E-ISSN: 2602-3741

Year 2025
Volume 35
Issue 2

GENEL TIP DERGİSİ

The Journal of General Medicine

SELCUK UNIVERSITY PRESS

GENEL TIP DERGİSİ

E-ISSN: 2602-3741

Sayı 35 | **Issue 2**

Nisan 2025 | **April 2025**

Yayıncı | **Publisher**
Selçuk Üniversitesi Yayınları | Selcuk University Press

Yayımlandığı Ülke | **Broadcast Country**
Türkiye | Türkiye

Yayın Modeli | **Release Model**
Açık Erişim | Open Access

Hedef Kitlesi | **Target Audience**
Genel Tıp Dergisi'nin hedef kitlesi, tıp alanında araştırmalarını sürdüren profesyoneller ile bu alana ilgi duyan öğrenciler, okurlar ve kurumlardır. | The target audience of Genel Tıp Journal is professionals who continue their research in the field of theology and students, readers and institutions who are interested in this field.

Yayın Dili | **Publication Language**
İngilizce | English

Ücret Politikası | **Price Policy**
Hiçbir ad altında yazar veya kurumundan ücret alınmaz. | No fee is charged from the author or institution under any name.

Hakemlik Türü | **Type of Arbitration**
En az iki uzman hakem tarafından çift taraflı kör hakemlik sistemine uygun olarak değerlendirilir. | It is evaluated by at least two expert referees in accordance with the double-blind refereeing system.

İntihal Kontrolü | **Plagiarism Check**
Ön kontrolden geçirilen makaleler, intihal.net yazılımı kullanılarak intihal için taranır. | Pre-checked articles are scanned for plagiarism using intihal.net software.

Tarandığı Dizin ve Endeksler | Abstracting and Indexing

EBSCO DOAJ CABI TR DİZİN ERIH PLUS EUROPEAN REFERENCE INDEX FOR THE HUMANITIES AND SOCIAL SCIENCES

Embase ELSEVIER

SELÇUK ÜNİVERSİTESİ KONYA - 1908

EDITORIAL BOARD

Editorial Correspondence

Prof. Dr. Bahadır ÖZTÜRK
Selcuk University, School of Medicine
Department of Department of Medical Biochemistry
Alaeddin Keykubat Campus Selçuklu/Konya 42075 TÜRKİYE

Phone: +90 (332) 241 21 81 - 82
Faks: +90 (332) 241 21 84

CONTENTS

Received: 31 Mar 2024 | **Accepted:** 10 Oct 2024 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 222-225
DOI: 10.54005/geneltip.1460859

ORIGINAL ARTICLE

Which Is Superior in Creating Scientific Article Titles in Plastic Surgery: Human Intelligence or Artificial Intelligence?

Plastik Cerrahide Bilimsel Makale Başlığı Oluşturmada Hangisi Üstündür: İnsan Zekâsı mı Yapay Zekâ mı?

[1]Gökce Yildiran, [1]Sare Demirtas, [1]Hande Akdeniz, [1]Zekeriya Tosun

[1]Selcuk University Faculty of Medicine, Plastic, Reconstructive and Aesthetic Surgery Department, Konya, Türkiye

Correspondence

Gokce Yildiran, M.D., Assoc. Prof. Selcuk University Faculty of Medicine, Plastic, Reconstructive and Aesthetic Surgery Department, Konya, Türkiye

E-Mail: ggokceunal@gmail.com

How to cite ?

Yildiran G, Demirtas S, Akdeniz H, Tosun Z. Which Is Superior in Creating Scientific Article Titles in Plastic Surgery: Human Intelligence or Artificial Intelligence?. Genel Tıp Derg. 2025;35 (2): 222- 225

ABSTRACT

Aim: This study explores the effectiveness of artificial intelligence (AI) versus human expertise in generating scientific article titles within the context of plastic surgery. Acknowledging the pivotal role titles play in attracting readership and conveying a study's significance, this research investigates whether AI can match or surpass human capability in crafting compelling titles for academic articles.
Methods: Utilizing a sample of original articles from the Plastic and Reconstructive Surgery Journal and published in January and February 2023, the study employs OpenAI's ChatGPT to generate alternative titles based on article abstracts. A survey among plastic, reconstructive, and aesthetic surgery experts, with a blinded setup regarding the origin of the titles (AI-generated or original), facilitates the comparison. Statistical analysis, including t-tests and the Mann-Whitney U test, assesses preferences across general and specific subject areas within plastic surgery.
Results: Findings indicate a predominant preference for original titles, yet in certain subjects like hand/peripheral nerve surgery, AI-generated titles were more favored. On the other hand, in experimental and cosmetic subjects original titles were more favored.
Conclusion: The study highlights the potential and limitations of AI in academic creativity, suggesting a nuanced view where AI's effectiveness varies by subject matter, such as experimental and cosmetic subjects. It concludes that while AI exhibits competence in title generation, human oversight remains crucial, especially in areas requiring deep expertise and nuanced understanding. This investigation contributes to the discourse on AI's role in academic publishing, emphasizing the need for balanced integration of AI tools in the scientific communication process.

Keywords: Artificial intelligence, article, plastic surgery, title

ÖZ

Amaç: Bu çalışma, plastik cerrahi alanında bilimsel makale başlıkları oluşturulması için yapay zekâ kullanımı ile orijinal başlıklar arasındaki farkı araştırmaktadır. Başlıkların temel rolü, okuyucu çekme ve çalışmanın önemini iletme olup, bu araştırma yapay zekanın akademik makaleler için çekici başlıklar oluşturma konusunda insan yeteneğine eşit veya onu aşma potansiyeline sahip olup olmadığını incelemektedir.
Gereç ve Yöntem: Ocak ve Şubat 2023'te yayımlanan Plastic and Reconstructive Surgery Journal isimli dergiden seçilen orijinal makalelerin makale özetlerine dayanarak alternatif başlıklar üretildi. Plastik, rekonstrüktif ve estetik cerrahi uzmanlarından, tek körleştirilmiş bir anketle hem orijinal başlık hem de yapay zekanın ürettiği başlık arasından makaleye daha uygun olanını seçmeleri istendi. İstatistiksel analiz yapıldı.
Bulgular: Bulgular, orijinal başlıklara yönelik yaygın bir tercihi göstermekle birlikte, el/periferik sinir cerrahisi gibi belirli konularda yapay zekâ tarafından üretilmiş başlıkların daha fazla tercih edildiği ortaya konulmuştur. Öte yandan deneysel araştırma makalelerinde ve estetik cerrahi alanında orijinal başlık daha fazla tercih edilmiştir.
Sonuç: Akademik yaratıcılıkta yapay zekanın potansiyeli ve sınırları çok geniştir, ancak etkinliği konu maddesine göre dahi değişebilmektedir. Deneysel araştırmalar ve estetik cerrahi gibi derin uzmanlık ve nüanslı anlayış gerektiren alanlarda, insan gözetimi halen kritik durumdadır. Bu araştırma, yapay zekanın akademik yayıncılıktaki rolü üzerine tartışmaya katkıda bulunarak, bilimsel iletişim sürecinde yapay zekâ araçlarının dengeli entegrasyonunun önemini vurgulamaktadır.

Anahtar Kelimeler: Başlık, makale, plastik cerrahi, yapay zekâ

Introduction

The role of article titles in disseminating scientific research and increasing its impact is undeniably important. Titles are critical in attracting the interest of potential readers and reflect the overall scope and significance of the study at first glance. Therefore, the title of an article has a direct effect on the audience it reaches. In rapidly evolving disciplines with wide interest, such as plastic, reconstructive, and aesthetic surgery, the ability to create effective titles becomes even more significant.

The use of artificial intelligence (AI) in academic writing is increasingly becoming a topic of interest and concern (1, 2). Thanks to the rapid advancement of

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

these technologies and their language-processing capabilities, they have come into the discussion of being able to interact and even compete with human intelligence in writing. Considering the development of scientific communication, the increasing use of AI in academic settings, and the contributions of these technologies to education, library services, and research processes, the potential use of AI in article titles is particularly noteworthy. However, despite many research topics, there is still not enough data on the creation of titles in scientific articles by AI.

This study aims to compare and evaluate the effectiveness of scientific article titles created by AI with those created by human experts in the field of plastic surgery.

Material And Methods

The Plastic and Reconstructive Surgery Journal (PRSJ) was selected through random sampling among academic journals related to plastic, reconstructive, and aesthetic surgery with impact factors above two (3). All original articles in the issues of January 2023 and February 2023 were included in the study. Articles that are not research articles, such as editors' perspectives, discussions, continuing medical education (CME) articles, ideas and innovations, special topics, letters, viewpoints, replies, corrections, and podcasts, were excluded from the study. The topics were classified according to the subject index of the same journal: Breast, cosmetic, experimental, hand/peripheral nerve, pediatric/craniofacial, head and neck, and trunk.

The AI tool ChatGPT, known for its natural language processing capabilities, was used in its 4th version to load the abstracts of articles without their titles, and the same question was posed to the AI for each article abstract: "I am providing you with an abstract of a scientific research article, what do you think should be the title of this article?" Both the title generated by AI and the original title of the article were recorded.

A survey was created on Google Forms, targeting plastic, reconstructive, and aesthetic surgery experts with an h-index of at least three, who were blind to the study. No information about AI was provided in the survey. The participants were informed with the following instructions: "In each of the following questions, you will find an abstract of an article published in PRSJ. We ask you to choose which title you think is more appropriate for this abstract."

The data were collected via GoogleForms and analyzed using the Statistical Package for Social Sciences (SPSS), version 21.0, focusing on AI-generated Title (AIT) versus Original-Title (OT). The distribution of the data was examined using the Shapiro-Wilk test, and the difference between the two groups was assessed with the independent samples t-test and the Mann-Whitney U test. A p-value of less than 0.05 was considered statistically significant.

The average preference for titles on a general level and by specific topics was investigated. The difference between the OT and AIT groups was evaluated. The t-test was applied to the preference rates for titles in the sample sizes, which were subgroups representing at least 10% of the universe, specifically for the topics of breast, cosmetic, and experimental. The differences between the OT and AIT groups within these subtopics were assessed.

Results

A total of 54 articles were evaluated, with their distribution across subjects as follows: breast (n=13), cosmetic (n=12), experimental (n=8), hand/peripheral nerve (n=6), pediatric/craniofacial (n=6), head and neck (n=4), trunk (n=4), and lower extremity (n=1).

Out of the survey participants, 15 individuals responded to all questions. When evaluating all titles, it was found that the original titles of 37 articles (68.5%) were deemed more appropriate by the participants, while the AI-generated titles were preferred for 17 articles (31.4%).

Subject-specific evaluations revealed that only in the hand/peripheral nerve subject did the AI-generated titles find greater appropriateness (66.6%). For all other subjects, the original titles were considered more suitable.

Based on the number of preferences, the original titles were found suitable by an average of 8.18 people, while AI titles were preferred by an average of 6.81 people, with a statistically significant difference ($p<0.05$).

The preference rates for titles in the breast, cosmetic, and experimental subgroups were also evaluated. In the breast subject, the averages for original title (OT) and AI-generated title (AIT) were 7.61 and 7.38, respectively (Table 1). For the cosmetic subject, the OT and AIT averages were 8.66 and 6.33, respectively (Table 2). In the experimental subgroup, the OT and AIT averages were 8.5 and 6.5, respectively (Table 3).

Table 1. Test Statistics

	Breast
Mann-Whitney U	76.000
Wilcoxon W	167.000
Z	-.442
Asymp. Sig. (2-tailed)	.658

Table 2. Test Statistics

	Cosmetic
Mann-Whitney U	18.000
Wilcoxon W	96.000
Z	-3.156
Asymp. Sig. (2-tailed)	.002

Table 3. Test Statistics

	Exp.
Mann-Whitney U	13.000
Wilcoxon W	49.000
Z	-2.028
Asymp. Sig. (2-tailed)	.043

While no significant difference was found between OT and AIT groups in the breast subjects ($p>0.05$), a statistically significant difference was found in the cosmetic and experimental subjects between the two groups ($p<0.05$).

