანი აუცილებლად უნდა იქნეს გათვალისწინებული დაავადების პროგრესირების კვალდაკვალ.

**თირკმლის დაზიანების სავარაუდო პირდაპირი მექანიზმები.** როგორც ცნობილია, SARS-CoV-2 რეცეპტორთან დამაკავშირებელი დომენის საშუალებით ახერხებს უჯრედში შეჭრას, ვინაიდან იგი უკავშირდება ACE2 რეცეპტორს, რომელიც წარმოდგენილია თირკმლის ტუბულარულ ეპითელიუმზე (განსაკუთრებით პროქსიმალური კლაკნილის მილაკის ეპითელიუმზე) და პოდოციტებზე.<sup>3</sup> არსებობს მოსაზრება, რომ ACE2-ის პოლიმორფიზმი ამცირებს ვირუსის უჯრედში შეჭრის შესაძლებლობას. როგორც კვლევებით დადგინდა, იმისთვის, რომ SARS-CoV-2-მა შეაღწიოს უჯრედში, აუცილებელია ACE2 და TMPRSS2 პროტეინებს თანაარსებობა უჯრედის ზედაპირზე.<sup>4</sup> ACE2 პროტეინი წარმოდგენილია პროქსიმალურ მილაკში (დაახლოებით, ასჯერ მეტი რაოდენობით, ვიდრე ფილტვებში), ხოლო TMPRSS2, ძირითადად, ექსპრესირდება დისტალურ კლაკნილი მილაკის ეპითელიუმზე და საშარდე ტრაქტის ეპითელიუმში.<sup>5</sup> შესაბამისად, SARS-CoV-2-თვის ნაკლებად შესაძლებელია პოდოციტებსა და პროქსიმალური მილაკების უჯრედებში შეღწევა ACE2 და TMPRSS1 მექანიზმით.

აღსანიშნავია პროტეინი CD147, რომელიც ლოკალიზებულია პოდოციტებზე და პროქსიმალური მილაკების უჯრედებზე.<sup>6</sup>

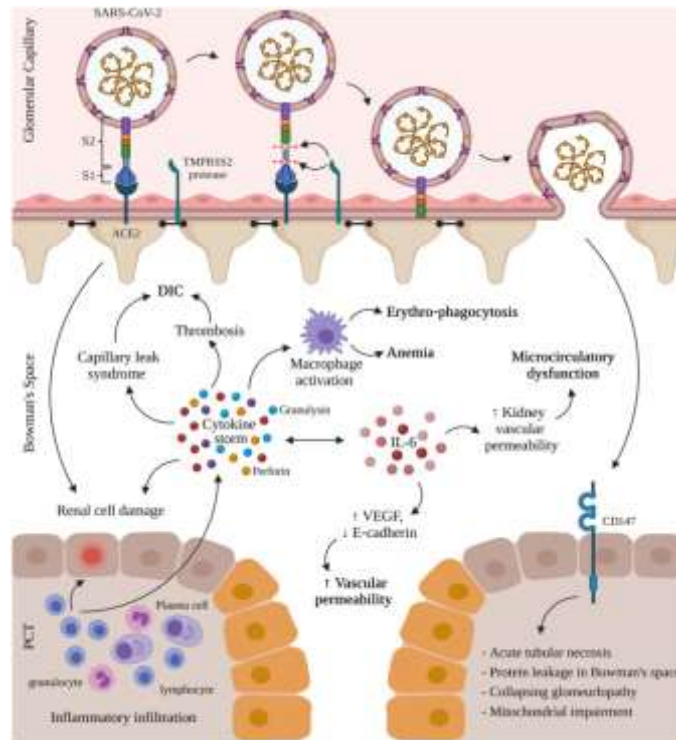
პირდაპირი დაზიანების სასარგებლოდ მიუთითებს კვლევები, რომელში მონაწილე პაციენტების აუტოფსიური მასალის მიკროსკოპულმა კვლევამაც გამოავლინა მნიშვნელოვანი ტუბულარული დაზიანებები და ვირუსის ნაწილაკები როგორც ტუბულარული ეპითელიუმში, ასევე პოდოციტებში.<sup>7</sup>

ენდოთელიუმის დისფუნქცია - ხასიათდება D-დიმერის მაღალი მაჩვენებლითა და მიკროვასკულარული დაზიანებით. იგი წარმოადგენს COVID-19-თან ასოცირებული კოაგულოპათიის განვითარების რისკის ძირითად ფაქტორს. სხვა თანდაყოლილი ან შეძენილი პროთრომბული მდგომარეობები, როგორცაა თრომბოზულ-თრომბოციტოპენიური პურპურა და ატიპიური ჰემოლიზურ-ურემიული სინდრომი, ასევე პირდაპირი, ვირემიით განპირობებული კომპლემენტის სისტემის აქტივაცია, შესაძლოა მონაწილეობდეს ენდოთელიარული დისფუნქციისა და კოაგულოპათიის განვითარებაში.<sup>8</sup> აღსანიშნავია, რომ კომპლემენტის აქტივაცია და თრომბოზული მიკროანგიოპათია წარმოადგენენ თირკმლის დაზიანების მნიშვნელოვან მექანიზმს კოვიდ პაციენტებში. კერძოდ, თირკმლის მილაკების უჯრედებში ხდება კომპლემენტის C5b-C9 კომპონენტის დეპოზიტების ჩალაგება, რომლებიც აფორმირებს MAC-ს (membrane attack complex), იწვევს პროქსიმალური კლაკნილი მილაკის პირდაპირი მექანიზმით დესტრუქციას.<sup>9</sup>

SARS-CoV-2 ინფექცია დაკავშირებულია ინფლამატორული პასუხის აქტივაციასთან, რომელიც „ციტოკინური შტორმის“ სახელით არის ცნობილი. ციტოკინური შტორმი დაკავშირებულია მცირე მონაკვეთში დიდი რაოდენობით ციტოკინების გამოთავისუფლებასთან და ის შესაძლოა წარმოადგენდეს ერთ-ერთ უმნიშვნელოვანეს რგოლს COVID-19-თან ასოცირებული მულტიორგანული დისფუნქციის განვითარების პათოგენეზში. ციტოკინური შტორმის განვითარებაში განსაკუთრებით დიდი მნიშვნელობა ენიჭება IL-6-ს.<sup>10</sup> თუმცა, IL-6-ის მატების ალტერნატიული ახსნა შესაძლოა მოსაზრებით,

რომ ეს პროცესი ასახავს მიმდინარე კრიტიკულ ავადმყოფობას და არა „ციტოკინურ შტორმს“. (სურ.1)

სურათი N1. თირკმლის დაზიანების პირდაპირი მექანიზმი.<sup>11</sup>



**არაპირდაპირი მექანიზმი.** გარდა პირდაპირისა, რენალური დისფუნქცია კოვიდის დროს ასევე შეიძლება განვითარდეს არაპირდაპირი მექანიზმით, რომელიც დაკავშირებულია ვირუსის სისტემურ ეფექტებთან. მაგალითად, ჰიპერპირექსიისა და გასტროინტენსტინალური მანიფესტაციების (მაგ.დიარეა, ლებინება) გამო სითხის მნიშვნელოვანი კარგვა. ნეფროტოქსინები, რომლებიც შესაძლოა წარმოადგენდნენ მკურნალობის ნაწილს (მაგ.ანტიბიოტიკები, რომლებსაც შეუძლიათ გამოიწვიონ თირკმლის მწვავე დაზიანება და მწვავე ინტერტიციული ნეფრიტი).<sup>12</sup> ამას გარდა, პაციენტებში, რომლებსაც უვითარდებათ მეორადი ინფექციები(ბაქტერიული, ვირუსული,სოკოვანი), მაღალია სეფსისთან ასოცირებული თირკმლის მწვავე დაზიანების განვითარების რისკი.<sup>13</sup> ხოლო პაციენტები, რომლებსაც ფილტვისმიერი გამოვლინებების (პნევმონია და/ან ARDS) გამო სჭირდებათ მექანიკური ვენტილაცია, გართულების სახით შესაძლოა განუვითარდეთ თირკმლის მწვავე დაზიანება. კონკრეტულად, COVID-19-თან ასოცირებული ARDS-ის დროს მკურნალობა ხშირად მიმდინარეობს ამოსუნთქვის ბოლოს დადებითი წნევით (PEEP). ეს იწვევს ინტრათორაკალური წნევის მატებას, საბოლოოდ კი შესაძლოა მოჰყვეს ვენური წნევის მატება თირკმელში და ფილტრაციის შემცირება, რაც, თავის მხრივ, მწვავედა თუ ინტრადომინალური წნევა არის მომატებული(მაგ.სითხით გადატვირთვის დროს).<sup>14</sup>

მნიშვნელოვანია ორგანული „კროს-ტოლქი“, რაც აღნიშნავს ერთმანეთისაგან დაშორებული ორგანოების კავშირს და ბიოლოგიურ კომუნიკაციას, რომელიც გაშუალებულია სასიგნალო მოლეკულებით, მათ შორის ციტოკინებითა და ზრდის ფაქტორებით, ასევე, დაზიანებული ქსოვილიდან დაზიანებასთან ასოცირებული მოლეკულური პატერნების(DAMPs) გამოთავისუფლებით.<sup>15</sup> მაგალითად, მწვავე ჰიპოქსემიამ შესაძლოა დააქვეითოს თირკმლის ფუნქცია და გაზარდოს თირკმლის ვასკულარული



რეზისტენტობა, რაც გამოიწვევს თირკმლის ჰიპოპერფუზიას და „მწვავე ტუბულარულ დაზიანებას. „კროსთოლქი“ არის თირკმლის დაზიანების ერთ-ერთი შესაძლო მექანიზმი ARDS-ის დროს. კერძოდ, ARDS-ის მიმდინარეობის დროს ფილტვების დაზიანება შესაძლოა მიმდინარეობდეს იმდენად მძიმედ, რომ გამოიწვიოს არამარტო DAMP-ების გამოთავისუფლება, არამედ ციტოკინების, ქემოკინების და ვაზოაქტიური ნივთიერებებისა, რაც შეიძლება გახდეს თირკმლის დაზიანების მიზეზი.<sup>16</sup>

ასევე აღსანიშნავია, რომ პაციენტის ასაკი, თირკმლის ქრონიკული დაავადება და სხვა დაავადებების თანაარსებობა(მაგ, დიაბეტი, ჰიპერტენზია, სიმსუქნე, გულის უკმარისობა და ფილტვის ქრონიკული ობსტრუქციული დაავადება) დაკავშირებულია დაავადების შედარებით ცუდ გამოსავალთან და წარმოადგენენ თირკმლის მწვავე დაზიანების განვითარების რისკის ფაქტორებს.<sup>17</sup>

**კვლევის მიზანი.** წარმოდგენილი კვლევის მიზანს წარმოადგენდა თირკმლის ფუნქციური ცვლილებების შესწავლა იმ პაციენტებში, რომლებიც დაავადების სიმპტომების გამოვლენიდან მინიმუმ 24 საათის შემდეგ მოთავსდნენ სტაციონარში და წარსულში არ აღენიშნებოდათ თირკმლის დაავადება.