Discussion

ChatGPT, an advanced chatbot developed by OpenAI, has the potential to significantly impact academia, libraries, and education (4, 5). The reason for specifically using the January and February 2023 issues in this study was to select issues published before the release of ChatGPT4, thereby eliminating the possibility of titles being previously generated by ChatGPT4. AI can enhance searching and discovery, reference and information services, and content creation, but its use should be approached responsibly and ethically (4). In education, ChatGPT can serve as an assistant for instructors and a virtual teacher for students, but its performance varies across subject areas and raises concerns about the generation of incorrect or misleading information (5). Nevertheless, these AI models can perform various language tasks and produce human-like responses, offering excitement for academic productivity (6).

The excitement generated by this potential for academic productivity has also brought along questions related to article writing in the academic world. While ChatGPT can be entertaining and may enhance the writing of review articles, thereby improving scientific communication, it's important to consider its limitations, such as the need for review and editing to avoid plagiarism, if academic support is to be sought (7, 8). Additionally, its capability to generate incorrect information is a handicap, suggesting that reliance on its outputs in academic writing could be problematic.

Nevertheless, since it could be considered a language robot, using it to generate titles for scientific papers without making scientific interpretations could be intriguing. This study investigated which is more successful: Titles generated by AI or those produced by the human brain? In the field of plastic surgery, finding that original titles were more successful than those generated by AI indicates that the human brain is capable of evaluating and interpreting the entire article and summarizing the scientific content more effectively in a title.

When investigated by subject, only in the hand and peripheral nerve category were the AI-generated titles found to be more preferred, but due to the small sample size, it couldn't be determined if this finding was coincidental. However, in the breast area, statistically, both AI and original titles created similarly liked titles. This could be interpreted as a significant development in this clinical area, which occupies a large space in plastic surgery journals, suggesting that AI can generate titles for articles that are at least as good as the originals. Conversely, in the cosmetic and experimental fields, original titles were found to be significantly superior. These findings could be interpreted to mean that AI may offer equivalent or even more appealing titles in some clinical areas of plastic surgery compared to human experts. It might be better to interpret clinical sciences solely from article abstracts. Despite this potential, the tendency of human authors to use more innovative or field-specific jargon in experimental or cosmetic fields could make the original titles more appealing in these areas. AI can be creative in specific subject areas, but its abilities are still developing in fields requiring deep expertise and specialized jargon.

Studies have been conducted on how to put a better title while generating article titles (9). These studies have emphasized the need for conciseness, accuracy, and informativeness in a title. Bowman (10) has further emphasized the importance of an effective title, as it can influence readers' decisions to read the article, affect the author's reputation, and contribute to the journal's impact factor. He also highlighted the

benefits of shorter titles with appropriate punctuation. In this context, AI and machine learning techniques have high potential in the realm of automatic title generation. AI-based systems, with their ability to learn from large datasets, can create effective titles that reflect the main theme and content of an article using information derived from extensive literature databases. Studies like Putra's (11) research on improving summarization tasks using rhetorical categories demonstrate how far AI can advance in text summarization and identifying key concepts. These capabilities can be directly adapted to the title generation process, allowing for the production of titles that are both appealing and consistent with the content of the articles.

This study was a survey that asked participants to choose one of two options to understand which title was more suitable. Future studies could include more comprehensive data by adding information to the survey on aspects such as the attractiveness of the title, the alignment of the emphasis in the title with the article, conciseness, accuracy, and informativeness of the title.

The existence of at least a 26.6% preference rate for AI-generated titles (when evaluating each article) indicates that AI is competitive with humans in generating academic titles. However, significant barriers remain before AI can perform at a human level in all academic fields. The inability to deeply and successfully interpret abstracts, especially on niche topics like cosmetic and experimental subjects, serves as an indication of this.

In conclusion, AI can be considered an effective tool in academic publishing, but its use should be carefully evaluated, and such tools should remain under human oversight and intervention. A collaboration between AI and the human brain during the title creation process could lead to the derivation of more successful article titles.

Acknowledgment

We would like to express our infinite gratitude to the plastic surgeons who participated in this survey, which took a long time to respond to, and dedicated their valuable time to this study.

Authors' Contribution:

Conception: GY. Design: GY, HA, SD. Data collection and processing: SD, GY. Data analysis and interpretation: GY, SD, HA Writing: GY Critical review: ZT

References

1.DuBose J, Marshall D. AI in academic writing: Tool or invader. Public Services Quarterly 2023; 19:125-130

2.Storey VA. AI Technology and Academic Writing: Knowing and Mastering the "Craft Skills". IJAET 2023; 14:1-15

3.https://journals.lww.com/plasreconsurg/pages/default.aspx

4.Lund BD, Wang T. Chatting about ChatGPT: how may AI and GPT impact academia and libraries? Library hi tech news 2023; 40: 26-29

5.Lo CK. What is the impact of ChatGPT on education? A rapid review of the literature. Education Sciences 2023; 13:410

6.Dergaa I, Chamari K, Zmijewski P, Ben Saad H. From human writing to artificial intelligence generated text: examining the prospects and potential threats of ChatGPT in academic writing. Biol Sport 2023; 40:615-622

7.Thorp HH. ChatGPT is fun, but not an author. Science 2023; 379:313-313

8.Huang J, Tan M. The role of ChatGPT in scientific communication: writing better scientific review articles. American journal of cancer research 2023; 13:1148

9.Bavdekar SB. Formulating the right title for a research. Journal of the Association of Physicians of India 2016; 64:53-56

10.Bowman D, Kinnan S. Creating effective titles for your scientific publications. VideoGIE 2018; 3:260-261

11.Putra JWG, Khodra ML. Automatic title generation in scientific articles for authorship assistance: a summarization approach. Journal of ICT Research and Applications 2017; 11:253-267

Received: 18 Sep 2024 | **Accepted:** 14 Nov 2024 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 226-231
DOI: 10.54005/geneltip.1552117

ORIGINAL ARTICLE

Evaluation of The Need for Angioembolization After Percutaneous Nephrolithotomy in Children and Adults

Çocuklarda ve Erişkinlerde Perkütan Nefrolitotomi Sonrası Anjiyoembolizasyon İhtiyacının Değerlendirilmesi

[1]Mehmet Sarikaya, [2]Emre Kandemir

[1]Selcuk University, Faculty of Medicine, Department of Pediatric Surgery, Konya, Türkiye
[2]Karamanoglu Mehmetbey University, Faculty of Medicine, Department of Urology, Karaman, Türkiye

Correspondence

Mehmet Sarıkaya MD
Selcuk University, Faculty of Medicine, Department of Pediatric Surgery, Konya, Turkey Yeni İstanbul Str. Str. No:369 Selcuklu/Konya Türkiye

E-Mail: drmehmetsarikaya@hotmail.com

How to cite ?

Sarikaya M, Kandemir E. Evaluation of The Need for Angioembolization After Percutaneous Nephrolithotomy in Children and Adults. Genel Tıp Derg. 2025;35 (2): 226-231

ABSTRACT

Aims: The present study aimed to evaluate the severe and resistant bleeding that may develop after percutaneous nephrolithotomy (PNL) operation and the need for transcatheter angioembolization (TAE) that may be required accordingly.
Methods: PNL operations performed in two clinics in the last eight years were evaluated retrospectively. Patients with persistent and severe bleeding and a need for TAE were assessed in terms of preoperative, perioperative, and postoperative findings.
Results: The number of patients who underwent TAE was 14. The mean age was 40.9 years. The mean duration of operation was 80.1 minutes. The duration of fluoroscopy was 7.7 minutes (2.2-16 min). The mean hematocrit decrease of the patients was 11.8% (4.4-22.1%). The mean time from surgery to embolization was 5.6 days (1-11 days). The mean nephrostomy time was 3.8 days (1-7), and the mean hospital stay was 4.9 days (2-10). 12 Fr access sheath was used in one patient, 20 Fr access sheath in one patient, 26 Fr access sheath in one patient, and 30 Fr access sheath in 11 patients.
Conclusions: Bleeding requiring intervention after PNL is a condition that should be managed and treated well. The patient's characteristics, PNL technique, and per-operative findings cannot predict this condition. Larger scale prospective randomized studies are needed for definitive results.

Keywords: Fluoroscopy, nephrolithiasis, percutaneous nephrolithotomy, transcatheter angioembolization,

ÖZ

Amaç: Perkütan nefrolitotomi (PNL) operasyonu sonrası gelişebilen şiddetli ve dirençli kanamalar ve buna bağlı gerekebilen transkatater anjiyoembolizasyon (TAE) ihtiyacının değerlendirilmesi amaçlandı.
Gereç ve Yöntem: Son sekiz yılda iki klinikte gerçekleştirilen PNL operasyonları retrospektif olarak değerlendirildi. İnatçı ve şiddetli kanaması olan ve TAE ihtiyacı olan hastalar ameliyat öncesi, ameliyat sırası ve ameliyat sonrası bulgular açısından değerlendirildi.
Bulgular: TAE uygulanan hasta sayısı 14, ortalama yaş 40.9, ortalama ameliyat süresi 80.1 dakika, floroskopi süresi 7.7 dakika (2.2-16 dakika) izlendi. Hastaların ortalama hematokrit düşüşü %11,8 (%4,4-22,1), ameliyattan embolizasyona kadar geçen süre ortalama 5,6 gün (1-11 gün), ortalama nefrostomi süresi 3,8 gün (1-7) ve ortalama hastanede kalış süresi 4,9 gün (2-10) olarak bulundu. 1 hastada 12 Fr erişim kılıfı, 1 hastada 20 Fr erişim kılıfı, 1 hastada 26 Fr erişim kılıfı ve 11 hastada 30 Fr erişim kılıfı kullanıldı.
Sonuç: PNL sonrası müdahale gerektiren kanama iyi yönetilmesi ve tedavi edilmesi gereken bir durumdur. Hastanın özellikleri, PNL tekniği ve per-operatif bulgular bu durumu öngöremez. Kesin sonuçlar için daha büyük ölçekli prospektif randomize çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Floroskopi, nefrolitiazis, perkutan nefrolitotomi, transkateter anjioembolizasyon

Introduction

Urinary system stone disease, whose first records are as old as human history, is seen as endemic in a population including our country. In studies conducted in our country, the prevalence of stone was 11.1% (1). Treatment-related complications that occur in parallel with the frequency of the disease necessitate renewal and progress in the treatment options of the disease.

The first steps of kidney stone treatment were taken with nephrostomy in 1941 (2). Standard percutaneous nephrolithotomy (PNL) was defined by Fernastrom and Johansson in 1976 (3). In the approximately 40-year period that has passed until today, new alternatives in treatment have emerged, and new treatment modalities such as shock wave lithotripsy (SWL) and flexible ureterorenoscopy (F-URS) have come to the fore. In addition, PNL treatment has also been renewed, and the mini-PNL technique has been developed using smaller-diameter instruments (4). Despite other treatment modalities, PNL is currently considered the

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

gold standard treatment in selected cases of kidney stones larger than two cm (5).

Percutaneous access to the kidney to reach the collecting system also carries some risks. The current series reports 20.5% overall complication rates and 1%-55% transfusion rates due to bleeding (6-11). Although most of these bleedings regress with conservative treatment, 0.8% of resistant bleedings require additional intervention (12). The surgeon's ability to predict these types of bleeding can be essential in preventing and treating bleeding. The type of operation, duration, size, localization of the stone, access site, number, and many other parameters may be related to resistant bleeding.

Bleeding in the kidneys due to the operation can threaten vital functions due to the hypervascular structure of the kidneys. This situation can occur as a pseudoaneurysm affecting the arterial system, arteriovenous fistula, or bleeding into the collecting system and perirenal area, depending on the damage to the renal parenchyma. Rapid and effective lesion treatment is essential in resistant bleeding that can threaten hemodynamics and vital functions.

Transcatheter arterial embolization (TAE) or classical surgical methods are preferred during treatment. In TAE treatment, the renal artery is reached with the help of catheterization from the femoral artery. The renal arterial system is visualized with contrast material, and vascular pathology is detected. The lesion is visualized with the help of microcatheters, and occlusion is provided with embolizing agents (peripheral coil, glue-liquid embolizing agent Liquid Band MEDLOGIC, PVA) (13). Although parenchymal loss secondary to ischemia is observed in this treatment; this loss is equal to TAE in alternative surgical treatments, and more parenchymal loss or direct renal loss can often be observed (14). The cost of surgery and the risk of general anesthesia are also added to this picture. All these reasons make TAE treatment a priority today (15).