ჩატარდა რეტროსპექტული კვლევა, რომლის ფარგლებშიც შეგროვდა 71 კოვიდ პაციენტის ინფორმაცია პირველი საუნივერსიტეტო კლინიკის მონაცემთა ბაზის მიხედვით (01.09.2022წ-30.09.2022წ). კვლევაში მონაწილე ყველა პაციენტს ჩატარებული ჰქონდა ანტიგენის სწრაფი ტესტი, რომლის მიხედვითაც ისინი აღმოჩნდნენ დაინფიცირებულები SARS-CoV-2-ით. პაციენტები მკურნალობდნენ პირველ საუნივერსიტეტო კლინიკაში. არცერთი პაციენტი არ იყო 18 წელს ქვემოთ და არცერთ მათგანს ანამნეზში არ აღენიშნებოდა თირკმლის დაავადება ან დადასტურებული თირკმლის ქრონიკული უკმარისობა.

ჩვენ შევკრიბეთ პაციენტების დემოგრაფიული ინფორმაცია, პერიოდი დაავადების გამოვლენიდან მის დადასტურებამდე, ლაბორატორიული მონაცემები, კლინიკური სიმპტომები და ნიშნები. ლაბორატორიული მონაცემები მოიცავდა თირკმლის ფუნქციურ ტესტებს, eGFR-ს, სისხლის ბიოქიმიურ კვლევას, შარდის საერთო ანალიზს და ელექტროლიტების განსაზღვრას სისხლის შრატში. COVID-19-ის დიაგნოზისა და მართვის გაიდლაინებზე დაყრდნობით, პაციენტები დაიყო 3 ძირითად ჯგუფად : მსუბუქი, საშუალო და მძიმე.

მსუბუქი- კლინიკური სიმპტომატიკა იყო მსუბუქი, რადიოლოგიური კვლევით არ მანიფესტირდებოდა პნევმონიისთვის დამახასიათებელი ნიშნები ან კლინიკა მიმდინარეობდა მსუბუქად, სატურაციის და სუნთქვის ნორმალური მაჩვენებლების შენარჩუნებით.

საშუალო - პაციენტებს გარდა იმისა, რომ აღენიშნებოდათ სიმპტომები, როგორცაა : ცხელება, რესპირატორული გამოვლინებები და ა.შ. , პნევმონია შეიძლება მანიფესტირებული ყოფილიყო რადიოლოგიური კვლევით.

მძიმე - პაციენტები, რომლებშიც აღინიშნება ჩამოთვლილი კრიტერიუმებიდან თუნდაც ერთი : სუნთქვის სიხშირე >30 სუნთქვა/წუთში, SpO2 ≤ 93% მოსვენებულ მდგომარეობაში, PaO2/FiO2 ≤300. პაციენტები, რომლებსაც უვითარდებათ ფილტვის 50%-ზე მეტი დაზიანება 24-48 სთ-ში, ასევე მიეკუთვნებოდნენ მძიმე ჯგუფის პაციენტებს.

ასევე, პაციენტები, რომლებსაც აღენიშნებათ თუნდაც ერთი ნიშანი ჩამოთვლილი კრიტერიუმებიდან : განვითარებული სუნთქვის უკმარისობა, რომელიც საჭიროებდა მექანიკურ ვენტილაციას, შოკის განვითარება, სხვა ორგანოს უკმარისობა, რომელიც მოითხოვდა ინტენსიური თერაპიის განყოფილებაში მონიტორინგსა და მკურნალობას.

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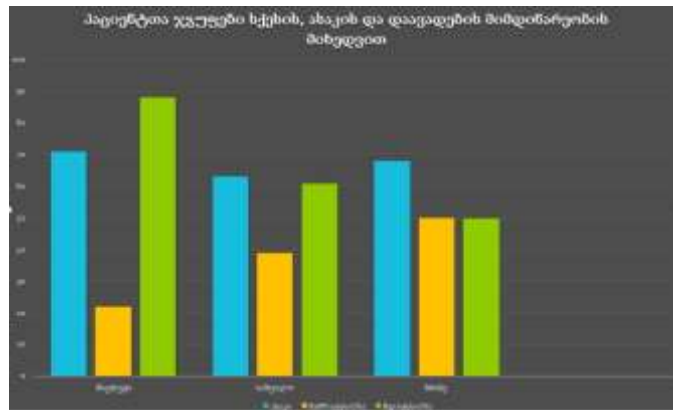
თირკმლის მწვავე დაზიანების დროული გამოვლენისათვის საჭირო იყო შემდეგი კლინიკური კვლევების ჩატარება: შარდის საერთო ანალიზი(ხვედრით წონა, ცილა, ერითროციტები, ლეიკოციტები), სისხლის ბიოქიმიური ანალიზი ( კრეატინინი, შარდოვანა, ნატრიუმი, კალიუმი, ქლორი),მწვავე-ტუტოვანი წონასწორობა (სისხლის pH, pCO<sub>2</sub>, pO<sub>2</sub>),თირკმლის ულტრასონოგრაფია.

თირკმლის დაზიანების დამატებით კრიტერიუმებად ჩაითვალა : პროტეინურია, ჰემატურია, ლეიკოციტურია, ჰიპერაზოტემია.

მიღებული მონაცემები დამუშავდა სტატისტიკურად. გამოითვალა M (მედიანა), საშუალო არითმეტიკული, საშუალო სტანდარტული გადახრა ჯგუფთა შორის მიღებულ მონაცემთა ანალიზისათვის. მონაცემთა შორის განსხვავების სარწმუნოობა შეფასდა სარწმუნოობის კოეფიციენტი(p).

**კვლევის შედეგები.** 71 პაციენტი იყო ჩართული კვლევაში. მათ შორის 22 მსუბუქი, 39 საშუალო, 10 მძიმე. სამივე ჯგუფში განაწილებულ პაციენტებში აღინიშნებოდა შედარებითი განსხვავება სქესში, ასაკში, დაავადების გამოვლენიდან დადასტურებამდე გასული დღეების რაოდენობაში.(სურ.2)

სურათი N2. პაციენტთა ჯგუფები სქესის, ასაკის და დაავადების მიმდინარეობის მიხედვით.



ჯგუფობრივად დაავადების სიმძიმის მატების პარალელურად, იზრდებოდა თანდართული დაზიანებების, რესპირაციის სიხშირის მაჩვენებლები, ხოლო ჟანგბადის სატურაცია მნიშვნელოვნად ქვეითდებოდა. ჰოსპიტალიზაციის დროს პაციენტების 41%-ში კრეატინინის დონე აღმოჩნდა მომატებული, ასევე, მომატებული იყო შარდოვანას დონე 15%-ში, ხოლო eGFR დაქვეითებული იყო 57%-ში. გფს საშუალო მაჩვენებელი შეადგენდა 46,9მლ/წთ. თირკმლის დაზიანების მარკერების დონე, მათ შორის შრატის კრეატინინი, სისხლის შარდოვანას აზოტი საგრძნობლად იმატებდა თირკმლის დაავადების გამწვავების პარალელურად. არ გამოვლინდა თირკმლის მწვავე უკმარისობის განვითარების შემთხვევა არცერთ ასაკობრივ ჯგუფში.

ცხრილი N1 . პაციენტთა განაწილება ასაკის სქესის და დაავადების მიმდინარეობის მიხედვით.

მონაცემთა ანალიზის მიხედვით გამოვლინდა დაავადების მიმდინარეობის დამძიმების პარალელურად თირკმლის ფუნქციური დაზიანების მაჩვენებლების ცვლილება.

დემოგრაფიული და კლინიკური მაჩვენებლები	მსუბუქი(n=22)	საშუალო(n=39)	მძიმე(n=10)
ასაკი(M)	71	63,7	68
სქესი (მამრ. %) (M)	22	39	50
დრო დაავადების გამოვლენიდან ჰოსპიტალიზაციამდე(დღე) (M)	3	4,12	3
ქრ. დაავადებები			
ჰიპერტენზია(%)	40	43,5	60
დიაბეტი(%)	4,5	7	40
გულის შეგუბებითი და კორონარული დაავადება(%)	18	9	30
თირკმლის ქრონიკული უკმარისობა(%)	0	0	0
რესპირატორული დაავადება(%)	0	9 (ქრ. ბრონქიტი, ბრონქული ასთმა)	0
ვიტალური რესპირატორული მონაცემები			
სუნთქვის სიხშირე (M)	22	24	28
SpO2(%) (M)	95	91	88
რადიოლოგიური მონაცემები(პმევმონია) (%)	18	51	100

კრეატინინის, შარდოვანასა და გფს-ის მაჩვენებლები უარესდებოდა პაციენტის მდომარეობის სიმძიმის შესაბამისად, კერძოდ, კრეატინინის და შარდოვანას დონე იმატებდა, ხოლო eGFR მნიშვნელოვნად ქვეითდებოდა. ასევე, დაავადების სიმძიმის პარალელურად იზრდებოდა პროტეინურიის, ჰემატურიისა და ლეიკოციტურიის მაჩვენებლები. ნაკლები განსხვავება აღმოჩნდა Na<sup>+</sup>, K<sup>+</sup>-სა და Cl<sup>-</sup> -ის მონაცემებში, რაც დაფუძვნირეთ საკვლევ მასალად ვენური სისხლის გამოყენებას.

ცხრილი N2. თირკმლის დაზიანების ლაბორატორიული მაჩვენებლები დაავადების სიმძიმის მიხედვით.

	მსუბუქი(n=22)	საშუალო(n=39)	მძიმე(n=10)
კრეატინინი	90	95.8	115
შარდოვანა	5.32	7.76	8.81
eGFR	73	64	49
Na+ (mmol/L)	137,5	139,5	137,5
K+ (mmol/L)	3,5	3,6	3,8
CL-- (mmol/L)	97,5	98	103
pH	7,4	7,4	7,4
შარდის ხვედრით წონა	1017	1015	1010
პროტეინურია	30	40	65
ჰემატურია(%)	23	51	62,5
ლეიკოციტურია(%)	20	42	50

**დასკვნა.** კვლევის მონაცემთა ანალიზის შედეგად მიღებული ინფორმაცია მიუთითებს კოვიდ ინფექციის ფონზე თირკმლის ფუნქციის დაქვეითებაზე. თირკმლის დაზიანების ხარისხი მატულობდა დაავადების სიმძიმესთან კორელაციაში, შესაბამისად, აუცილებელია თირკმლის ფუნქციის მონიტორინგი იმ პაციენტებშიც, რომელთაც აღენიშნებათ კოვიდ-19-ის მსუბუქი კლინიკური მიმდინარეობა.

**რეკომენდაციები.** თირკმლის დაზიანების ნაადრევი გამოვლენა, თირკმლის ფუნქციების აქტიური მონიტორინგი, მისი ფუნქციის (ფილტრაციული და გამომყოფი) კორექცია, ადეკვატური ჰემოდინამიკური ღონისძიებები და ნეფროტოქსიკური პრეპარატების შეზღუდვა აუმჯობესებს კოვიდ-19-ით დაავადებული პაციენტების პროგნოზს.

ასევე აუცილებელია თირკმლის დაზიანების ახალი ბიომარკერების განსაზღვრა კოვიდინფიცირებულ პაციენტებში(KIM1, L-AFBP, TIMP-2, IGFBP-7, UMOD, NGAIL). ეს დაგვეხმარება განვსაზღვროთ ნეფრონში დაზიანების ლოკალიზაცია და შევიმუშავოთ თანამედროვე მკურნალობის ოპტიმალური სტრატეგიები.

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**TÜRKİYE’DE DİNDARLIK, RUH VE BEDEN SAĞLIĞI İLİŞKİSİ İLE İLGİLİ YAPILMIŞ ÇALIŞMALARIN DEĞERLENDİRİLMESİ**

**AN EVALUATION OF THE STUDIES DONE IN TURKEY ON THE RELATIONSHIP BETWEEN RELIGIOSITY AND MENTAL AND PHYSICAL HEALTH**

***Mehmet Emin KALGI***

*Dr. Öğr. Üyesi, Ardahan Üniversitesi, Felsefe ve Din Bilimleri Bölümü, Din Psikolojisi Anabilim Dalı, Ardahan, Türkiye*

*Assist. Prof. Dr., Ardahan University, Theology Faculty, Department of Psychology of Religion, Ardahan/Türkiye*

*ORCID NO: 0000-0001-6999-5059*

**ÖZET**

Dinin ruh ve beden sağlığı üzerinde ne denli etkili olduğu ile ilgili çalışmalar günümüzde giderek yaygınlaşmaktadır. Bu sahada yapılan çalışmalar din psikolojisi başta olmak üzere, psikoloji, psikiyatri ve sosyal psikoloji gibi bilim dalları alanında yoğunlaşmaktadır. Bu çalışmaların bazıları teorik bazı da ampirik şekilde yapılmıştır. Bu alanda bu iki yöntemin araştırmacılar tarafından kullanılması, konunun anlaşılması ve detaya inilmesi bakımından son derece önem arz etmektedir. Nitekim araştırmacılar bu yöntemlerle konuyu daha anlaşılır kılmaktadır. Bu iki yöntem konunun zenginleştirilmesi adına önemli bir gelişme olarak değerlendirilebilir.

Biz de çalışmamızda konu ile ilgili yapılmış çalışmaların genel bir değerlendirilmesini hedefledik. Bu bağlamda geniş bir literatür taraması yaptık. Yaptığımız inceleme sonucunda yukarıda zikrettiğimiz gibi çalışmaları teorik ve ampirik olarak iki kategoride değerlendirdik. Şimdiye kadar yapılan ampirik çalışmalarda dindarlığın ruh ve beden sağlığı üzerinde ne gibi etkilerinin olduğunu irdelerken aynı zamanda bu yöntemin yapılan çalışma ile ilgili işlevselliğine de değindik. Bununla birlikte, teorik olarak yapılan çalışmalarda ise konu ile ilgili detayları ve kullanılan kavramların sıklığını belirlemeye çalıştık.

Yaptığımız araştırma sonucuna göre konunun değişkenleri arasında çok yönlü bir ilişki ağının olduğunu belirledik. Ampirik çalışmalarda bu ilişki ağı şu şekilde ortaya konulmuştur: Dindarlık olgusu ile özsaygı, anksiyete, depresyon, ölüm duygusu gibi değişkenler arasında ilişkilere bakılmıştır. Teknik olarak da genelde korelasyon kullanılmıştır. Bununla birlikte çalışmalarda genelde dindarlık olgusu bağımsız değişken olarak ele alınmış ve dindarlığın bu değişkenler üzerindeki etkisi tespit edilmeye çalışılmıştır. Teorik çalışmalarda ise en çok vurgulanan unsur birinci derecede dindarlık olgusu olmuştur. Dindarlık olgusundan sonra ikinci derecede değinilen unsurlar ise olumsuz diye nitelendirilen psikolojik kavramlar olmuştur. Üçüncü derecede ise olumlu olarak nitelendirilen psikolojik kavramların etkili olduğu ortaya çıkmıştır.

**Anahtar Kelimeler:** Din Psikolojisi, Dindarlık, Ruh Sağlığı, Beden Sağlığı.

**ABSTRACT**

Studies on the effect of religion on mental and physical health are becoming more common nowadays. Studies in this field focus on disciplines such as psychology, psychiatry, and social psychology, especially the psychology of religion. Some of these studies have been done theoretically and some empirically. The use of these two methods by researchers in this field is extremely important in terms of understanding the subject and delve more into detail. As a matter of fact, researchers can make the subject more understandable through these methods. These two methods can be considered as an important development in terms of enriching the subject.

In our study, we aimed at making a general evaluation of the studies done on this subject area. In this sense, we conducted an extensive literature review. As a result of our analysis, as mentioned above, we

evaluated the studies in two categories as theoretical and empirical. While examining the effects of religiosity on mental and physical health in the empirical studies conducted so far, we also tried to touch on the functionality of this method in relation to the study. Additionally, in theoretical studies, we tried to determine the details about the subject and the frequency of the concepts used.

According to the results of our research, we came to the conclusion that there is a multi-directional relationship network among the variables of the subject. In empirical studies, this relationship network has been revealed as follows: Relationships between the phenomenon of religiosity and variables such as self-esteem, anxiety, depression, and death have been examined. And technically, correlation is generally used in examining these relationships. Further, in these studies, the phenomenon of religiosity was generally considered as an independent variable and the effect of religiosity on these variables was tried to be found out. Considering the theoretical studies, the most emphasized element was religiosity with the highest degree of effect. After the phenomenon of religiosity, the elements mentioned in the second degree were psychological concepts that were described as negative. As for the third degree, it was revealed that psychological concepts described as positive were the most effective ones.

**Keywords:** Psychology of Religion, Religiosity, Mental Health, Physical Health.

## GİRİŞ

Din ve ruh sağlığı ilişkisi ilk dönem psikologların üzerinde önemle durduğu konuların başında gelmektedir. Mesela, William James “*Dinsel Deneyim Çeşitleri: İnsan Doğası Üstüne Bir İnceleme*” adlı eserinin bir bölümünü bu konuya ayırmıştır.<sup>1</sup> James’ten başka Jung, Freud, Adler, Fromm, Allport gibi daha birçok araştırmacı bu konuya yönelmiş ve bu konu ile ilgili akademik çalışmalar ortaya koymuştur.<sup>2</sup> Bu araştırmacıların bazıları dinin ruh sağlığı üzerinde olumlu bir etkisi olduğunu ortaya koyarken, bazı araştırmacılar ise bu görüşün aksine ruh sağlığının bozulmasında dinin etkisi olduğunu öne sürmüşlerdir.<sup>3</sup> Bunun en güzel örneklerinden biri Freud ve Jung’un çalışmalarında görülebilir. Freud, nevrozların sebebinin din olduğunu ifade ederken,<sup>4</sup> Jung ise dinden uzak bir hayatın hastalığın kaynağı olabileceğini belirtmektedir.<sup>5</sup>

Bu konu ile ilgili ilk çalışmalar yapıldığı dönemden günümüze katlanarak artmaktadır. Ayten’in ifadesi ile 1960’lardan önce teorik olarak ağırlık verilen bu çalışmalar, 1960’lardan sonra yöntem ve teknik olarak değişikliğe gidilerek ampirik çalışmalara dönülmüş ve bu minval üzerine ilgili çalışmalarla dinin ruh sağlığına nasıl bir etkisi olduğu ortaya konulmaya çalışılmıştır. Öncüllüğünü Amerika’nın yaptığı bu çalışmalar artık dünya genelinde yaygınlaşmakta ve çalışmalar hız kesmeden devam etmektedir. Örneğin bugün Koenig vd. 2001’de yaptığı araştırmada bu tarihe kadar Amerika genelinde konu ile ilgili 850 çalışmanın yapıldığını tespit etmiştir.<sup>6</sup>

Türkiye özelinde konuya bakıldığında ise ilk dönemlerde teorik olarak yapılan çalışmalara 2000’lerden sonra saha çalışmalarına dönüşerek hız kazanmıştır. Özellikle konuya ilgi duyma ve araştırma yapma bakımında Türkiye’de din psikologları bu alanı sahiplendiği ve en fazla araştırmanın yapıldığı bilim dalının din psikolojisi olduğu görülmektedir. Türkiye’de bu konu ile ilgili çalışmaları olan Mustafa Koç, Asım Yapıcı, Ali Ayten, Mustafa Naci Kula, Hayati Hökelekli, Ali Köse vb. birçok din psikoloğu örnek gösterilebilir. Tabiki bu konunun Türkiye özelinde sadece din psikologlarının çalıştığı veya sadece din

<sup>1</sup> William James, *Dinsel Deneyimin Çeşitleri: İnsan Doğası üzerine Bir İnceleme*, çev. İsmail Hakkı Yılmaz (İstanbul: Pinhan Yayıncılık, 2017).

<sup>2</sup> Ali Ayten, *Din ve Sağlık: Kavram, Kuram ve Araştırma* (İstanbul: Marmara Akademi Yayınları, 2018), 7.

<sup>3</sup> Taha Yılmaz, “İslâm Hukuku’nun Güncel Meseleler Karşısındaki Dinamizmi”, *Sosyal Bilimler Dergisi* 57 (2022b), 131-140; Taha Yılmaz, “Kadınların İslâm Hukukuna Katkıları: Hz. Aişe Örneği”, *Diyanet İlmî Dergisi* 58/3 (2022a), 979-1002; Taha Yılmaz, “İslâm Hukuku’nda Hak İspatı Bağlamında Karînenin İspat Değeri”, *The Journal of Turk-Islam World Social Studies* 9/33 (2022c), 157-175; Taha Yılmaz, “İslâm Hukuku’na Göre Hak İspatı Bağlamında Türk Hukuku’nda Kullanılan Modern Karînelerin İspat Değeri”, *Pearson Journal of Social Sciences & Humanities* 7/19 (2022d), 228-242.