This study examined PNL operations performed by the same surgeons in different clinics in the last eight years, and cases requiring intervention after resistant hematuria were evaluated. Factors related to bleeding and the applied treatment methods were examined.

Material and Methods

Approval for the study was obtained from the local ethics committee (Etic number: 04-2021/17). Seven hundred eighty-one conventional and mini percutaneous nephrolithotomy operations performed by different surgeons in two State Hospitals were evaluated retrospectively between August 2016 and April 2024. Data from patients whose hematuria or hemorrhage continued in the postoperative period and who underwent additional treatment interventions to control bleeding were recorded. Preoperative demographic data preoperative and postoperative results of patients who required open surgery or TAE in the postoperative period were attempted to be examined. Patients who were referred for postoperative embolization but were reported as usual after embolization and patients whose necessary data could not be fully accessed were excluded from the study. Patients who underwent TAE represent a tiny portion of patients in the postoperative period. Therefore, the aim was to examine the general characteristics of patients who underwent TAE rather than compare these patients with the group that did not require TAE. Values were expressed as a number, mean, percentage, and standard deviation.

Results

Of the 781 patients who underwent PNL, 53 (6.7%) were children under the age of 18 years. The mean age of pediatric patients was 15.4±3.1 years (11-18). The mean age of adult patients was 41.2±8.3 years. When the patients who underwent PNL were analyzed, complete data on the TAE procedure performed in 14 patients were obtained and evaluated. It was remarkable that 13 (92.9%) of these patients were male. Only one patient was in the pediatric age group (15 years). The mean age was 40.9 years, while the patients' mean body mass index (BMI) was 26.9 kg/m2. The mean preoperative hematocrit values were calculated as 41.2, while the mean creatinine values indicating the preoperative renal reserves of the patients were seen as 1.02 mg/dl (range 0.78-2.0). The mean preoperative stone areas of the patients were seen as 8.6±6.4 cm2 (range 1.2-24 cm2 and median 8.35 cm2). Stone localization was noted as multiple calyceal localization in 78.6% of the patients, while only 14.3% had isolated lower calyceal localization, and 7.1% had isolated upper calyceal localization. In one of the stones located in the lower calyx, the stone area was 1.2 cm2, and in the other, 4 cm2.

The procedure was performed on the right kidney in 8 patients and on the left in 6 patients. When evaluated in terms of hydronephrosis, it was seen that 92.9% of the patients had mild (Grades 1 and 2) hydronephrosis.

Regarding stone opacity, it was seen that the stone was opaque in 92.9% of the patients. It was noticed that four (28.6%) patients had undergone a PNL operation before. It was noted that one of the patients with a history of PNL had bilateral kidney stones. PNL was performed from the other side three months ago, and the patient required PTE in the previous PNL. It was seen that another patient who underwent a PNL operation had previously undergone PNL from the other side; one patient had PNL from the same side three times before, and a resting stone remained, and the PNL operation performed on the same side of one patient was unsuccessful. The operation was terminated without being entered into the system or the stone removed. Of the patients with a history of open surgery, one had previously undergone open ureterolithotomy, one had previously undergone open nephrolithotomy, and one had previously undergone pyeloplasty. The preoperative demographic data of the patients are summarized in Table 1.

Table 1. Demographic data of the patients

		% or Range
Number of units	14	
Gender		
Male	13	92.9
Female	1	7.1
Age (mean - years)	40.9±12.2	15-61
Body mass index (mean-kg/m^2)	26.9±6.1	19.8-37.1
Preoperative hematocrit (mean-%)	41.2±4.7	32.2-49
Preoperative creatinine level (mean-mg/dL)	1.02±0.32	0.78-2.0
Stone size (mean-cm^2)	8.6±6.4	1.2-24
Stone localization		
Upper±Middle	1	7.1
Upper ±Lower	1	7.1
Middle±Lower	1	7.1
Lower	2	14.3
Upper	1	7.1
Complete coralliform	2	14.3
Pelvis±lower calyx	3	21.4
Pelvis±multiple calyx	3	21.4
Side		
Left	6	57.1
Right	8	42.9
Hydronephrosis (grade)		
1	8	41.2
2	5	35.7
3	1	7.1
Stone opacity		
Non-opaque	1	7.1
Opaque	13	92.9
Previous PNL surgery	4	28.6
Previous open surgery	3	21.4

PNL: Percutaneous nephrolithotomy

When the perioperative data of the patients who developed persistent hemorrhage were examined, it was seen that the mean duration of operation was 80.1 minutes (range 40-180 minutes, median 78.5 minutes), and the mean duration of fluoroscopy was 7.7 minutes (range 2.2-16 minutes, median 5.7 minutes). It was observed that only 3 of the patients (21.4%) had a hemorrhagic operation in the operation note. It was observed that a single percutaneous entry was made in 13 operations (92.9%), and two entries were made in one patient. It was observed that lower calyceal entry was made in 11 operations (78.6%), multiple (lower calyceal and middle calyceal entries) in one operation, isolated upper calyceal entry in one operation, and isolated middle calyceal entry in one operation. It was noted that the bleeding occurred from the middle calyceal entry during embolization in the patient who underwent multiple calyceal entries. In other words, two of the operations were seen to be hemorrhagic after the middle calyx, 11 after the lower calyx entry, and one after the upper calyx entry. 12 Fr access sheath was used in 1 patient, 20 Fr access sheath in one patient, 26 Fr access sheath in one patient, and 30 Fr access sheath in 11 patients. The perioperative data of the patients were summarized in Table 2.

Table 2. Perioperative data of the patients

		% or Range
Duration of operation (min)	80.1±35.0	40-180
Duration of fluoroscopy (min)	7.7±5.0	2.2-16
Severe bleeding during surgery	3	21.4
Number of access		
1	13	92.9
2	1	7.1
Access localization		
Multiple	1	7.1
Lower	11	78.6
Middle	1	7.1

Upper	1	7.1
Intercostal	2	14.3
Size of amplatz sheat		
12	1	7.1
20	1	7.1
26	1	7.1
30	11	78.6

When the information obtained from the patient's postoperative follow-ups was examined, it was seen that the mean nephrostomy time was 3.8 days (range 1-7 days, median four days) and the mean hospital stay was 4.9 days (range 2-10 days, median five days). In the postoperative blood values, it was seen that the mean hematocrit decrease of the patients was 11.8% (range 4.4-22.1%), and all of these patients were transfused at least one unit of erythrocyte suspension (ES). The mean transfusion amount was 2.57 units, and it was seen that the patient with the most transfusions was five units of ES. It was seen that two patients underwent open exploration for the treatment of bleeding and hemodynamic disorders that developed in the postoperative period, three patients underwent nephrectomy, and nine patients underwent PTE. It was seen that 3 of the patients who underwent open surgery had a history of previous open surgery. The mean time from surgery to the onset of symptoms related to bleeding was 3.1 days (0-11 days). The mean time from surgery to embolization was 5.6 days (1-11 days). When evaluated regarding postoperative stone-free status, it was noted that the operation resulted in residual stones in 50% of the patients. In addition to bleeding, chest tube placement due to pulmonary effusion or hemothorax was observed in the patient who underwent only upper calyceal access and intercostal access as additional complications. Information on the results of the operation is summarized in Table 3.

Table 3. Postoperative results

		% or Range
Duration of nephrostomy (days)	3.8±1.9	1-7
Duration of hospitalization (days)	4.9±2.2	2-10
Hemoglobin drop (mg/dL)	3.1±2.2	0.4-6.7
Hematocrit drop (%)	11.8±5.4	4.4-22.1
Number of patients transfused	14	100
Transfusion units (mean)	2.57±1.4	1-5
Intervention		
Exploration or nephrectomy	5	35.7
Transcatheter arterial embolization	9	64.3
Duration from surgery to the onset of severe Hematuria (days)	3.1±4.7	0-11
Additional postoperative complications		
Pulmonary effusion and chest tube insertion	1	7.1
Duration from surgery to intervention (days)	5.6±3.9	1-11
Success		
Residual stone	7	50
Stone-free or CIRF	7	50

CIRF: Clinically insignificant residual fragment

Discussion

PNL is widely used today as a minimally invasive method in treating kidney stones. Its effectiveness in treatment stands out with features such as less postoperative pain, smaller incisions, shorter hospital stays, and faster return to daily life compared to open surgery (16). Despite all these advantages, it should be remembered that PNL surgery has serious complications that may require additional intervention.

PNL complications include extravasation (7.2%), bleeding requiring blood transfusion (11.2-17.5%), fever (21-32.1%), septicemia (0.3-4.7%), colon injury (0.2-4.8%) and pleural injury (0-3.1%) (17). To standardize all these complications, complications were classified according to the Clavien grading system in the study conducted by Tefekli et al (18).

Resistant bleeding seen after PNL is one of the most important conditions to manage and treat correctly. Procedures such as calyceal puncture, dilatation, lithotripsy, and manipulation with a nephroscope, which are among the steps of the operation, can lead to bleeding from renal parenchymal sources. In studies, transfusion rates can reach up to 23% (7-10,12,19-23).

In bleeding requiring transfusion, additional intervention is required in resistant patients who do not respond to conservative treatment. Since it is an infrequent complication in the literature (0.3% - 1.4%) (7-10,12,19-23). A limited number of patient groups will inevitably be obtained in our study. Instead of comparing patients with the group without bleeding, it seems more appropriate to examine their current characteristics.

An essential point for the operation is determining the patient's current stone burden. In cases where there is an increased stone burden in the patients,

the operation time is extended, or a second access is needed since it is aimed at achieving complete success. This situation may create an additional bleeding risk. Erbin et al. In a study conducted by Ateş et al. with 2300 patients, the average stone size was 7.5±4.1 cm2 (24). In another study conducted by Ateş et al., when the data of 194 patients who underwent PNL were evaluated, it was seen that the average stone size was 3.87-4.75 cm2 in different groups (25). In our study, the average stone size was 8.6±6.4 cm2. Although the average stone burden in our patients who required additional intervention after resistant bleeding was seen to be larger than in the general patient group, the increased stone burden may increase the risk of bleeding.

Another essential condition for the operation is the localization of the stones. In parallel with the increased stone burden, the presence of stones in more than one localization instead of isolated calyces affects the operation time and necessitates manipulation in the calyceal system. In our study, stones were seen in more than one calyces in 11 patients (78.5%). It is thought that this situation may be related to increased bleeding risk.

In studies examining the effect of obesity on PNL success and complications, it is seen that PNL does not lead to an increase in complications in obese patients (26). When the demographic data of the patients were evaluated in our study, the average BMI was found to be 26.9 kg/m2, and obesity and resistant bleeding could not be associated.

When the hemoglobin and creatinine values of the patients were examined, almost all of them were seen to be within the standard value range. (Table 1) When the gender distribution is examined, it is seen that M/F is 13/1. There may be an increased risk for bleeding in male patients, but larger-scale prospective studies are needed.

The number, location, and diameter of the accesses applied during the operation are becoming increasingly important today. Our study observed that single access was used in 13 patients (92%), and lower calyceal access was applied in 11 patients (78.5%). It was thought that this situation could not be attributed as a risk since standard operations are usually performed with the lower calyceal-single access technique. Studies have shown that bleeding and morbidity decrease with the decrease in percutaneous tract width (27,28). In parallel, the effectiveness and reliability of mini PNL performed using a smaller diameter Amplatz sheath in adult patients has been demonstrated (29). In our study, it was observed that 26Fr and 30Fr Amplatz sheaths were used in 12 patients (85.7%), 12Fr in one patient, and 20Fr in one patient. Although the number of operations performed using 12Fr and 20Fr Amplatz sheaths is low, it has been noted that this type of complication can be seen even in operations performed with small-diameter access sheaths. Another issue that the surgeon will pay attention to during the operation is per-operative bleeding. This situation often causes the operation to be terminated early and may affect the success. In our study, per-operative bleeding was reported in three patients (21%). This situation suggests that not all bleeding resistant to conservative treatment can be predicted with per-operative findings. The mean hemoglobin decrease of the patients was 3.1±2.2%, and the mean hematocrit decrease was 11.8±5.4 g/dl. In a study by Çalışkan et al., the hemoglobin cut-off value was reported as 10 mg/dl, and angiographic control and treatment were recommended for bleeding below this value (13). The time until severe hematuria after the operation was found to be 3.1±4.7 days, and all patients received transfusion. Caution should be exercised, especially in hematuria, which requires transfusion at a late stage.