<sup>4</sup> Sigmund Freud, *Bir Yanılsamanın Geleceği* (Ankara: Tutku Yayınevi, 2014).

<sup>5</sup> Ali Ayten, *Psikoloji ve Din: Psikologların Din ve Tanrı Görüşleri* (İstanbul: İz Yayıncılık, 2012).

<sup>6</sup> Harold Koenig vd., *Handbook of Religion and Health* (New York: Oxford University Press, 2001).

psikologları çalışabilir anlamına gelmemektedir. Psikiyatri uzmanı olan Kemal Sayar'ın ve Mustafa Merter'in bu konu ile ilgili çalışmaları dikkate değerdir.

Alan taramasında dindarlık ve ruh sağlığı ilişkisine yönelik yapılan çalışmalarla ilgili üç (3) farklı veri olduğu görülmüştür. Birincisi, dinin insan sağlığına yönelik olumlu etkisi olduğuna yönelik verilerdir. İkincisi, dinin insan sağlığına zararlı olduğu yönündeki verilerdir. Bu veriden çıkan sonuca göre bazı dinî inanç ve uygulamalar sağlıklı bir insanı hasta edebilir. Üçüncüsü ise dindarlık biçimlerine göre insan sağlığının etkilendiği ile ilgili elde edilen verilerdir.<sup>7</sup>

Amerika'da yapılan çalışmalar Batı'da yapılan çalışmalara oranla dinin ruh sağlığına daha fazla olumlu yönde katkı sağladığı bulgular mevcuttur.<sup>8</sup> Bu bulgular İslam ülkelerinde daha fazla olduğu ifade edilmektedir.<sup>9</sup> Dinin ruh ve beden sağlığına olumlu etkisi olduğuna dair verilerin daha yoğunlukta olması dindarlık-ölçek ilişkisini eleştirel bir bakışla incelemekte fayda vardır.<sup>10</sup> Özellikle korelasyonel çalışmalarda geliştirilen hipotezlerde, “*Dindarlık neden, dindarlığın ruh sağlığı ilişkisi üzerindeki etkisinden kaynaklı olarak ortaya çıkan durum ise sonuçtur.*” Diğer yöntemlere bağlı olarak kullanılan tekniklerden de genelde kurulan hipotezlerin dindarlığın ruh sağlığı üzerinde olumlu etkisi olduğu yönündedir. Hipotez örgüsüne göre kullanılacak yöntem ve tekniklerde de benzer bir öngörü varsa genelde hipoteze paralel bir sonuç ortaya çıkmaktadır. Yapıcı'nın da üzerinde önemle durduğu konulardan biri olan ölçek-olgu ilişkisi için şu noktaya dikkat çekmektedir: “*Sadece olgudan hareket edildiği zaman ise ölçeğin nasıl şekillendirileceği, bunun da ötesinde bir ölçek oluşturma da karşılaşılan güçlüklerin olgudan ne derece bağımsız olduğu meselesi de önemli bir problem olarak kendisini hissettirmektedir.*”<sup>11</sup>

## YÖNTEM

Türkiye'de ruh sağlığı ve dindarlık ile ilgili yapılmış birçok teorik ve ampirik çalışma tespit edilmiştir. Bu çalışmalardan hepsinin analiz etmek mümkün olmadığı için farklı yıllarda yapılan ve türden yapılan çalışmalar alınmış olup ve bu çalışmalardan genel bir sonuç çıkarılması amaçlanmıştır. Bu amaçla çalışmamızda ampirik verilere yönelik 2 kitap, 2 makale ve 3 kitap bölümünün verisi analiz edilmiştir. Bununla birlikte bu çalışmaların 3'ü teorik ve 4'ü ise ampirik olarak yapılmıştır. Ampirik çalışma grubunun özellikleri ile ilgili bilgiler Tablo-1'de sunulmuştur.

**Tablo 1.** Analize Tabi Tutulan Ampirik Çalışmalar ve Çalışma Grubunun Özellikleri Tablosu

	Araştırmacı (lar) ve Yayın Yılı	Çalışma Grubunun Özellikleri			
		Örneklemin Seçildiği Alan	Yaş Aralığı	Sayısı	Türü
1	Kaplan & İşbilen Esendir, 2017	Çanakkale Onsekiz Mart Üniversitesi Tıp Fakültesi Öğrencileri, Çanakkale ve çevresinde görev yapan doktorlar	-	398	Kitap Bölümü
2	Kurt, 2017	Bursa Ali Osman Sönmez Onkoloji Hastanesi'ne bir yıl (2013) içinde başvuran ve meme kanseri tanısı almış kadın hastalar	30 ile 80 üstü	360	Kitap Bölümü
3	Gürsu, 2017	Madde bağımlısı gençler	22-28	8	Kitap Bölümü
4	Yapıcı, 2013	Çukurova üniversitesi	17-32	634	Kitap

<sup>7</sup> Emine Kurt, “Kanser Hastalarında Depresyon, Yaşam Kalitesi ve Dindarlık”, *Din, Değerler ve Sağlık*, ed. Hayati Hökelekli (2017: DEM Yayınları, 2017), 152.

<sup>8</sup> Yılmaz, “İslâm Hukuku'nun Güncel Meseleler Karşısındaki Dinamizmi”; Taha Yılmaz, “İslâm Yargı Sistemine Göre DNA ve Parmak İzinin Delil Olma Değeri”, *Danısname Beşeri ve Sosyal Bilimler Dergisi 2* (2021), 131-140.

<sup>9</sup> Aytan, *Din ve Sağlık: Kavram, Kuram ve Araştırma*, 12.

<sup>10</sup> Asım Yapıcı, “Din Bilimleri Alanında Yapılan Empirik Çalışmalarda Karşılaşılan Metodolojik Bir Problem: Ölçek mi Olguyu, Olgu mu Ölçeği Oluşturmakta?”, *Çukurova Üniversitesi İlahiyat Fakültesi Dergisi (ÇÜİFD)* 4/1 (2004), 85-118; Taha Yılmaz, *Asr-ı Saadette Kadın Sahabîler ve İslâm Hukukuna Katkıları* (Ankara: Sonçağ Akademi Yayınları, 2022e).

<sup>11</sup> Yapıcı, “Din Bilimleri Alanında Yapılan Empirik Çalışmalarda Karşılaşılan Metodolojik Bir Problem: Ölçek mi Olguyu, Olgu mu Ölçeği Oluşturmakta?”, 87.



Dindarlık ile ruh ve beden sağlığı ilişkisini ortaya koymak amacıyla dört çalışmanın verisi analiz edilmiştir. Bu çalışmaların verileri 3'ü nicel ve 1'i ise nitel yöntemle elde edilmiştir. Analize tabi tutulan ampirik çalışmalar, Türkiye'nin birçok şehrinde ikamet çalışma 1400 kişiyi kapsamaktadır. Nicel yöntemle elde edilen veriler korelasyon, bağımsız t-testi ve tek yönlü varyans (ANOVA) analizi ile çözümlenirken, nitel yöntemle elde edilen veriler ise betimsel ve içerik analiz tekniğiyle çözümlenmiştir.

### **Araştırmada Cevap Aranılan Sorular**

Türkiye'de yapılan ampirik araştırmalarda çoğunlukla dindarlığın ruh ve beden sağlığını pozitif yönde yordadığına yönelik sonuçlar elde edilmiştir. Bununla birlikte ruh ve beden sağlığı için genellikle psikolojinin temel kavramlarıyla dindarlık arasındaki ilişkiye bakılmaktadır? Bu bağlamda araştırmamızda aşağıdaki sorulara cevap aranmıştır;

1. Dindarlık ile ruh ve beden sağlığı arasında bir ilişki var mıdır?
2. Teorik çalışmalarda dindarlık ve ruh sağlığına ilişkin en çok hangi konular ya da kavramlar vurgulanmaktadır?

### **BULGULAR**

Bu başlık altında ruh sağlığı ve dindarlık konusuna ilişkin hem ampirik hem de teorik veriler analiz edilecektir. Ampirik veriler için dört çalışma incelenmiş olup bu çalışmaların biri (1) kitap diğer üçü (3) ise kitap bölümüdür. Ampirik verilere ilişkin bulgular Tablo 2'de sunulmuştur.

#### **1. Ampirik Verilere İlişkin Bulgular**

**Tablo 2.** Analize Tabi Tutulan Ampirik Çalışmalar ile İlgili Elde Bulgular Tablosu

	<b>Araştırmacı(lar) ve Yayın Yılı</b>	<b>Veri Toplama Şekli</b>	<b>Araştırmanın Konusu</b>	<b>Dindarlık ile Ruh ve Beden Sağlığı İlişisine Dair Bulgular</b>
1	Kaplan & İşbilen Esendir, 2017	Anket Tekniği	Sağlık uzmanlarının inançla iyileşme konusundaki görüşleri	- Çoğunlukla Tanrı'ya ya da yüce bir varlığa inanılmaktadır. - Katılımcıların çoğunluğu inanç kaynaklı mucizevi iyileşmeye inanmamaktadır. - Fakat büyük çoğunluğu dinî inancın hastaların iyileşmesinde olumlu rol oynayabileceğine sıcak bakmaktadır.
2	Kurt, 2017	Ölçek Tekniği	Meme kanseri hastalarda depresyon ve yaşam kalitesi değişkenlerin din tutum ile ilişkisi	Meme kanseri hastalarda fiziksel sağlık, ruhsal sağlık, hastalığa uyum ve hastalıkla başa çıkma sürecinde dindarlık etkili bir faktördür.
3	Gürsu, 2017	Görüşme Tekniği	Madde bağımlılığı ile mücadelede inanç eksenli yaklaşım	Madde bağımlılığı ile mücadelede dini eğitim ve uygulamalar etkili faktörlerdir.
4	Yapıcı, 2013	Ölçek Tekniği	Dindarlık ve ruh sağlığı ilişkisi	- Dindarlık ile özsaygı arasında ilişki yoktur. - Dindarlık arttıkça depresyon düşmektedir. - Dindarlık arttıkça umutsuzluk düşmektedir. - Allah'a iman intihar olasılığını düşürmektedir.

Tablo 2'deki bulgulara bakıldığında dindarlığın ruh ve beden sağlığı üzerinde bir etkisi olduğu görülmektedir. Kaplan ve İşbilen Esendir'in yaptığı çalışmada tıp öğrencileri ve doktorların büyük çoğunluğunun dinî inancın hasatların iyileşmesinde önemli rolü olabileceğini belirtmektedir. Fakat katılımcıların çoğunluğu mucizevi kaynaklı iyileşmeye inanmamaktadır. Fakat bu kişilerin çoğu Tanrı inancı olmakla birlikte çok azı kendini oldukça dindar kategorisinde olduğunu kabul etmektedir. Çoğunluğu kendini biraz dindar olarak tanımlamaktadır.<sup>12</sup>

Kurt, nicel yöntemle dayalı olarak 360 kişi ile meme kanseri hastalarda dinî tutum ile depresyon ve yaşam kalitesi değişkenleri arasında ilişkisinin olup olmadığını ortaya koymak amacıyla yaptığı çalışmada, dinî tutumun depresyon ve yaşam kalitesi değişkenlerini etkilediğini tespit etmiştir. Bununla birlikte çalışmada fiziksel sağlık, ruhsal sağlık, hastalığa uyum ve hastalıkla başa çıkma sürecinde dindarlığın önemli bir faktör olabileceği görülmüştür.<sup>13</sup>

Gürsu, madde bağımlılığı ile mücadelede inancın etkisinin olup olmadığı ortaya koymak amacıyla nitel yöntemle dayalı olarak yaptığı çalışmada, madde bağımlılığı ile mücadelede dinî eğitimin ve uygulamaların önemli bir etkisini olduğunu ortaya koymuştur. Bununla birlikte araştırmacı, dinî eğitim ve uygulamaların, grup dinamiğinin oluşturduğu sosyal desteğin düzelmeye sürecinde bir etkisi olduğunu tespit etmiştir.<sup>14</sup>

Yapıcı, dindarlık ile ruh sağlığı arasında bir ilişki olup olmadığını ortaya koymak amacıyla kapsamlı bir çalışma yapmıştır. Bununla birlikte Yapıcı, dindarlık ile ruh sağlığının göstergeleri olan özsaygı, depresyon, umutsuzluk, intihar gibi kavramlar ile ilişkisine bakmıştır. Araştırmacı, elde ettiği bulgulara göre dindarlık artıkça kişinin depresyona girme, intihar etme ve umutsuz olma duygusuna düştüğünü tespit etmiştir. Yani çalışmada genel anlamda dindarlığının ruh sağlığı üzerinde olumlu bir etkisi olduğu tespit edilmiştir.<sup>15</sup>

## 2. Teorik Verilere İlişkin Bulgular

Dinin ruh ve beden sağlığı ile ilişkisini ortaya koymak için literatür taraması yapılmış olup 2'si makale ve 1'i kitap olmak üzere toplam 3 çalışma incelemiştir. Bu çalışmalarda konu ile ilgili en çok atıf yapılan başlık ve kavramlar tespit edilmiştir. Bununla ilgili veriler Tablo 3'e işlenmiştir.

**Tablo 3.** Analize Tabi Tutulan Teorik Çalışma Verileri ile İlgili Bulgular Tablosu

	<b>Araştırmacı ve Yayın Yılı</b>	<b>Konu</b>	<b>Konu ile İlgili Vurgulanan Başlık ve Kavramlar ile İlgili Elde Edilen Bulgular</b>
1	Ayten, 2018	Dindarlık ve sağlık ilişkisi	- Dindarlık ile başa çıkma, ölüm kaygısı, depresyon, obsesif-kompulsif bozukluklar ve intihar ilişkisi - Dindarlık ile fiziksel sağlık arasındaki ilişki - Dindarlık ile sağlık davranışları, diyet, obezite ve yeme bozuklukları ilişkisi - Bağımlılıkla mücadelede dindarlık ve maneviyat
2	Apaydın, 2010	Dindarlık ile ruh sağlığı ilişkisi	Dindarlık ile yaşam memnuniyeti, depresyon, ölüm kaygısı, intihar, psiko-sosyal uyum, oto-kontrol, başa çıkma gibi kavramlarla ilişkisi
3	Köylü, 2010	Dindarlık ile ruh ve beden sağlığı ilişkisi	- Dindarlık ile ruh sağlığı kavramlarına (depresyon, intihar, mutluluk, yaşam memnuniyeti gibi) yönelik vurgulanan kavramlar - Dindarlık ile beden sağlığı kavramlarına (fizikî sağlık, bağışıklık sistemi, kolesterol gibi) yönelik vurgulanan kavramlar

<sup>12</sup> Hasan Kaplan - Nihal İşbilen Esendir, "Tıp Öğrencileri ve Doktorlarda Mucize ve Mucizevi İyileşme İnanç: Çanakkale Örneği", *Din, Değerler ve Sağlık*, ed. Hayati Hökelekli (2017: DEM Yayınları, 2017), 163-165.

<sup>13</sup> Kurt, "Kanser Hastalarında Depresyon, Yaşam Kalitesi ve Dindarlık", 201-202.

<sup>14</sup> Orhan Gürsu, "Madde Bağımlılığı ile Mücadelede İnanç Eksenli Yaklaşım: Sincan Örneği", *Din, Değerler ve Sağlık*, ed. Hayati Hökelekli (İstanbul: DEM Yayınları, 2017), 218-224.

<sup>15</sup> Asım Yapıcı, *Ruh Sağlığı ve Din: Psiko-Sosyal Uyum ve Dindarlık* (Adana: Karahan Kitapevi, 2013).

Ayten, dindarlığın ruh ve beden sağlığı ile ilişkisi ortaya koymak için detaylı bir çalışma yapmıştır. Çalışmada hem yerli hem yabancı birçok araştırmannın verisini incelemiş ve incelediği bu verilerden genel bir sonuca ulaşmaya çalışmıştır. Ayrıca dinin ruh sağlığı ile ilişkisinin olup olmadığını belirlemek için, *dindarlık ile başa çıkma, ölüm kaygısı, depresyon, obsesif-kompulsif bozukluklar ve intihar* ilişkisini ayrıntılı incelemiştir. İkinci bir durum ise dindarlık ile fiziksel sağlık arasındaki nasıl bir ilişki olduğunu belirlemek için bu konu ilgili yapılmış çalışmalardan genel bir sonuca varmaya çalışmıştır. Son olarak bağımlılıkla mücadelede dinî inancın etkisini belirlemek için bu konu başlıkları ile ilgili yapılmış çalışmaları analiz etmiştir.<sup>16</sup>

Apaydın, çalışmasında dindarlık ile ruh sağlığı arasında nasıl bir ilişki olduğunu ortaya koymak amacıyla yerli ve yabancı literatür taramış ve iki temel sonuca ulaşmıştır. Bunlardan birincisi dindarlığın *ruh sağlığı değişkenlerinden olan yaşam memnuniyeti, mutluluk, oto kontrol, psiko-sosyal, başa çıkma* gibi olumlu kavramlarla pozitif yönde; *depresyon, ölüm kaygısı, intihar* gibi olumsuz psikolojik kavramlarla ise negatif yönde bir ilişkisi olduğunu tespit etmiştir. İkinci bulgu ise dindarlığın ruh sağlığı ile olumsuz yönde bir ilişkisi olduğu yönündedir. Araştırmacı, literatür taraması ile elde ettiği çalışmalarda ulaştığı sonuca göre dindarlık arttıkça ölüm kaygısı, öfke, stres artmakta ve kişiliğin bazı yönlerini olumsuz yönde etkilemektedir. Ona göre çalışma verilerine göre birbirinden iki farklı zıt sonucun ortaya çıkmasında çalışmalarda kullanılan yöntem, teknik ve ölçme araçları ile birlikte deneklerin sosyo-demografik yapısı, kişilik özellikleri, kültürel özellikleri gibi birçok faktörün etkisi vardır.<sup>17</sup>

Köylü, teorik olarak yaptığı çalışmayı üç başlık altında incelemiştir: Ruh sağlığı ve din; beden sağlığı ve din; uyuşturucu madde kullanımı, alkol ve din. Araştırmacı, ruh sağlığı ve din konusu ile ilgili genel bir sonu çıkarmak için *depresyon ve din, intihar ve dinî inanç, kaygı ve din, iyimserlik ve din, psikolojik iyi hal ve din* başlıklarını incelemiştir. Bununla birlikte beden sağlığı ve din başlığı altında ise *kanser ve din, ameliyat ve din, kalp hastaları ve din, fizikî fonksiyon ve din, sağlıklı uzun yaşama ve din* başlıklarını ele almıştır. Araştırmacı, en son olarak din ve ruh sağlığına etki eden faktörleri belirlemek için ise *uyuşturucu madde kullanımı, alkol ve din* başlıklarını analiz etmiştir.<sup>18</sup>

## SONUÇ ve TARTIŞMA

Popüler bir konu olma hüviyetine kavuşan dinin ruh ve beden sağlığı ilişkisi ile ilgili çalışmalar her geçen gün artmakta ve bu da zengin bir literatürün ortaya çıkmasını sağlamaktadır. Zenginleşen bu literatür ile ilgili üç temel veri elde edilmektedir. Birincisi dinin ruh ve beden sağlığına olumlu yönde etkisi olduğuna yönelik oluşan literatür; ikincisi dinin ruh ve beden sağlığını olumsuz etkisi olduğuna yönelik literatür ve üçüncüsü ise dindarlık biçimlerine göre insan sağlığının etkilendiği ile ilgili elde edilen verilerdir.<sup>19</sup> Bu üç farklı literatürün ortaya çıkmasında temel faktörün araştırmacıların dinin kökeni ve gelişimine yönelik yapılan tanım ve itirazlardan kaynaklı olduğu düşünülmektedir. Bununla birlikte araştırmannın yapıldığı katılımcı gruplarının sosyo-demografik yapıları, kültürel etkenler, kişilik özellikleri vb. birçok tali faktörün etkisinden de söz edilebilir.<sup>20</sup>

<sup>16</sup> Ayten, *Din ve Sağlık: Kavram, Kuram ve Araştırma*.

<sup>17</sup> Halil Apaydın, "Ruh Sağlığı-Din İlişkisi Araştırmalarına Bir Bakış", *Dinbilimleri Akademik Araştırma Dergisi* 10/2 (2010), 59-77.

<sup>18</sup> Mustafa Köylü, "Ruh ve Beden Sağlığı ile Din İlişkisi Üzerine Yapılan Araştırmaların Bir Değerlendirmesi", *Ondokuz Mayıs Üniversitesi İlahiyat Fakültesi Dergisi* 28 (2010), 5-36.

<sup>19</sup> Kurt, "Kanser Hastalarında Depresyon, Yaşam Kalitesi ve Dindarlık".