Among the treatment options, TKE stands out. Diagnosing the lesion causing bleeding and its rapid and effective treatment are possible in this way. In addition, the morbidity and general anesthesia risks added by surgical treatment are also prevented. It should be considered that the parenchymal losses observed after TKE occlusion are equal to or less than those observed with surgical treatment (14,15). In our study, TAE treatment was applied to 9 patients (64%), and open surgery was preferred in 5 patients (36%) due to deterioration in hemodynamics. It is thought that TAE treatment should be applied as a priority in hemorrhages where hemodynamics are stable.

Among the limitations of our study is that it is retrospective. In addition, since hemorrhages requiring intervention are rare in PNL, the comparison could not be made with the group without complications.

In conclusion, bleeding requiring intervention after PNL is a condition that should be managed and treated well. The patient's characteristics, PNL technique, and per-operative findings cannot predict this condition. However, caution should be exercised in patients with complex stones. Larger scale prospective randomized

studies are needed for definitive results.

Author Contributions

MS conceived the study, and all authors participated in the study design. EK collected and analyzed the data. EK and MS drafted the manuscript. All authors commented on the earlier versions of the manuscript. All authors edited the manuscript and approved the final version.

Conflict of Interest

The authors declare no conflict of interest.

References

1.Muslumanoglu AY, Binbay M, Yuruk E, Akman T, Tepeler A, Esen T, et al. Updated epidemiologic study of urolithiasis in Turkey. I: Changing characteristics of urolithiasis. Urol Res. 2011 Aug;39(4):309-14

2.Rupel E, Brown R. Nephroscopy with removal of stone following nephrostomy for obstructive calculous anuria. J Urol 1941;46: 177-82

3.Fernstrom I, Johansson B. Percutaneous pyelolithotomy: a new extraction technique. Scand J Urol Nephrol 1976;10:257-9

4.Helal M, Black T, Lockhart J, Figueroa TE. The Hickman peel-away sheath: an alternative for pediatric percutaneous nephrolithotomy. J Endourol. 1997; 11(3):171-2

5.Guidelines on Urolithiasis, European Urology Association, 2013, pp 1-100

6.Labate G, Modi P, Timoney A, Cormio L, Zhang X, Louie M, et al. The percutaneous nephrolithotomy global study: classification of complications. J Endourol 2011;25:1275-80

7.Lee WJ, Smith AD, Cubelli V, Badlani GH, Lewin B, Vernace F, et al. Complications of percutaneous nephrolithotomy. AJR Am J Roentgenol 1987;148:177-80

8.Stoller ML, Wolf JS Jr, St Lezin MA. Estimated blood loss and transfusion rates associated with percutaneous nephrolithotomy. J Urol 1994;152(6 Pt 1):1977-81

9.Turna B, Nazli O, Demiryoguran S, Mammadov R, Cal C. Percutaneous nephrolithotomy: variables that influence hemorrhage. Urology 2007;69:603-7

10.Segura JW, Patterson DE, LeRoy AJ, Williams HJ Jr, Barrett DM, Benson RC Jr, et al. Percutaneous removal of kidney stones: review of 1,000 cases. J Urol 1985;134:1077-81

11.Liatsikos EN, Kallidonis P, Stolzenburg JU, Ost M, Keeley F, Traxer O, et al. Percutaneous management of staghorn calculi in horseshoe kidneys: a multi-institutional experience. J Endourol 2010;24:531-6

12.Kessaris DN, Bellman GC, Pardalidis NP, Smith AG. Management of hemorrhage after percutaneous renal surgery. J Urol 1995;153(3 Pt 1):604-8

13.Çalışkan KC, Ulusay SM, Tanrıverdi O, Çakmakçı E, Sönmez NC, Arısan S. Iyatrojenik Renal Hemorajilerde Transkateter Embolizasyon Ne Zaman ve Nasıl Yapılmalı? Yeni Bir Algoritim. Okmeydanı Tıp Dergisi 28(2):84-93, 2012

14.Clark RA, Gallant TE, Alexander ES. Angiographic management of traumatic arteriovenous fistulas: clinical results. Radiology 1983;147:9-13

15.Heyns CF, van Vollenhoven P. Increasing role of angiography and segmental artery embolization in the management of renal stab wounds. J Urol 1992;147:1231-1234

16.White EC, Smith AD. Percutaneous stone extraction from 200 patients. J Urol 1984;132:437-8

17.Michel MS, Trojan L, Rassweiler JJ. Complications in percutaneous nephrolithotomy. Eur Urol 2007;51:899-906

18.Tefekli A, Ali Karadag M, Tepeler K, et al. Classification of percutaneous nephrolithotomy complications using the modified Clavien grading system: looking for a standard. Eur Urol 2008;53:184-90

19.el-Kenawy MR, el-Kappany HA, el-Diasty TA, Ghoneim MA. Percutaneous nephrolithotripsy for renal stones in over 1000 patients. Br J Urol 1992;69:470-5

20.Sacha K, Szewczyk W, Bar K. Massive hemorrhage presenting as a complication after percutaneous nephrolithotomy (PCNL). Int Urol Nephrol 1996;28:315-8

21.Patterson DE, Segura JW, LeRoy AJ, Benson RC Jr, May G. The etiology and treatment of delayed bleeding following percutaneous lithotripsy. J Urol 1985;133:447-51

22.Martin X, Murat FJ, Feitosa LC, Rouviere O, Lyonnet D, Gelet A, et al. Severe bleeding after nephrolithotomy: results of hyperselective embolization. Eur Urol 2000;37:136-9

23.Srivastava A, Singh KJ, Suri A, Dubey D, Kumar A, Kapoor R, et al. Vascular complications after percutaneous nephrolithotomy: are there any predictive factors? Urology 2005;66:38-40

24.Erbin A, Berberoğlu Y, Sarılar Ö, Akbulut MF, Özgör F, Sönmezay E, et al. Percutaneous Nephrolithotomy: Our Results of a Single-Centre Analysis in 2300 Cases. Haseki Tıp Bülteni 2014; 52: 19-24

25.Ateş M, Karalar M, Tüzel E, Pektaş F, Yıldırım B. Safety and efficacy of percutaneous nephrolithotomy in obese patients. Üroloji Dergisi 2011;37(2):105-111

26.Carson CC, Danneberger JE, Weinerth JL. Percutaneous lithotripsy in morbid obesity. J Urol 1988;139:243-247

27.Bader MJ, Gratzke C, Seitz M, Sharma R, Stief CG and Desai M: The "all-seeing needle": initial results of an optical puncture system confirming access in percutaneous nephrolithotomy. Eur Urol 2011; 59: 1054-9

28.Desai MR, Sharma R, Mishra S, Sabnis RB, Stief C and Bader M: Single-step percutaneous nephrolithotomy (micro-perc): the initial clinical report. J Urol 2011; 186: 140-5

29.Akbulut MF, Küçüktopçu O, Kandemir E, Sonmezay E, Şimşek A, Gürbüz ZG. Experiences of mini percutaneous nephrolithotomy in adult patients: Results of the pilot study. New J Urol 2015; 10 (1): 29-33

Received: 06 Sep 2024 | **Accepted:** 05 Dec 2024 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 232-241
DOI: 10.54005/geneltip.1544758

ORIGINAL ARTICLE

The Relationship Between Inflammatory Blood Cells and Executive Functions in Medication-Free Children with ADHD

İlaç Kullanmayan DEHB'li Çocuklarda İnflamatuar Kan Hücrelerinin Yürütücü İşlevler İle İlişkisi

[1]Mustafa Esad Tezcan, [1]Elif Kimya Balcı

[1]Department of Child and Adolescent Psychiatry, Selçuk University Faculty of Medicine, Konya, Türkiye

Correspondence

Mustafa Esad Tezcan,
Department of Child and Adolescent Psychiatry, Present Address: Ardıçlı, Akademi, Celal Bayar St., No:313, 42250 Selçuklu/Konya/Türkiye

E-Mail: esadaxe@gmail.com

How to cite ?

Tezcan ME, Kimya Balcı E. The Relationship Between Inflammatory Blood Cells and Executive Functions in Medication-Free Children with ADHD. Genel Tıp Derg. 2025;35 (2): 232-241

ABSTRACT

Background: The present study aimed to compare blood neutrophil, lymphocyte, platelet, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), erythrocyte and systemic inflammatory index levels in children with attention deficit hyperactivity disorder (ADHD) with typically developing (TD) healthy controls and to investigate the relationship between these levels and executive functions.
Materials and Methods: In this study, 79 ADHD children aged 8-14 years who did not use medication and 34 healthy controls were included. Participants' blood levels were based on routine complete blood count analysis. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) was used for clinical diagnosis in children, and the Stroop color test and serial digit learning test were applied to evaluate executive functions.
Results: No significant difference was found between the groups in neutrophil, lymphocyte, platelet, NLR, PLR, erythrocyte, and systemic inflammatory index levels. Compared to TDs, patients with ADHD were observed to perform significantly worse on executive function tests. Platelets, neutrophils, and lymphocytes were positively correlated with Stroop first section correction scores, platelets were positively correlated with Stroop second section time scores, lymphocytes were positively correlated with Stroop second section correction scores, NLR was negatively correlated with Stroop second section correction scores and platelets was positively correlated with Stroop third section time scores. Platelets and lymphocytes were positively correlated with Stroop section fourth time scores and NLR was positively correlated with Stroop section fourth error scores.
Conclusion: This study suggests that serum lymphocyte, neutrophil, NLR, and platelet levels may be associated with impaired executive tests in ADHD.

Keywords: Attention deficit hyperactivity disorder, child, executive function, systemic immune inflammation index

ÖZ

Arka plan: Bu çalışmanın amacı dikkat eksikliği ve hiperaktivite bozukluğu (DEHB) olan çocuklarda kan nötrofil, lenfosit, platelet, nötrofil-lenfosit oranı (NLR), platelet-lenfosit oranı (PLR), eritrosit ve sistemik inflamatuar index düzeylerini tipik olarak gelişen (TG) sağlıklı kontrollerle karşılaştırmak ve bu düzeylerin yürütücü işlevler ile ilişkilerini araştırmaktır.
Yöntemler: Bu çalışmaya 8-14 yaşları arasında ilaç kullanmayan 79 DEHB'li çocuk ve 34 TG sağlıklı kontrol dahil edilmiştir. Katılımcıların kan düzeyleri rutin tam kan sayımı analizine dayanmaktadır. Çocuklarda klinik tanı için Ruhsal Bozuklukların Tanısal ve Sayımsal El Kitabı, Beşinci Baskı (DSM-5) kullanılmış ve yürütücü işlevleri değerlendirmek için stroop renk testi ve sayı dizisi testi uygulanmıştır.
Bulgular: Nötrofil, lenfosit, platelet, NLR, PLR, eritrosit ve sistemik inflamatuar index düzeylerinde gruplar arasında anlamlı bir fark bulunmadı. Kontrol grubu ile karşılaştırıldığında, DEHB'li hastaların yürütücü işlev testlerinde anlamlı olarak daha kötü performans sergilediği gözlenmiştir. Platelet, nötrofil ve lenfositin stroop 1.bölüm düzeltme skorları ile pozitif, plateletin stroop 2.bölüm süre skorları ile pozitif, lenfositin stroop 2.bölüm düzeltme skorları ile pozitif korelasyon, NLR'nin ise stroop 2.bölüm düzeltme skorları ile negatif korelasyon, plateletin stroop 3.bölüm süre skorları ile pozitif korelasyon gösterdiği belirlenmiştir. Platelet ve lenfosit stroop 4.bölüm süre skorlarıyla pozitif, NLR stroop 4.bölüm hata skorlarıyla pozitif korelasyon göstermiştir.
Sonuç: Bu çalışma serum lenfosit, nötrofil, nötrofil-lenfosit oranı ve platelet düzeylerinin DEHB'deki bozulmuş yürütücü testlerle ilişkili olabileceğini göstermektedir.