<sup>20</sup> Fatma Baynal, "Yetişkinlerde Dindarlık ve Ruh Sağlığı İlişkisinin Çeşitli Değişkenlere Göre İncelenmesi", *İnsan ve Toplum Bilimleri Araştırmaları Dergisi* 4/1 (2015), 206-231; Elif Baykal, "Spiritüelite (Ruhsallık) ve İş Ortamında Anlam Arayışı", *Alanya Akademik Bakış* 2/1 (2018), 9-20; Steven Pirutinsky vd., "Is Attachment to God a Unique Predictor of Mental Health? Test in a Jewish Sample", *The International Journal for the Psychology of Religion* 29 (2019), 1-11; Simon Dein vd., "Covid-19, Mental Health and Religion: An Agenda for Future Research", *Mental Health, Religion & Culture* 23/1 (2020), 1-9; Luisauny Gomez - Jeremiah Sullins, "The Relationship Between Religiosity and Mental Health During the COVID-19 Quarantine", *McNair Scholars Research*, (2020); Ernst T. Bohlmeijer vd., "Promoting Gratitude as a Resource for Sustainable Mental Health: Results of a 3-Armed Randomized Controlled Trial up to 6 Months Follow-Up", *Journal of Happiness Studies* 22/3 (2021), 1011-1032.

Araştırmamızda yedi (7) çalışmanın verisi analiz edilmiştir. Bu çalışmaların dördü ampirik ve üçü ise teorik olarak yapılmıştır. Ampirik çalışmalarda ulaşılan sonuca göre dinin ruh ve beden sağlığı üzerinde olumlu bir etkisi olduğu yönündedir. Bununla birlikte araştırma deneklerinin dinî inanç ve tutumları ne kadar yüksek olursa ruhsal ve bedensel olarak da o oranda sağlıklı olduğu görülmüştür. Teorik çalışmaların verilerinde ulaşılan sonuca göre dinin ruh ve beden sağlığı ile ilişkisini ortaya koymak için daha önce yapılan çalışmaların verilerinden genel bir sonuca ulaşılmaya çalışılmıştır. Bu bağlamda ruh sağlığı ile ilgili daha çok ölüm kaygısı, depresyon, intihar, stres, yaşam memnuniyeti, oto-kontrol vb. olumlu-olumsuz psikolojik kavramlara sıklıkla başvurulurken; beden sağlığı için ise diyet, beslenme, obezite, bağışıklık sistemi gibi kavramlara başvurulmuştur.

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**MODERN TIBBIN GELİŞMİ SÜRECİNDE TIBBA DAİR FETVA VERİRKEN İSLAM HUKUKUNUN TAKİP ETTİĞİ TEMEL PRENSİPLER**

**THE FUNDAMENTAL PRINCIPLES FOLLOWED BY ISLAMIC LAW WHILE ISSUING FATVA ON MEDICINE IN THE DEVELOPMENT PROCESS OF MODERN MEDICINE**

**Taha YILMAZ**

*Dr. Öğr. Üyesi, Ardahan Üniversitesi, Temel İslami Bilimler Bölümü, Fıkıh Anabilim Dalı.*

*Assist. Prof. Dr., Ardahan University, Teology Faculty, Department of Fıkh, Ardahan/Türkiye*

*ORCID NO: 0000-0001-9503-3937*

**Mehmet Emin KALGI**

*Dr. Öğr. Üyesi, Ardahan Üniversitesi, Felsefe ve Din Bilimleri Bölümü, Din Psikolojisi Anabilim Dalı, Ardahan, Türkiye*

*Assist. Prof. Dr., Ardahan University, Teology Faculty, Department of Psychology of Religion, Ardahan/Türkiye*

*ORCID NO: 0000-0001-6999-5059*

**ÖZET**

İslam din olarak müntesiplerine iki dünya saadetini temin etmek için birtakım ilke ve kurallar vaz etmiştir. Bu ilke ve kurallar çerçevesinde hayatını sürdüren Müslümanlar klasik fıkıh döneminde var olmayan sosyal, iktisadi ve tıp alanıyla ilgili birçok problemle karşı karşıya kalmıştır. İslam dini bu problemlere Fıkıh Usûlü perspektifinden çözümler sunarak bazı ilkeler ortaya koymuştur. Özellikle modern tıp teknolojisi ve yeni tedavi yöntemleri genel olarak din, özel olarak da fıkıh bakımından birtakım problemi içinde barındırmaktadır. Haram maddelerle tedavi, vücut üzerinde gerçekleştirilen tıbbî müdahaleler, organ, doku ve kan nakli, estetik ameliyat, cinsiyet değişimi, doğumla ilgili yapay /suni dölleme, kürtaj, doğum kontrolü, genetiğe müdahale, ötenazi gibi birçok problem İslam hukukunu ilgilendiren konulardandır. Bu amaçla İslam hukuku bu problemlere fetva verirken bir taraftan şer'i hüküm diğer taraftan da maslahat-mefsedet, zâruret ve ihtiyacı esas alan bir metot takip etmiştir. Modernist, yeni selefci, gelenekselci ve akademik yaklaşımlar günümüzde modern tıpla ilgili problemleri değerlendirmektedirler. Çalışmamızda temel dini naslar şemsiyesi altında asli ve fer'i delilleri ölçü alarak ayrıca İlk dönem İslam Tarihinde meydana gelen tarihsel vakıaları da sosyal değişim ve akıl ölçeğinde analiz ederek tıp sahasında yaşanan bu yeni gelişmelerin İslam hukuku açısından ne denli meşru olduklarını değerlendirdik. Böylelikle fikhî açıdan bu yeni meselelere çözüm ararken ahlaki ve hukuki olarak ne gibi prensiplere riayet edilmesi gerektiği hususlarını ortaya koyduk.

**Anahtar Kelimeler:** İslam Hukuku, Modern Tıp, Fetva, Tedavi, Şer'i Hüküm.

**ABSTRACT**

As a religion, Islam has given its followers some principles and rules to ensure the happiness of both worlds. Muslims who lead their lives within the framework of these principles and rules have faced many social, economic and medical problems that did not exist in the classical fiqh period. The religion of Islam has revealed some principles by offering solutions to these problems from the perspective of Fiqh Method. Especially modern medical technology and new treatment methods contain some problems in terms of religion in general and fiqh in particular. Many problems such as treatment with haram substances, medical interventions on the body, organ, tissue and blood transplantation, plastic surgery, sex change, artificial / artificial insemination, abortion, birth control, genetic intervention, euthanasia are among the issues that concern Islamic law. For this purpose, while giving fatwa to these problems, Islamic law has followed a method based on shar'i rule on the one hand and on the other hand, maslahat-mafsedet, necessity and need. Modernist, neo-salafist, traditionalist, and academic approaches

are currently assessing the problems of modern medicine. In our study, we evaluated the legitimacy of these new developments in the field of medicine in terms of Islamic law by measuring the primary and secondary evidence under the umbrella of basic religious scriptures, and also analyzing the historical events that occurred in the Early Islamic History on the scale of social change and reason. Thus, we put forward the issues of what moral and legal principles should be followed while seeking solutions to these new issues in terms of jurisprudence.

**Keywords:** Islamic Law, Modern Medicine, Fatwa, Treatment, Sharia Rule

## GİRİŞ

Günümüzde birçok alanda olduğu gibi, tıp teknolojisi ve tedavi yöntemleri konusunda da önemli gelişmeler ve değişiklikler yaşanmaktadır.<sup>21</sup> Bu gelişmeler, genel olarak insan sağlığı ve yaşamı için olumlu birtakım neticelerin açığa çıkmasına sebep olsa da dinî, hukukî açıdan bazı sorunları da beraberinde getirmektedir. Zira bu gelişmeler insan, hayvan ve diğer canlılar üzerinde yapılan birtakım çalışmalar ve deneyler sonucu açığa çıkmaktadır.

Modern tıp teknolojisi ve yeni birtakım tedavi yöntemlerinin, genel anlamda din, özel olarak da fıkıh bakımından bir sorun olarak ortaya çıkmasının iki farklı yönü bulunmaktadır. Öncelikli olarak tıpla ilgili yaşanan bu güncel problemlerin birçoğunun hükmü, tabii olarak bazı metodolojik yaklaşım farklılıklarının ortaya çıkmasına sebep olmaktadır. Diğer taraftan klasik fıkıhta hükmü olan bazı problemlerin yeniden ele alınması gerekir. Maslahat-mefsedet ölçüğüne başvurulup vurulmayacağı, zarûret ve ihtiyacın neye göre tayin edileceği hususları söz konusu olan problemlerin başında gelmektedir.<sup>22</sup>

Tıp konusuna oldukça fazla fikhî sorun vardır. Bu problemlerin başında haram maddeyle tedavi, otopsi, organ nakli, estetik cerrahi müdahale ve sünni döllenme gibi çokça başvurulmuş tıbbî uygulamalar gelmektedir. İnsan hayatının bütünü düzenleyen ve yaşamın tüm alanlarını kapsayarak şekillendiren İslam bu konularda da bazı hükümler ortaya koymuştur. Makâsîdüş-şerîa adına beş temel ilke ortaya koymuştur. Bu ilkelerin bir tanesi de canın ve nefsin korunmasıdır. Canın nefsin korunması için insanın hastalıklardan uzak durması adına birtakım koruyucu önlemlere başvurulması gerekir.<sup>23</sup> Günümüzde önleyici/koruyucu tıp bu alana hizmet etmektedir. Yine kişinin hastalandığında tedavi olması da bu meyanda zikredilen hususların arasındadır. Günümüzde var olan teknoloji ile bu alana sıkça başvurulmaktadır.

Bu zaviyeden konuyu ele aldığımızda eski dönemde bilinmeyen birçok hastalık ve tedavi yöntemi ortaya çıkmıştır.<sup>24</sup> Bu hastalık ve tedavi yöntemlerini şu şekilde sıralaya biliriz: Palyatif sedasyon, kök hücre ve embriyonik kök hücre tedavisi, haram madde ile tedavi, Domuz kalp kapağının insan kalbine takılması, Anne sütünün tedavi ve kozmetik amaçlı kullanılması, aşırı kilolardan kaynaklı vücutta bulunan fazla yağların alınması, kanser hastası çocuklarda kullanılmak üzere saç bağıışı, tedavi amaçlı kullanılan tırnak cilasının abdest ve gusle mani oluşu problemi, ağız ve burun ameliyatı olan bir kimsenin nasıl abdest alacağı, diş dolgusu ve kaplatılması, trombosit verildiğinde abdestin bozulma meselesi, protez göz ve gözden akan iltihabın abdeste mani oluşu, periton diyalizine giren hastanın ve kolostomi ameliyatı geçiren kişinin abdesti, ameliyat, kemoterapi, radyoterapi gibi tedaviler gören kimselerin abdest durumu, orucu bozan ve bozmayan muayene ve tedavi yöntemleri ibadet alanında yaşanan bazı fikhî problemlerdir. Estetik, kadın sağlığı ile ilgili olan âdet ve menopoz dönemlerindeki haller, gebelik ve lohusalık, doğum kontrolü ve kürtaj, tüp bebek ve embriyo, yeni doğan bebeklere yönelik yapılan bazı uygulamalar ve programlar, hekimlik ve etik konusunda yaşanan bazı problemler, beyin ölümü, yaşam desteğinin sonlandırılması, organ nakli ve bağıışı, ötanazi, otopsi, kadavra bağıışı,

<sup>21</sup> Yunus Apaydın, “İctihâd: Dinin Hayatla Buluşması”, *İslam'a Giriş-Ana Konulara Yeni Yaklaşımlar* (İstanbul: Diyanet İşleri Başkanlığı Yayınları, 2007), 81-101.

<sup>22</sup> Mehmet Erdoğan, *İslam Hukukunda Ahkâmın Değişmesi* (İstanbul: Marmara Üniversitesi İlahiyat Fakültesi Vakfı Yayınları, 1990), 4-6.

<sup>23</sup> Ertuğrul Boynukalın, “Makâsduş-Şerîa”, *Türkiye Diyanet Vakfı Yayınları* (Ankara: TDV Yayınları, 2003), 27/423-427.

<sup>24</sup> Komisyon, *Tıp ve Sağlıkla İlgili Fetvalar* (Ankara: DİB Yayınları, 2020), 1-18.

ameliyatla kesilen azaların defni, DNR gibi ileriye dönük talimatlar, cinsiyet değiştirmek, alternatif veya tamamlayıcı tıp uygulamalarıyla tedavi olmak, hipnoz, dua ve rukye, bioenerji ile tedavi olmak, Alzheimer ve zihinsel engellilerin kaybolmaması için sevgi izi adlı dövme uygulaması, hayvanların tıbbi deneylerde kullanılması ve daha bir çok tıp alanındaki problemler günümüzde fıkıh ilminin okumaları ve problemlere bakışıyla çözüm beklemektedir. Bu alanda yaşanan problemlere fıkıh ilminin hangi prensipler ile çözüm ürettiği önemli bir konudur.<sup>25</sup> Dolayısıyla bu ilkeler üzerinde durarak fetvâ verirken başvuru prensipleri ortaya koymaya çalıştık.

## **1. İctihadın Gerekliği İlkesi**

İslam kükunun temel kaynaklarından olan Kur'an ve sünnet naslarını içlerinde birer söz ve metin şeklinde barındırmaktadır. Bu dini naslardan hüküm çıkarmanın da birtakım kuralları vardır. Bunun için öncelikli olarak Arapça dil kurallarını iyi bilmek gerekir. Çünkü vahiy ürünü olan Kur'an ve onun bir tefsiri halinde tezahür eden sünnet Arapça olarak nesilden nesle aktarılarak gelmiştir.<sup>26</sup> Bu nasların içinde barındırdıkları anlamları yorumlamak bir ihtiyaçtan ileri gelmektedir. Anlam ve yorum da metnin durumuna göre belirli düzeylerde zihni bir gayreti gerektirmektedir. İslam ilim geleneğinde bu entelektüel çabalar fıkıh ilmi şemsiyesinde değerlendirilmektedir. Fıkıh ilmi de nasların içinde barındırdığı anlamları yorumlama faaliyetidir. Bu faaliyet birinci derecede bilgi ve birikimin yanında belirli ölçüde akıl yürütmeyi de gerektirmektedir.

Müslümanların bireysel ve toplumsal davranışlarının dinle bağlantısının kurulması fıkıhın daha dar ve teknik bir mekanizması olan icthad vasıtasıyla sağlanmaktadır. Bu çerçevede fıkıh denildiğinde icthad akla gelmektedir. İctihad müessesesi adeta fıkıh ilminin ana eksenini oluşturmaktadır. İctihad faaliyetinde bulunan kişiye de fakih ve müçtehit adı verilmektedir. İctihad faaliyetinde bulunmak için üç temel unsur hayati öneme sahiptir. Binci derecede naslar ikinci derecede akıl yürütme ve üçüncü derecede ise sosyal gerçeklik/sosyal değişim birbiriyle ilişkilendirilmekte ve icthad müessesesi de fıkıh donukluktan kurtararak ortaya çıkan problemlere çözümler üretmektedir.<sup>27</sup>

Fıkıh bir yönüyle ilahi tebliğe yani Kur'an ve sünnette yer alan bilgi ve açıklamalara dayanmakta diğer yönüyle de fakihlerin zihni çıkarımlarına, üretim, gözlem ve tecrübelerine bağlıdır. Fakihlerin bu faaliyeti de yaşadıkları toplumun kültür ve geleneklerine, zamanın icraat ve değişimine, coğrafi şartlara göre değişiklik göstermektedir. Günümüzde ise çeşitli nedenlere bağlı olarak dini açıdan birçok problem ortaya çıkmış ve çıkmaya devam etmektedir. İslam dini de yaşamın tüm alanlarını kuşattığı için güncel dini meseleler başlığı altında ibadet hayatından yiyeceklerdeki helal- haramlara, aile hayatından tıbbi tedaviye, ticaret, iş, meslek ve eğlence hayatına kadar hayatın her alanıyla ilgilenmektedir. Bu alanlarda çıkan meseleler her ne kadar birbirinden farklı gözükseler de temelde ortak bir teorik çerçeve ve metodolojiye dayanmaktadır.<sup>28</sup> Bu çerçeve ve metodoloji ise fıkıh usulü ve fıkıh ilminin kaide ve kurallarıdır. Klasik fıkıh konuları içinde nüveleri bulunan bu yeni meseleler de icthad müessesesini gerekli kılmaktadır.

## **2. Kolaylaştırma ve Zarûret İlkesi**

Fıkıh ilminde hükümlerin esnekliğini sağlayan önemli vasıtalarından biri de kolaylaştırma ve zarûret ilkesidir. Yapılan inceleme ve tecrübeler sonucunda bütün toplumsal kurallar gibi din kurallarının da belirli ölçüde bir takım zorluk ve meşakkat içermesi tabiidir. Nitekim teklifin özelliği de bunu gerektirmektedir. Fakat teklifte bazı meşakkatler bulunsa da asıl olan teklifin yapıldığı muhatabın buna güç yetirebilmesidir. Çünkü kolaylaştırma İslam dininin temel prensipleri arasında yer almaktadır.<sup>29</sup> Allah hâkim-i ezeli olmasından dolayı mükellefin güç yetiremeyeceği hükümleri kendisine teklif etmemiştir. Hükümler güçleştikçe kolaylaştırma ilkesi işlettirilmiştir.<sup>30</sup>

<sup>25</sup> Mustafa Baktır, *İslam Hukukunda Zaruret Hali* (İstanbul: Akçağ Yayınları, ty.), 45.

<sup>26</sup> Hayreddin Karaman, *İslam Hukukunda İctihad* (İstanbul: Akademi Yayıncılık, 2002), 23-27.

<sup>27</sup> Abdullah Kahraman, *İslam'da İbadetlerin Değişmezliği* (İstanbul: Akademi Yayıncılık, 2002), 67.

<sup>28</sup> Eyyüp Said Kaya, "Nevâzil", *Türkiye Diyanet Vakfı İslam Ansiklopedisi* (Ankara: TDV Yayınları, 2007), 33/34-35.

<sup>29</sup> Ahmet Ekşi, *İslam Tıp Hukuku* (İstanbul: Ensar Neşriyat, 2011), 12-15.

<sup>30</sup> el- Bakara, 2/185.



İslam hukukunun temel kaynakları olan Kur'ân-ı Kerim ve sünnette bu konuyla ilgili birçok nas bulunmaktadır. Bunlar şu şekilde sıralanabilir. "Allah dinde sizin için bir zorluk kılmamıştır."<sup>31</sup> "Allah size kolaylık ister, zorluk istemez"<sup>32</sup>, "Allah yükünüzü hafifletmek istiyor, nitekim insan zayıf yaratılmıştır"<sup>33</sup>. Hz. Peygamber de hadislerinde dinde kolaylaştırma ilkesinden bahsetmiş ve bu ilkeyi bizzat yaşamında uygulamıştır. "Eğer ümmetime meşakkat ve zorluk verecek olmasaydım, onlara devamlı olarak misvak kullanmalarını emrederdim"<sup>34</sup> Mecelle-i Ahkâm-ı adliyyede de birçok kaide kolaylaştırma ilkesiyle ilgilidir. Bu açıdan fikhî hükümlerin kolaylık prensibiyle hafiflediğine yapılan inceleme sonucunda rastlamak mümkündür.

Kolaylık ilkesiyle ilgili olan ve fıkıh alanında kullanılan bir diğer prensip de zarûrettir. Zarûret yasaklanmış bir şeyin işlenmesini mübâh kılan özür hali olarak tarif edilmektedir. Bu ilke gereği insan zor durumda kaldığı zaman birtakım ruhsatlardan yararlanabilir. Bazen hayati tehlike veya bir uzvun yok olması durumunda haram olan bir şeyi ruhsat ölçüsünde yapabilir. Bu konuda Kur'ân-ı Kerim'de bulunan şu ayet bunun delilidir: "Şu kadar var ki, kim, gönülden günaha yönelmiş olmaksızın dayanılmaz açlık durumunda çaresiz kalırsa (haram kılınanlardan yiyebilir ve bunlardan istifade edebilir) Allah çok bağışlayıcı ve esirgeyicidir."<sup>35</sup> Zarûret ilkesi İslam alimleri tarafından "Zarûretler yasakları mübah kılar"<sup>36</sup> biçiminde kurallaştırılmıştır. Bu ilke gereği haramlık hükmü devam etmekle birlikte haram olan bu şeyler geçici olarak, zarûreten mübah hale gelmektedir. "Zarûretler miktarınca takdir olunur"<sup>37</sup> Kaidesi gereği olarak da zarûret ortadan kalktığı anda haramlık vasfı tekrar eski haline döner.