Anahtar kelimeler: Çocuk, dikkat eksikliği hiperaktivite bozukluğu, sistemik immün inflamasyon indeksi, yürütücü işlev

Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by persistent symptoms of inattention, hyperactivity, and impulsivity (1). One widely accepted theory of ADHD symptomatology states that children and adolescents with this disorder show immature executive function development (2). In cognitive functioning, ADHD is most consistently associated with deficits in executive functions such as sustained attention, working memory, timing, psychomotor speed, and reaction time variability (3). Increased serum inflammatory markers have been reported to be associated with impaired executive function tests (4). In addition, in recent years, there has been increasing interest in investigating the role of systemic inflammation and immune dysregulation in the pathogenesis of ADHD (5). Genetic studies have also shown links between ADHD and polymorphisms

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

in genes associated with inflammatory pathways (6). Studies to date have shown that inflammatory cytokine levels in patients with ADHD are higher than in healthy individuals (7). Increased levels of cytokines in the central nervous system (CNS) can lead to neuroinflammation and consequent impairment of neuronal plasticity or alterations in synaptic processes (8). Increased risk of ADHD has been reported in children of mothers with inflammatory and immune system diseases (9). Changes in inflammatory cytokines have been shown to cause neurotransmission changes in dopaminergic pathways in the brain similar to those seen in ADHD (10). It has also been reported that there are inconsistent findings in studies on inflammatory changes in ADHD (11).

Ongoing inflammatory processes in the body can be recognized by complete blood count (CBC) tests, which are frequently used in clinical practice. CBC includes levels of erythrocytes, white blood cells (WBCs), neutrophils, lymphocytes, and platelets (12).

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) reflect the balance between adaptive immune responses and can be used to assess their use in routine clinical practice in chronic low-grade inflammation (13, 14). In recent years, NLR and PLR have been reported to be elevated in patients with depressive, bipolar, or non-affective psychosis (15). A recent meta-analysis showed that ADHD patients had higher NLR and PLR values compared to controls, and no significant difference was observed in inflammatory markers in studies including analyses according to ADHD subtypes. (16). However, higher WBC, neutrophil and NLR levels have been reported in women with ADHD compared to men with ADHD (17).

Changes in platelet function can affect common pathways with neurons by triggering inflammatory processes (18). PLR is a widely used marker that is thought to be associated with malignancies and infections (19).

A new index defined as the systemic immune inflammation index (SII) has been developed concerning inflammation variability. This index (Platelet × Neutrophil/Lymphocyte) is based on platelet, neutrophil, and lymphocyte counts (20). High SII appears to be associated with subclinical low-grade inflammation (21).

This study aimed to investigate whether neutrophil, erythrocyte, NLR, PLR, lymphocyte, platelet, and SII levels, which are an easy option for use in clinical practice in children with ADHD who have not received drug treatment, are different from typically developing (TD) healthy children and whether this is associated with inflammatory response and ADHD. In addition, the relationship between these parameters and executive functions in ADHD will be evaluated.

Materials and Methods

In the Child and Adolescent Psychiatry Outpatient Clinic of the Faculty of Medicine at Selcuk University, patients diagnosed with eating disorders, visual and hearing loss, chronic blood disease, organic brain damage, chronic physical illness, obesity, overweight, active infection, specific learning disability, genetic disorders, intellectual disability, substance abuse, schizophrenia, major depressive disorder (MDD), autism spectrum disorder (ASD) and language disorders and patients who had previously used any psychiatric medication were excluded from the study. Children with ADHD were included in the study considering the above-mentioned conditions. The selection process of participants with ADHD is shown in Figure 1.

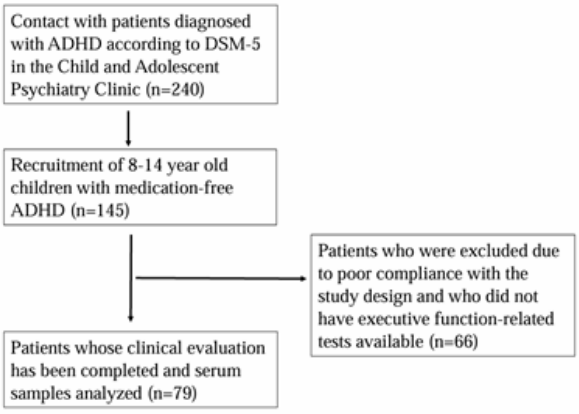


Figure 1. Flowchart of the patients' inclusion. ADHD: attention deficit hyperactivity disorder, n: number.

The TD control group consisted of healthy children who came to our clinic for consultation and were randomly selected under the exclusion criteria. Seventy-nine children were included in the ADHD group and 34 children were included in the TDs.

After the examination, sociodemographic data forms were completed by the clinician for both groups. Written informed consent was obtained from the parents of the children in both groups. The ages of the children ranged between 8 and 14 years. Children in both groups were similar in terms of age, height, weight, and body mass index (BMI).

The study was conducted under the Declaration of Helsinki and approved by the ethics committee of the Selçuk University Faculty of Medicine (Date: July 30, 2024, number: 2024/14).

Clinical assessment

The children in both groups were evaluated by a certificated interview using the Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (KSADS-PL) and diagnosed based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), criteria (22, 23). The validity and reliability of the K-SADS-PL for Turks were confirmed by Ünal et al. (24).

Stroop Test and Serial Digit Learning Test (SDLT) were administered to the participants by the clinician (25). Validity and reliability studies of the Stroop Test for the Turkish population were performed by Karakaş et al (26).

The SDLT was first proposed by Zangwill (1943) as a method for assessing short-term memory deficits (27). Studies on the standardization of the SDLT to Turkish culture were carried out by Karakaş et al (26). In the evaluation, the number of attempts by which the mastery learning was achieved and the total score were considered (28).

Blood Samples

Blood samples were taken from all children in both groups between 09.00 and 10.00 hours after 9 hours of fasting. All blood analyses were performed in the Biochemistry Laboratory of Selcuk University Medical Faculty Hospital using an automatic hematological analyzer (BC 6200). SII, NLR, and PLR values were obtained from CBC results based on quantitative analysis of blood cells.

Statistical analysis

The Statistical Package for Social Sciences, software version 24.0 (SPSS Inc., Chicago, IL) was used for the statistical analysis. Clinical, demographic, and blood variables were compared between the groups according to their distributions, as determined using the Student t-test or Mann-Whitney U test. The chi-square test was used for categorical data, and skewness and kurtosis values between −2 and +2 were used to determine a normal distribution (George, 2011). A p-value <0.05 was accepted as significant at the 95% CI. Effect sizes (ESs) were estimated using Cohen's d (parametric-nonparametric comparisons) and Cramér's V (categorical variables; Ess: ≥0.8, large; 0.5–0.7, intermediate; 0.2–0.4, small; and <0.2, no effect) (29). The Pearson and Spearman tests were used to determine any correlations between the blood parameters and executive function tests.

Results

A total of 113 children (34 in the TDs and 79 in the ADHD group) were included in the study. There was no statistically significant difference between ADHD and TD control groups in terms of weight, height, age, and BMI, but a significant difference was observed in terms of sex.

Regarding executive functions, Stroop's third, fourth, and fifth section times were significantly longer in the ADHD group than in the TDs. Stroop third, fourth, and fifth segment corrections were significantly higher in the ADHD group than in the TDs. Serial Digit Learning Test scores were significantly lower in the ADHD group compared to TDs.

No significant difference was found between the two groups in terms of neutrophil, erythrocyte, lymphocyte, NLR, PLR, SII, and platelet levels (z = −0,644; p =0,519, z = 0,136; p = 0,892, t = 0,705; p = 0,482, t = 1,201; p= 0,232, z = −0,745; p= 0,456, z = −0,472; p =0,637, t =-0,080; and p= 0,936, respectively).

Height, sex, weight, age, BMI, blood variables, and executive function-related test data of the two groups are shown in Table 1.

Platelets, neutrophils, and lymphocytes were positively correlated with Stroop 1 correction scores (p= 0,048; r= 0,223, p= 0,047; r= 0,224, p= 0,011; r= 0,286, respectively), platelets were positively correlated with Stroop 2 times scores, lymphocytes were positively correlated with Stroop 2 correction scores, NLR was negatively correlated with Stroop 2 correction scores (p= 0,037; r= 0,235, p= 0,007; r= 0,299, p= 0,015; r= -0,273, respectively) and platelets were positively correlated with Stroop 3 times scores (p=0,017; r= 0,267) (Table 2).

Platelet and lymphocyte correlated positively with Stroop section 4 time scores and NLR correlated positively with Stroop section 4 error scores (p= 0,002; r= 0,344, p= 0,016; r= 0,271, p= 0,014; r= 0,277, respectively) (Table 3).

Discussion

To the best of our knowledge, this is the first study to examine the relationship between neutrophil, erythrocyte, lymphocyte, NLR, PLR, SII, platelet levels,

Table 1. Data regarding the comparison of serum neutrophil, lymphocyte, NLR, PLR, erythrocyte, platelet, and SII levels and demographic and clinical variables of the two groups.

	ADHD (79)	TD (34)	p	$t/x^2/z$	d
Age (years)	10.43±2.57	10.74±2.24	0.550	-0.600	0.012
Sex	Erkek (47) Kız (32)	Erkek (13) Kız (21)	0.038	4.313	0.195[a]
Height	142.97 ±13.32	139.20 ±13.19	0.169	1.383	0.028
Weight[b]	38.98 ±11.44	37.58 ±15.44	0.758	-0.308	0.010
BMI	18.72±3.19	18.72 ±4.04	1.000	0.000	0.000
S1T[b]	13.95 ±5.47	10.98±2.59	0.251	-1.148	0.069
S1E	-	-	-	-	-
S1C[b]	0.13±0.46	0.06±0.23	0.598	-0.527	0.018
S2T[b]	14.78±6.25	12.59±3.42	0.537	-0.617	0.043
S2E[b]	0.03 ±0.17	-	-	-	-
S2C[b]	0.32 ±0.69	0.09 ±0.28	0.311	-1.012	0.043
S3T	19.81±5.40	17.59±4.71	0.041	2.072	0.043
S3E[b]	0.11±0.42	0.09 ±0.28	0.655	-0.447	0.005
S3C	1.20±1.31	0.38±0.65	0.001	3.454	0.079
S4T	30.16±10.95	21.28±5.11	<0.001	4.512	0.103
S4E[b]	0.30±1.07	0.15±0.35	0.711	-0.371	0.018
S4C	2.30±1.95	0.68±0.72	<0.001	4.716	0.110
S5T	44.12±18.24	29.37±8.12	<0.001	4.517	0.104
S5E[b]	1.37±2.83	0.59±0.65	0.848	-0.191	0.037
S5C[b]	3.75±2.71	1.26±0.89	0.036	-2.095	0.123
SDLT[b]	4.95±6.44	19.85±4.99	<0.001	-7.578	0.258
Neutrophil[b]	3.95±1.46	3.40±0.96	0.519	-0.644	0.044
Lymphocyte	2.88±0.77	2.77±0.66	0.482	0.705	0.014
NLR	1.43±0.61	1.29±0.50	0.232	1.201	0.025
PLR[b]	115.47±31.91	121.48±37.94	0.456	-0.745	0.017
Erythrocyte[b]	4.89±0.35	4.88±0.32	0.892	0.136	0.002
Platelet	318.84±71.14	319.97±64.31	0.936	-0.080	0.001
SII[b]	459,96±221,29	422,01±217,57	0,637	-0,472	0.172

[a]Cramer's V effect size, [b]Mann-Whitney U. ADHD: Attention deficit hyperactivity disorder, TD: Typically developing healthy controls, BMI: Body mass index, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, S1T: Stroop 1. Part-Time, S1E: Stroop 1. Part Error, S1C: Stroop 1. Part Correction, S2T: Stroop 2. Part-Time, S2E: Stroop 2. Part Error, S2C: Stroop 2. Part Correction, S3T: Stroop 3. Part-Time, S3E: Stroop 3. Part Error, S3C: Stroop 3. Part Correction, S4T: Stroop 4. Part-Time, S4E: Stroop 4. Part Error, S4C: Stroop 4. Part Correction, S5T: Stroop 5. Part-Time, S5C: Stroop 5. Part Correction, S5E: Stroop 5. Part Error, SDLT: Serial Digit Learning Test, SII: Systemic inflammatory index, d: Cohen's d effect size,

and executive functions in children with ADHD who are not taking medication. In our study, no significant difference was found between the two groups in terms of neutrophil, erythrocyte, lymphocyte, NLR, PLR, SII, and platelet levels.