İslam hukukçuları zaruret ve kolaylaştırma ilkesinin gereği olarak fetvada Müslümanların karşılaştıkları günümüz fıkıh problemlerine, "İhtiyaç zarûret menzilesinde tenzil olunur"<sup>38</sup> kuralını işleterek zarûret ve maslahat ilkelerini fazlaca işletmişlerdir. Yeni çıkan fikhî problemlere dair bu ilkeler perspektifinde fikhî'n-nevâzil, kadâyâ mu'âsıra, kadâyâ mustecede, mesâil mu'âsıra, fetâvâ mu'âsıra başlıkları altında bu güncel meselelere dair eserler telif etmişlerdir. Bu başlıklar altında ele aldıkları ulaşım araçlarındaki gelişme ve yerleşim merkezlerinin büyümesi; yolculuk mesafesi, namazların birleştirilmesi, uçakta ve otobüste namaz, mîkat yerleri gibi konular yeniden ele alınmıştır.<sup>39</sup> Yine çağımızda bilimsel ve teknolojik gelişmeler sonucunda tıp ve gen teknolojisi, organ, doku, yumurtalık nakli, beyin ölümü, ötenazi, tüp bebek, taşıyıcı annelik, kürtaç, cinsiyet tercihi, kök hücre ve klonlama, estetik operasyonları sağlık ve zarûret bileşeninde yeniden değerlendirilmiş ve bu konuda ahlak, fitrat ve mekâsîdü's- şeriâ bağlamında bir takım fetvalar verilmiştir. İktisat hayatıyla ilgili modern şirket tipleri, bankacılık, yeni para sistemi, kıymetli evrak, faiz, kredi kartı, enflasyon, sigorta, yeni akit türlerinden olan teverruk ve sukûk (eşit değere sahip şâyi hisseli belgeler) konuları, gıda ürünlerinde koruyucu ve tatlandırıcı, renklendirici ve kıvam artırıcı olarak yeni bir çok maddenin kullanımı, sosyal hayatla ilgili sanat spor ve eğlence faaliyetleri ve daha bir çok konuda bu kural ve ilkeler işlettilerle, bireysel ve kurumsal kurullar olarak zarûrât-ı dinîye çerçevesinde dinin ana gayeleri göz önünde bulundurularak, fetvâ siyaseti de gözetilerek eşyada asl olan mübahlıktır, sıkıntı kolaylaştırmayı gerektirir, zarar izale olunur ilkeleri ölçüde çözüm yolları sunulmaya çalışılmıştır.

### **3. Tedavi Olma ve Sağlık Koruma İlkesi**

İslam dini de "Eşyada asıl olan mübahlıktır." ilkesiyle hayata bakmış ve insanoğluna hizmet eden tüm araçları temel naslarla çelişmediği sürece kabul etmiştir. Tıp alanında yaşanan son gelişmeler de insan hayatına çoğu zaman olumlu yönde hizmet etmektedir.<sup>40</sup> İslam dini bu bakımdan fitratı değiştirmedeği

<sup>31</sup> el-Hac, 22/78.

<sup>32</sup> el-Bakara, 2/185.

<sup>33</sup> Nesâi, 4/28.

<sup>34</sup> Buhârî, "Cuma", 8.

<sup>35</sup> el-Mâide, 5/3.

<sup>36</sup> Mecelle, mad. 22, 32.

<sup>37</sup> Mecelle, mad. 22.

<sup>38</sup> Halit Çalış, "Zaruret", *Türkiye Diyanet Vakfı İslam Ansiklopedisi* (İstanbul: TDV Yayınları, 2013), 141-144.

<sup>39</sup> Hayreddin Karaman, *İslam Işığında Günün Meseleleri* (İstanbul: İz Yayıncılık, 2001), 10-13.

<sup>40</sup> Hasan Petek, "Güzelleştirme Amaçlı Estetik Ameliyatlardan Kaynaklanan Hukukî Sorumluluk", *Dokuz Eylül Üniversitesi, Hukuk Fakültesi Dergisi* (2006), 8/177-239.

sürece insan sağlığına hizmet eden birçok yeni tedavi yöntemini kabul etmiştir. Nitekim Hz. Peygamber sağlığı iki nimetten biri olarak saymış hastalanıldığında da tedavi olunmasını ümmetinden istemiştir.

İslam dini bir medeniyet mefkûresiyle daima cihana hükmetmiştir. Mekân, imkân ve insan sac ayağında insanı önclemiştir. İnsanlar içerisinde ise en önde olanlar peygamberler olmuştur. Sosyal, kültürel, eğitim ve ekonomik alanda insanlık tarihi daima bir değişim ve gelişim içinde olmuştur. Tıp alanında da tarihi süreçte birçok değişim ve gelişim yaşanmıştır.<sup>41</sup> Bu bağlamda Allah her alanda peygamberlerini örnek olarak gösterdiği gibi yine tıp alanında da peygamberlerin insanlığa sundukları tedavi yöntemlerini örnek olarak göstermiştir.<sup>42</sup> Nitekim Hz. İsa'nın mucize olarak anadan doğma körleri ve alaca hastalığına yakalananları iyileştirmesi, ölüleri diriltmesi tıp alanında her müzmin/çaresiz derde ilaç ve tedavi aranacağına işaret olarak delalet etmektedir.<sup>43</sup> Çoğu zaman insanoğlu peygamberin elinden çıkan mucizelere bakarak birçok icat ve buluşa imza atmıştır. Tedavinin nihai sınırını Allah peygamberlerine nasip etmiş fakat bu yolu da insanoğluna kapatmamıştır. Hz. Peygamber "Tedavi olunuz; zira Allah her hastalık için bir de deva (ilaç ve tedavisini) yaratmıştır; bundan sadece ihtiyarlık müstesnadır."<sup>44</sup> "Her hastalığın bir ilacı vardır, bu ilaç bulunduğu zaman hastalık Allah'ın izniyle iyileşir."<sup>45</sup> buyurmuş ve kendisi de hastalandığında tedavi olmuştur. Bu bakımdan İslâm dininin sağlık ile ilgili görüşü koruyucu ve tedavi edici olmak üzere iki kısımda ele alınmaktadır. Helal ve temiz gıdalarla dengeli beslenme<sup>46</sup>, bulaşıcı hastalıkların olduğu muhite girmeme<sup>47</sup>, misvak kullanma, el, ağız ve beden temizliğine önem verme<sup>48</sup> gibi ayet ve hadisler sağlığın korunması adına konulan teşvik edici ilkelerdir. Dolayısıyla insan tedavi olmadığında herhangi bir organın zarar görmesi veya yok olması da caiz değildir.

### **Sonuç**

İslam dini varlık içerisinde insanı önclemiştir. Onun için bütün varlığı onun emrine vermiş ve onu halife-i arz kılarak teklifle mükellef kılmıştır. Bu bakımdan da insan hayatına hizmet edecek tüm imkânlar kıymetlidir. Günümüzde insanoğlu nimet ve külfet dengesi bağlamında birçok yeni problemle karşılaşmıştır. Dünya adeta bir köy haline gelmiş, insan da bu hızlı değişim ve gelişim rüzgârından etkilenmiştir. Sosyal, ekonomik ve kültürel olarak birçok yeni imkân ve fırsatla buluşmuştur. Bu teknolojik imkânlar tıp alanında da kendini daha fazla göstermiştir. Tıbbın tedavi yönü olduğu kadar estetik ve sanat boyutu da vardır. Bu perspektiften baktığımızda klasik fıkıh konuları içerisinde bulunmayan birçok tıbbi konu günümüzde fıkıh alanında meşru olup olmama konusunda fetva beklemektedir. Fıkıh usûlü ve fıkıh kuralları çerçevesinde Müslüman alimler bu yeni problemleri ele alarak içtihat müessesesi içerisinde zaruret ve kolaylaştırma ilkeleri ile fetva vermişlerdir. Fetvada ahlakîliği ve fitrata uygunluğu esas alarak ruhsatlar boyutunda bu yeni konulara bir takım çözümler üretmişlerdir. Bu amaçla vahyi esas alarak akıl ve sosyal değişim şemsiyesi altında ilcaat-ı zamana uygun olarak fetvalar vermişlerdir. Makâsıdü's-şeriâ ve zarurat-ı diniyye ile çelişmemek kastıyla heva ve hevsten uzak günümüz tıp dünyasında birtakım ilkeler vaz etmişlerdir. Zarurat, haciyat ve tahsiniyat prensipleriyle meselelere yaklaşmış, ahlak ve dini naslar bağlamında bütün İslam fıkıh mirasını kullanarak asrımızda meydana gelen ve yeni fıkıh problemlerinden olan organ, doku, gen, yumurtalıkların nakli, beyin ölümü, ötenazi, tüp bebek, taşıyıcı annelik, kürtaj, cinsiyet tercihi, kök hücre, klonlanma ve estetik ameliyatı konularında fetvalar vermişlerdir. İslam hukuk dini, ahlaki ve manevi olarak ilkeler koymuş, bu çerçevede fitrat ve nesli bozmayacak, dünyada bozgunculuk çıkarmayacak tıp alanındaki her türlü gelişmeyi desteklemiştir.

<sup>41</sup> İrfan İnce "Organ Nakli", *Türkiye Diyanet Vakfı İslam Ansiklopedisi* (İstanbul: TDV Yayınları, 2007), 33/373-375.

<sup>42</sup> Hacı Mehmet Günay, "Tıbbî Uygulamalar", *Günümüz Fıkıh Problemleri* (Eskişehir: Anadolu Üniversitesi, 2010), 104-129.

<sup>43</sup> "Allah'ın izniyle anadan doğma körleri ve alaca hastalığına yakalananları iyileştirir ve ölüleri diriltirim." Âl-i İmrân, 3/49.

<sup>44</sup> Ebû Davûd, "Tıbb", 1.

<sup>45</sup> Müslim, "Selam", 69.

<sup>46</sup> el-A'râf, 7/31; Mü'minun, 23/51

<sup>47</sup> Buhârî, "Tıbb", 19, 30.

<sup>48</sup> Buhârî, "Savm", 27; Şuarâ, 26/80; Müslim, "Selam", 69.

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**THE EFFECTS OF DOG PARKS (ECO ZONES) ON THE REDUCTION OF DOG FACES POLLUTION OF PARKS - BELGRADE'S EXPERIENCES**

*Ivan Pavlovic*

*Scientific Institute of Veterinary of Serbia, Belgrade, Serbia*

*ORCID ID: 0000-0003-4751-6760*

**Abstract**

In an urban environment such as Belgrade, green areas and parks are the main place where children play and are resting places for city people, but they are also places where dog owners walk their pets.. During their stay in these areas, dogs defecate on them, and apart from their unpleasant appearance and smell, dog excrement represents a kind of epidemiological danger, considering that dogs are carriers and real hosts of a large number of species of zoonotic parasites. As one of the possible solutions to this problem in a number of urban Eco-zones or dog parks are arranged in parks where owners can let their animals out. In this paper, we present the contamination of park areas that are included in the eco center program during 2019 the period when programs of owner-owned dog excrement removal through the dogi-pot system (baskets for disposing of dog excrement) and after the introduction of dog parks (Eco zones) within the parks themselves came to life in these municipalities. We also provide an overview of soil contamination in ecozones before and after their remediation, which is carried out periodically. A total of 250 samples of soil and dog excrement were examined using sedimentation-flotation methods. Parasite eggs were determined by morphometric analysis. Based on the performed parasitological control of soil contamination from parks, the presence of parasites during the first inspection was found in 48.12% and polyparasitism in 45.53%. Three months after the release of the dog parks, a second analysis was conducted that included the same parks where the ecosomes were placed. The presence of parasites was found in 11.23% and polyparasitism in 23.27%. The results clearly show that there has been a significant decrease in the intensity and extent of infection with dog parasite eggs in the mentioned parks.

**Keywords:** dogs, parks, dog parks, pollution, Belgrade