Platelets, neutrophils, and lymphocytes were positively correlated with Stroop first section correction scores, platelets were positively correlated with Stroop first section time scores, lymphocytes were positively correlated with Stroop second section correction scores, NLR was negatively correlated with Stroop second section correction scores. Also, platelets were positively correlated with Stroop's third section time scores. Platelets and lymphocytes were positively correlated with Stroop section four-time scores and NLR was positively correlated with Stroop section fourth error scores.

Previous studies between children with ADHD and controls revealed that NLR and PLR values in the ADHD group were significantly higher than in controls (30, 31). Although a recent meta-analysis reported that ADHD patients had higher NLR and PLR values compared to controls, another recent review reported inconsistent results regarding adolescents with ADHD (16, 32).

Tablo 2. Correlation coefficients between blood variables and Stroop test subscores.

		S1T	S1C	S2T	S2C	S3T	S3E
SII	p	0.110	0.285	0.395	0.130	0.747	0.826
	r	0.181	0.122	0.097	-0.172	0.037	0.025
Ntrphl	p	0.131	**0.047**	0,454	0,576	0,860	0,962
	r	0.171	**0,224**	0,085	-0,064	-0,020	0,006
Lymp	p	0,481	**0,011**	0,261	**0,007**	0,113	0,875
	r	0,080	**0,286**	0,128	**0,299**	0,180	0,018
NLR	p	0,380	0,996	0,949	0,015	0.506	0.956
	r	0,100	-0,001	0,007	-0.273	-0.076	0.006
PLR	p	0.292	0.262	0.453	0.126	0.327	0.650
	r	0.120	-0.128	0.086	-0.174	0.112	0.052
Erythc	p	0.904	0.422	0.774	0.427	0.510	0.744
	r	-0.014	0.092	0.033	0.091	0.075	0.037
Platelet	p	0.058	**0.048**	**0.037**	0.116	**0.017**	0.413
	r	0.214	**0.223**	**0.235**	0.178	**0.267**	0,093

NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, S1T: Stroop 1. Part-Time, S1C: Stroop 1. Part Correction, S2T: Stroop 2. Part-Time, S2C: Stroop 2. Part Correction, S3T: Stroop 3. Part-Time, S3E: Stroop 3. Part Error, SII: Systemic inflammatory index, Ntrphl: Neutrophil, Lymp: Lymphocyte, Erythc: Erythrocyte

Tablo 3. Correlation coefficients between blood variables and Stroop and serial digit learning test subscores.

		S3C	S4T	S4E	S4C	S5T	S5E	S5C	SDLT
SII	p	0.463	0.739	0.055	0.957	0.864	0.694	0.366	0.843
	r	-0.084	0.038	0.217	-0.006	0.020	0.045	0.103	-0.023
Ntrphl	p	0.378	0.882	0.078	0.973	0.752	0.487	0.899	0.881
	r	-0.101	0.017	0.199	-0.004	-0.036	-0.079	0.015	0.017
Lymp	p	0.338	**0.016**	0.421	0.423	0.501	0.176	0.861	0.729
	r	0.109	**0.271**	-0.092	0.091	0.077	-0.154	0.020	-0.040
NLR	p	0.177	0.291	0.014	0.461	0.703	0.807	0.904	0.496
	r	-0.153	-0.120	0.277	-0.084	-0.044	0.028	-0.014	0.078
PLR	p	0.951	0.721	0.243	0.834	0.398	0.125	0.326	0.582
	r	-0.007	0.041	0.133	-0.024	0.096	0.174	0.112	-0.063
Erythc	p	0.171	0.992	0.520	0.552	0.379	0.785	0.913	0.492
	r	0.156	-0.001	-0.073	0.068	-0.100	-0.031	0.013	0.078
Platelet	p	0.293	**0.002**	0.958	0.256	0.193	0.829	0.071	0.145
	r	0.120	**0.344**	-0.006	0.129	0.148	0.025	0.204	-0.166

NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, S3C: Stroop 3. Part Correction, S4T: Stroop 4. Part-Time, S4E: Stroop 4. Part Error, S4C: Stroop 4. Part Correction, S5T: Stroop 5. Part-Time, S5C: Stroop 5. Part Correction, S5E: Stroop 5. Part Error, SDLT: Serial Digit Learning Test, SII: Systemic inflammatory index, Ntrphl: Neutrophil, Lymp: Lymphocyte, Erythc: Erythrocyte

Neutrophil, platelet, and SII levels have been reported to be higher in children with ADHD compared to controls in various studies (33, 34). However, similar to the results of our study, it was reported that there was no significant difference in platelet, WBC, NLR, PLR, and SII levels in adults and children with ADHD when compared with healthy controls (35-37).

It is known that increased inflammation may be associated with the development of psychopathology or resistance to treatment (9). Regarding other inflammatory markers, recent meta-analyses have shown that peripherally measured IL-6 levels are significantly higher and tumor necrosis factor-alpha (TNF-a) levels are lower in individuals with ADHD compared to healthy controls (11, 38). Contradictory results have been reported in studies on c-reactive protein (CRP) in children with ADHD (39, 40). Other studies showed that there was no significant difference

in IL-1 and TNF- a levels between participants with ADHD and controls (41, 42).

NLR, PLR, and platelet levels can be easily calculated from CBC analysis (43). NLR, platelets, and PLR are observed to be associated with inflammatory pathways and have been used as a diagnostic biomarker model in various psychiatric disorders (44, 45). However, increased SII levels may contribute to increased neuronal apoptosis in ADHD brains by causing the release of reactive oxygen species in neutrophils (46). There is a reciprocal relationship between platelets and inflammation. Numerous inflammatory cytokines released during inflammation, such as IL-1, may contribute to platelet activation (47).

Systemic inflammation has been suggested to play an important role in psychiatric disorders such as ASD and ADHD; however, the relationships between these neurodevelopmental disorders and systemic inflammation are still poorly understood (48). In contrast to ASD, less evidence has been presented to date for targeting inflammation in ADHD (49). The fact that the blood parameters examined in our study did not differ from the controls may be due to methodological differences such as sample characteristics, measurement methods, and study design. Conflicting results in the literature may also contribute to this situation. In addition, the fact that children with ADHD did not use medication in our study may affect blood parameters. Due to the retrospective design of other studies, active or chronic infections and autoimmunity-related conditions that may affect inflammatory markers may not be assessed. Further studies including repeated measurements with a larger study group are needed to demonstrate this situation.

In our study, platelets, neutrophils, and lymphocytes were positively correlated with Stroop first section correction scores, platelets were positively correlated with Stroop second section duration scores, lymphocytes were positively correlated with Stroop second section correction scores, NLR was negatively correlated with Stroop second section correction scores, and platelets were positively correlated with Stroop third section duration scores. Platelets and lymphocytes were positively correlated with Stroop section fourth duration scores and NLR was positively correlated with Stroop section fourth error scores. A negative correlation between NLR and Montreal Cognitive Assessment has been reported in patients with Parkinson's disease (50). It was reported that NLR and PLR were inversely significantly correlated with the working memory test (Direct Digit Span) but not with the Stroop test in women (51). High NLR is associated with visuospatial impairments and executive function deficits (52, 53). An association between high levels of NLR and cognitive impairment in Alzheimer's disease has been reported (54, 55). It has been reported that higher neutrophil counts are associated with an increased risk of dementia and higher lymphocyte counts are associated with a lower risk of dementia (56). While a significant negative correlation was observed between NLR and Stroop interference score in bipolar patients, no statistically significant difference was found between patients and controls in terms of NLR and PLR (57).

Elevated inflammatory cytokines are associated with worse cognitive function in patients with bipolar disorder (58). Increased neutrophil and NLR values and decreased lymphocyte levels were significantly associated with worsening Stroop interference in women with schizophrenia (59). Concerning this condition, studies provide preliminary evidence that elevated inflammatory status negatively affects frontotemporal cognitive abilities such as memory, attention, and executive functions (60). The correlation of platelet, lymphocyte, neutrophil, and NLR levels with the scores in the Stroop color test in our study may refer to previous studies. To clearly show the relationship between inflammatory response and executive tests, further studies are needed to understand this situation with repeated blood measurements throughout the day and related advanced executive function tests. The strengths of this study include the fact that the patients did not receive any medical treatment and the blood parameter measurements were performed within a certain period. To the best of our knowledge, this is the first study to examine the relationship between neutrophil, erythrocyte, lymphocyte, NLR, PLR, SII, platelet levels, and executive functions in children with ADHD who are not taking medication.

However, this study also has limitations. Considering neuroinflammation in our study, further repeated measurements of tests related to executive functions in patients with ADHD were not performed and comorbid psychiatric disorders that may occur with prospective follow-up could not be examined and other inflammatory cytokines were not investigated. Anxiety disorders and other depressive disorders comorbid with ADHD that may affect blood values were not excluded, and the severity of these symptoms was not assessed in participants with ADHD. Furthermore, daily

variations in blood levels have not been analyzed or correlated with executive function-related tests through repeated measurements. To understand the inflammatory variability in the participants, we measured only complete blood counts and did not measure other body fluids such as saliva cerebrospinal fluid, or neuronal tissue.

Conclusion

This study suggests that lymphocyte, neutrophil, neutrophil-to-lymphocyte ratio, and platelet levels in the blood may be related to impaired executive tests in ADHD. Neutrophil, erythrocyte, lymphocyte, NLR, PLR, SII, and platelet levels in ADHD patients aged 8-14 years who did not use medication did not differ significantly compared to the TD control group.

However, further studies are needed to examine the roles of inflammatory cytokines and blood cells in ADHD etiopathogenesis and their ability to identify executive dysfunctions in ADHD.

Authors' Contribution Statement

MET: Conceptualization, data curation, formal analysis, investigation, methodology, supervision, validation, visualization, writing – original draft, writing – review and editing.

EKB: Conceptualization, formal analysis, methodology, supervision, writing – original draft, writing – review and editing.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

Acknowledgments

The authors wish to thank the patients and families who participated in this study.

References

1.Posner J, Polanczyk GV, Sonuga-Barke E. Attention-deficit hyperactivity disorder. Lancet (London, England). 2020;395(10222):450-62.

2.Ramos-Galarza C, Pérez-Salas C. Moderator Role of Monitoring in the Inhibitory Control of Adolescents With ADHD. J Atten Disord. 2021;25(2):188-98.

3.Isfandnia F, El Masri S, Radua J, Rubia K. The effects of chronic administration of stimulant and non-stimulant medications on executive functions in ADHD: A systematic review and meta-analysis. Neuroscience and biobehavioral reviews. 2024;162:105703.

4.Lawrence KA, Gloger EM, Pinheiro CN, Schmitt FA, Segerstrom SC. Associations between IL-1β, IL-6, and TNFa polymorphisms and longitudinal trajectories of cognitive function in non-demented older adults. Brain, behavior, & immunity - health. 2024;39:100816.

5.Saccaro LF, Schilliger Z, Perroud N, Piguet C. Inflammation, Anxiety, and Stress in Attention-Deficit/ Hyperactivity Disorder. Biomedicines. 2021;9(10).

6.Dunn GA, Nigg JT, Sullivan EL. Neuroinflammation as a risk factor for attention deficit hyperactivity disorder. Pharmacology, biochemistry, and behavior. 2019;182:22-34.

7.Donfrancesco R, Nativio P, Borrelli E, Giua E, Andriola E, Villa MP, et al. Serum cytokines in pediatric neuropsychiatric syndromes: focus on Attention Deficit Hyperactivity Disorder. Minerva pediatrics. 2021;73(5):398-404.

8.Siniscalco D, Schultz S, Brigida AL, Antonucci N. Inflammation and Neuro-Immune Dysregulations in Autism Spectrum Disorders. Pharmaceuticals (Basel, Switzerland). 2018;11(2).

9.Núñez-Jaramillo L, Herrera-Solís A, Herrera-Morales WV. ADHD: Reviewing the Causes and Evaluating Solutions. Journal of personalized medicine. 2021;11(3).

10.Kozłowska A, Wojtacha P, Równiak M, Kolenkiewicz M, Huang ACW. ADHD pathogenesis in the immune, endocrine, and nervous systems of juvenile and maturating SHR and WKY rats. Psychopharmacology. 2019;236(10):2937-58.

11Chang JP, Su KP, Mondelli V, Pariante CM. Cortisol and inflammatory biomarker levels in youths with attention deficit hyperactivity disorder (ADHD): evidence from a systematic review with meta-analysis. Translational psychiatry. 2021;11(1):430.

12.Pogorzelska K, Krętowska A, Krawczuk-Rybak M, Sawicka-Żukowska M. Characteristics of platelet indices and their prognostic significance in selected medical condition - a systematic review. Advances in medical sciences. 2020;65(2):310-5.

13.Zahorec R. Neutrophil-to-lymphocyte ratio. Sixteen-year-long history since publication of our article in Bratislava Medical Journal. Bratislavske lekarske listy. 2017;118(6):321-3.

14.Urbanowicz T, Olasińska-Wiśniewska A, Michalak M, Rodzki M, Witkowska A, Straburzyńska-Migaj E, et al. The Prognostic Significance of Neutrophil to Lymphocyte Ratio (NLR), Monocyte to Lymphocyte Ratio (MLR), and Platelet to Lymphocyte Ratio (PLR) on Long-Term Survival in Off-Pump Coronary Artery Bypass Grafting (OPCAB) Procedures. Biology. 2021;11(1).

15.Cheng Y, Wang Y, Wang X, Jiang Z, Zhu L, Fang S. Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Monocyte-to-Lymphocyte Ratio in Depression: An Updated Systematic Review and Meta-Analysis. Frontiers in psychiatry. 2022;13:893097.

16.Gędek A, Modrzejewski S, Gędek M, Antosik AZ, Mierzejewski P, Dominiak M. Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and monocyte to lymphocyte ratio in ADHD: a systematic review and meta-analysis. Frontiers in psychiatry. 2023;14:1258868.

17.Chang SJ, Kuo HC, Chou WJ, Tsai CS, Lee SY, Wang LJ. Cytokine Levels and Neuropsychological Function among Patients with Attention-Deficit/Hyperactivity Disorder and Atopic Diseases. Journal of personalized medicine. 2022;12(7).

18.Ghoshal K, Bhattacharyya M. Overview of platelet physiology: its hemostatic and nonhemostatic role in disease pathogenesis. TheScientificWorldJournal. 2014;2014:781857.

19.Topal E, Celiksoy MH, Catal F, Karakoç HT, Karadağ A, Sancak R. The Platelet Parameters as Inflammatory Markers in Preschool Children with Atopic Eczema. Clinical laboratory. 2015;61(5-6):493-6.

20.Hu B, Yang XR, Xu Y, Sun YF, Sun C, Guo W, et al. The systemic immune-inflammation index predicts the prognosis of patients after curative resection for hepatocellular carcinoma. Clinical cancer research: an official journal of the American Association for Cancer Research. 2014;20(23):6212-22.

21.Yang YL, Wu CH, Hsu PF, Chen SC, Huang SS, Chan WL, et al. Systemic immune-inflammation index (SII) predicted clinical outcomes in patients with coronary artery disease. European journal of clinical investigation. 2020;50(5):e13230.

22.Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. Journal of the American Academy of Child and Adolescent Psychiatry. 1997;36(7):980-8.

23.APA. Diagnostic and statistical manual of mental disorders (DSM-5®): American Psychiatric Pub; 2013.

24.Ünal F, Öktem F, Çetin Çuhadaroğlu F, Çengel Kültür SE, Akdemir D, Foto Özdemir D, et al. [Reliability and Validity of the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version, DSM-5 November 2016-Turkish Adaptation (K-SADS-PL-DSM-5-T)]. Turk Psikiyatri Dergisi = Turkish Journal of Psychiatry. 2019;30(1):42-50.

25.Kılıç BG, Koçkar Aİ, Irak M, Şener Ş, Karakaş S. STROOP TESTİ TBAG FORMU NUN 6-11 YAŞ GRUBU ÇOCUKLARDA STANDARDİZASYON ÇALIŞMASI. 2002.

26.KARAKAŞ S, ERDOĞAN E, Soysal Ş, ULUSOY T, Yüceyurt ULUSOY İ, ALKAN S. Stroop test TBAG form: standardization for Turkish culture, reliability and validity. Journal of Clinical Psychiatry. 1999;2(2):75-88.

27.Hamsher KdS, Benton A, Digre KJJoC, Neuropsychology E. Serial digit learning: Normative and clinical aspects. 1980;2(1):39-50.

28.KaraKaş S. BİLNOT bataryası el kitabı: Nöropsikolojik testler için araştırma ve geliştirme çalışmaları [BILNOT Battery Handbook: research and development studies for neuropsychological tests]. Ankara, turkey: eryılmaz Offset Matbaacılık; 2006.

29.Cohen J. Statistical power analysis for the behavioral sciences: Academic press; 2013.

30.Avcil S. Evaluation of the neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and mean platelet volume as inflammatory markers in children with attention-deficit hyperactivity disorder. Psychiatry and clinical neurosciences. 2018;72(7):522-30.

31.Önder A, Gizli Çoban Ö, Sürer Adanır A. Elevated neutrophil-to-lymphocyte ratio in children and adolescents with attention-deficit/hyperactivity disorder. International journal of psychiatry in clinical practice. 2021;25(1):43-8.

32.Popov M, Popov Y, Kosterin D, Lepik O. Inflammatory Hematological Ratios in Adolescents with Mental Disorders: A Scoping Review. Consortium psychiatricum. 2024;5(2):45-61.

33.Topal Z, Tufan AE, Karadag M, Gokcen C, Akkaya C, Sarp AS, et al. Evaluation of peripheral inflammatory markers, serum B12, folate, ferritin levels, and clinical correlations in children with autism spectrum disorder (ASD) and attention deficit hyperactivity disorder

(ADHD). Nordic journal of psychiatry. 2022;76(2):150-7.

34.Öz E, Parlak ME, Kapıcı Y, Balatacı U, Küçükkelepçe O, Kurt F. Pre- and post-treatment evaluation of routine blood analysis in patients with attention deficit hyperactivity disorder and comparison with the healthy control group. Scientific reports. 2023;13(1):16233.

35.Ceyhun HA, Gürbüzer N. New Hematological Parameters as Inflammatory Biomarkers: Systemic Immune Inflammation Index, Platerethritis, and Platelet Distribution Width in Patients with Adult Attention Deficit Hyperactivity Disorder. Advances in neurodevelopmental disorders. 2022;6(2):211-23.

36.Binici NC, Kutlu A. Is ADHD an inflammation-related disorder?/DEHB inflamasyonla iliskili bir bozukluk olabilir mi? Anadolu Psikiyatri Dergisi. 2019;20(3):313-21.

37.Abdel Samei AM, Mahmoud DAM, Salem Boshra B, Abd El Moneam MHE. The Interplay Between Blood Inflammatory Markers, Symptom Domains, and Severity of ADHD Disorder in Children. J Atten Disord. 2024;28(1):66-76.

38.Misiak B, Wójta-Kempa M, Samochowiec J, Schiweck C, Aichholzer M, Reif A, et al. Peripheral blood inflammatory markers in patients with attention-deficit/hyperactivity disorder (ADHD): A systematic review and meta-analysis. Progress in neuro-psychopharmacology & biological psychiatry. 2022;118:110581.

39.Chang JP, Mondelli V, Satyanarayanan SK, Chiang YJ, Chen HT, Su KP, et al. Cortisol, inflammatory biomarkers and neurotrophins in children and adolescents with attention deficit hyperactivity disorder (ADHD) in Taiwan. Brain, behavior, and immunity. 2020;88:105-13.

40.Leffa DT, Caye A, Santos I, Matijasevich A, Menezes A, Wehrmeister FC, et al. Attention-deficit/hyperactivity disorder has a state-dependent association with asthma: The role of systemic inflammation in a population-based birth cohort followed from childhood to adulthood. Brain, behavior, and immunity. 2021;97:239-49.

41.Mahmoud IM, El-Keiy M, Hammad K, Mostafa A. Serum interleukin-6 level in children with attention-deficit hyperactivity disorder. Al-Azhar J Pediatr. 2020;23:1315-37.

42.Verlaet AAJ, Breynaert A, Ceulemans B, De Bruyne T, Fransen E, Pieters L, et al. Oxidative stress and immune aberrancies in attention-deficit/hyperactivity disorder (ADHD): a case-control comparison. European child & adolescent psychiatry. 2019;28(5):719-29.

43.Karageorgiou V, Milas GP, Michopoulos I. Neutrophil-to-lymphocyte ratio in schizophrenia: A systematic review and meta-analysis. Schizophrenia research. 2019;206:4-12.

44.Mazza MG, Lucchi S, Tringali AGM, Rossetti A, Botti ER, Clerici M. Neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in mood disorders: A meta-analysis. Progress in neuro-psychopharmacology & biological psychiatry. 2018;84(Pt A):229-36.

45.Ehrlich D, Humpel C. Platelets in psychiatric disorders. World journal of psychiatry. 2012;2(6):91-4.

46.Yun HS, Park MS, Ji ES, Kim TW, Ko IG, Kim HB, et al. Treadmill exercise ameliorates symptoms of attention-deficit/hyperactivity disorder by reducing Purkinje cell loss and astrocytic reaction in spontaneous hypertensive rats. Journal of exercise rehabilitation. 2014;10(1):22-30.

47.Margetic S. Inflammation and haemostasis. Biochemia medica. 2012;22(1):49-62.

48.Chen X, Yao T, Cai J, Fu X, Li H, Wu J. Systemic inflammatory regulators and 7 major psychiatric disorders: A two-sample Mendelian randomization study. Progress in neuro-psychopharmacology & biological psychiatry. 2022;116:110534.

49.Ferencova N, Visnovcova Z, Ondrejka I, Hrtanek I, Bujnakova I, Kovacova V, et al. Peripheral Inflammatory Markers in Autism Spectrum Disorder and Attention Deficit/Hyperactivity Disorder at Adolescent Age. International journal of molecular sciences. 2023;24(14).

50.Lucero J, Gurnani A, Weinberg J, Shih LC. Neutrophil-to-lymphocyte ratio and longitudinal cognitive performance in Parkinson's disease. Annals of clinical and translational neurology. 2024.

51.Frota IJ, de Oliveira ALB, De Lima DN, Jr., Costa Filho CWL, Menezes CES, Soares MVR, et al. Decrease in cognitive performance and increase of the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios with higher doses of antipsychotics in women with schizophrenia: a cross-sectional study. BMC psychiatry. 2023;23(1):558.

52.Shang T, Ma B, Shen Y, Wei C, Wang Z, Zhai W, et al. High neutrophil percentage and neutrophil-lymphocyte ratio in the acute phase of ischemic stroke predict cognitive impairment: A single-center

retrospective study in China. Frontiers in neurology. 2022;13:907486.

53.Fang Y, Doyle MF, Alosco ML, Mez J, Satizabal CL, Qiu WQ, et al. Cross-Sectional Association Between Blood Cell Phenotypes, Cognitive Function, and Brain Imaging Measures in the Community-Based Framingham Heart Study. Journal of Alzheimer's disease: JAD. 2022;87(3):1291-305.

54.An P, Zhou X, Du Y, Zhao J, Song A, Liu H, et al. Association of Neutrophil-Lymphocyte Ratio with Mild Cognitive Impairment in Elderly Chinese Adults: A Case-control Study. Current Alzheimer research. 2019;16(14):1309-15.

55.Liu JH, Zhang YJ, Ma QH, Sun HP, Xu Y, Pan CW. Elevated blood neutrophil to lymphocyte ratio in older adults with cognitive impairment. Archives of gerontology and geriatrics. 2020;88:104041.

56.van der Willik KD, Fani L, Rizopoulos D, Licher S, Fest J, Schagen SB, et al. Balance between innate versus adaptive immune system and the risk of dementia: a population-based cohort study. Journal of Neuroinflammation. 2019;16(1):68.

57.Sağlam Aykut D, Civil Arslan F, Özkorumak Karagüzel E, Aral G, Karakullukçu S. The relationship between neutrophil-lymphocyte, platelet-lymphocyte ratio and cognitive functions in bipolar disorder. Nordic journal of psychiatry. 2018;72(2):119-23.

58.Lotrich FE, Butters MA, Aizenstein H, Marron MM, Reynolds CF, 3rd, Gildengers AG. The relationship between interleukin-1 receptor antagonist and cognitive function in older adults with bipolar disorder. International journal of geriatric psychiatry. 2014;29(6):635-44.

59.Karahan A, Manzak Saka I, Sağlam Aykut D, Civil Arslan F, Selçuk Özmen E, Özkorumak Karagüzel E. The relationship between peripheral immune cell markers and cognitive functions in patients with schizophrenia. International journal of psychiatry in medicine. 2024:912174241266059.

60.Bauer IE, Pascoe MC, Wollenhaupt-Aguiar B, Kapczinski F, Soares JC. Inflammatory mediators of cognitive impairment in bipolar disorder. Journal of psychiatric research. 2014;56:18-27.

Received: 25 Nov 2024 | **Accepted:** 06 Jan 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 242-247
DOI: 10.54005/geneltip.1591194

ORIGINAL ARTICLE

The Relationship Between Fetal Cardiac Echogenic Foci Detected in Fetal Echocardiography and Congenital Heart Diseases: A Cross-sectional Study

Fetal Ekokardiyografide Saptanan Fetal Kardiyak Ekojenik Odakların Konjenital Kalp Hastalıkları İle İlişkisi: Kesitsel Bir Çalışma

[1]Hayrullah Alp, [2]Gamze Savcı, [3]Fatmagül Şencan

[1]Professor, M.D. Karamanoğlu Mehmetbey University, Faculty of Medicine, Department of Pediatric Cardiology, Karaman, Türkiye
[2]Karamanoğlu Mehmetbey University, Faculty of Medicine, Department of Obstetrics and Gynecology, Karaman, Türkiye
[3]Karaman Training and Research Hospital, Department of Obstetrics and Gynecology, Karaman, Türkiye

Correspondence

Hayrullah Alp, M.D., Prof. Karamanoğlu Mehmetbey University, Faculty of Medicine, Department of Pediatric Cardiology, Karaman, Türkiye

E-Mail: drhayrullahalp@hotmail.com

How to cite ?

Alp H, Savcı G, Şencan F. The Relationship Between Fetal Cardiac Echogenic Foci Detected in Fetal Echocardiography and Congenital Heart Diseases: A Cross-sectional Study. Genel Tıp Derg. 2025;35 (2): 242-247

ABSTRACT

Aim: To determine the prevalence of intracardiac echogenic focus and investigate the possible association of congenital heart diseases in risky pregnancies.
Methods: A total of 380 pregnant women in the 17th to 36th weeks of gestation were included in our study. The patients were classified as low-risk and high-risk groups according to various referral reasons such as any drug usage, presence of chromosomal or fetal anomalies, number and characteristics of previous pregnancies, congenital or acquired heart diseases in the family, and presence of family history.
Results: Based on the selective criteria 134 (35.26%) pregnant women were classified as the low-risk group while 246 (64.74%) pregnant were classified as the high-risk group. Maternal diabetes (13.16%) was the most common reason for referral in the high-risk group. However, in low-risk pregnancies, the lack of a good image of the fetal heart by ultrasound was the major reason for referral (21.05%). Intracardiac echogenic foci were detected in a total of 77 (20.26%) cases, 68 (50.75%) of whom were in the low-risk group and nine (3.66%) cases were in the high-risk group. Left ventricular echogenic foci were detected in 59 (44.03%) fetuses in low-risk pregnancies and four (1.63%) fetuses in high-risk pregnancies (p=0.001). Additionally, only one fetus in a low-risk pregnancy and one fetus in a high-risk pregnancy had echogenic foci in one of the ventricles with congenital heart diseases.
Conclusion: In conclusion, we found the prevalence of intracardiac echogenic foci in low-risk pregnancies as 50.75%, higher than in high-risk pregnancies. This can be attributed to ethnicity, tertiary hospital referrals, a relatively low number of patients, and other associated factors. Additionally, in our study, no correlation was found between congenital heart diseases and intracardiac echogenic foci in both low- and high-risk pregnancies.

Keywords: Congenital heart diseases, intracardiac echogenic focus, risky pregnancies

ÖZ

Amaç: Çalışmamızın amacı intrakardiyak ekojenik odak prevalansını belirlemek ve riskli gebeliklerde konjenital kalp hastalıklarıyla olası ilişkisini araştırmaktır.
Yöntem: Çalışmamıza 17-36. gebelik haftasında olan toplam 380 gebe dahil edildi. Hastalar herhangi bir ilaç kullanımı, kromozomal veya fetal anomalilerin varlığı, önceki gebeliklerin sayısı ve özellikleri, ailede konjenital veya edinilmiş kalp hastalıkları ve aile öyküsünün varlığı gibi çeşitli sevk nedenlerine göre düşük riskli ve yüksek riskli gruplar olarak sınıflandırıldı.
Bulgular: Seçici kriterlere göre 134 (%35,26) gebe düşük riskli grup olarak sınıflandırılırken, 246 (%64,74) gebe yüksek riskli grup olarak sınıflandırıldı. Yüksek risk grubunda en sık sevk nedeni maternal diyabet (%13,16) idi. Ancak düşük riskli gebeliklerde, ultrasonografi ile fetal kalbin iyi görüntülenmemesi sevk için en önemli nedendi (%21,05). Toplam 77 (%20,26) gebede intrakardiyak ekojenik odaklar tespit edildi, bunlardan 68 (%50,75) tanesi düşük risk grubunda ve 9 (%3,66) tanesi de yüksek risk grubundaydı. Düşük riskli gebeliklerde 59 (%44,03) fetüste ve yüksek riskli gebeliklerde 4 (%1,63) fetüste sol ventrikülde ekojenik odaklar tespit edildi (p=0,001). Ek olarak, konjenital kalp hastalığı tespit edilen düşük ve yüksek risk grubundaki birer fetüste sol ventrikülde yerleşimli ekojenik odaklar tespit edildi. Sonuç: Sonuç olarak, düşük riskli gebeliklerde intrakardiyak ekojenik odakların prevalansını %50,75 olarak bulduk ki bu yüksek riskli gebeliklere göre daha yüksekti. Bu durum; etnik kökene, üçüncü basamak hastane sevklerine, nispeten düşük hasta sayısına ve diğer ilişkili faktörlere bağlanabilir. Ek olarak, çalışmamızda, hem düşük hem de yüksek riskli gebeliklerde konjenital kalp hastalıkları ile intrakardiyak ekojenik odaklar arasında bir ilişki tespit edilmedi.

Anahtar Kelimeler: Riskli gebelikler, intrakardiyak ekojenik odak, konjenital kalp hastalığı

Introduction

Schechter et al. first described fetal intracardiac echogenic focus (ICEF) in 1987 (1). ICEF is a condition frequently encountered during routine fetal echocardiography (ECG) and can sometimes be a reason for referral for fetal ECG. ICEF is a small structure seen in the fetal heart with either an isolated or multiple echogenic foci that are as bright as bone (2). Also, during the routine fetal ECG, ICEF is found within the papillary muscles of the ventricles on a four-chamber view. Although its etiology is unknown, it is thought to occur due to a normal variant or increased mineralization in the development of the papillary muscle or chordae within the ventricle (2). Also, the study of Levy and Mintz suggested that ICEF may be incomplete fenestration of the chordae tendineae or papillary muscle (3). Additionally, Brown et al. identified

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

fetuses with an echogenic focus with histologically clarified mineralization present in the papillary muscle in 1994 (4). In this way, many studies reported that ICEF is a benign variant with no clinical significance (5,6). Some of the studies conducted on this subject have reported that ICEF is a variation of normal development, while others have drawn attention to its relationship with chromosomal abnormalities and congenital heart diseases (7-10).

The reported incidence of ICEF varies between 0.5 and 20% with an overall frequency of 5.6% (11,12). On the other hand, the prevalence of ICEF also varies among races, ethnicities, and populations (7). Also, the incidence would depend on the reason for the ultrasound (US) referral. In patients at high risk for perinatal problems studies suggested a possible association of ICEF with fetal aneuploidy (7-10). Further studies showed that ICEF might be a benign finding in low-risk populations (13,14).

Many studies showed that ICEF is frequently found in the left ventricle neither than in the right ventricle with rare cases being bilateral (5,15)., Also, Wax and Philput, reported that the biventricular location of ICEF is associated with fetal aneuploidy in a high-risk population, not cardiac structural defects in 1998 (16). Also, Bronshtein and colleagues suggested that ICEF located in the right ventricle may be a signal of poor prognosis (17).

To shed light on this issue, in our study, ICEF and congenital heart diseases detected in high- and low-risk pregnant women undergoing fetal ECG in our hospital were investigated. The purpose of this study was to determine the prevalence of ICEF and to investigate the possible association of congenital heart diseases in low and high-risk pregnancies.

Materials And Methods

Study population

The study with a retrospective design was approved by the Medical Research Ethics Committee of the Medical School of Karamanoğlu Mehmetbey University (Date: 26.09.2024, decision no: 10-2024/01, and reg. no: E-11095095-050.04-216359). The study was performed under the 1961 Declaration of Helsinki and its later amendments. Written informed consent was obtained from all patients for the use of data from medical records.

This study is a retrospective research performed between January 2023 and September 2024. A total of 380 pregnant women between the 17th to 36th weeks of gestation were included in our study. The patients consisted of pregnant women referred by obstetricians due to various reasons classified as high-risk and low-risk groups (18). The study population was analyzed in detail for pregnancy history, reasons for referral to our clinic, any drug usage, presence of chromosomal or fetal anomalies, number and characteristics of previous pregnancies, congenital or acquired heart diseases in the family, and presence of family history. Also, all pregnant women were grouped as either high-risk or low-risk pregnancies according to these parameters. Also, echocardiographic confirmation was done in the babies after birth for congenital heart diseases.

Fetal echocardiography (ECG)

Fetal heart examinations were performed using a Philips Affiniti 50 (Philips Healthcare, Andover, Netherlands) ECG device with 2.5-5 MHz transducers by the same echocardiographic scanner. All fetal echocardiographic examinations were performed using standard techniques determining the fetal position and heart axis and providing Doppler and M-mode measurements (19,20). In all the cases, four-chamber views, outflow-tract views, three-vessel views, and aortic and ductal arch views were done. Fetal heart rate was noted and any arrhythmia was confirmed with M-mode imaging, color Doppler, and pulse-wave Doppler were used whenever necessary. All the images were recorded.

Statistical analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 16.0 software program(Chicago, IL, USA). Data in parametric tests were given as mean and ± standard deviation. Data were presented as percentage values. The chi-square test was used to compare parametric values between groups, and the student t-test was used for non-parametric data. A p-value of <0.05 was considered statistically significant.

Results

A total of 380 pregnant women were included in the study. The low-risk and high-risk pregnancy groups constituted under the criteria during referrals are seen in Table 1. In this way, 134 (35.26%) pregnant women were classified as the low-risk group while 246 (64.74%) pregnant were classified as the high-risk group. Maternal diabetes mellitus (13.16%), dysrhythmia

(5.26%), and a history of a previous child or fetus with extracardiac abnormality (8.42%) were the most common reasons for referral in the high-risk group. However, in low-risk pregnancies, the lack of a good image of the fetal heart by US was the major reason for referral (21.05%).

Table 1. Distribution of pregnant women by low-risk and high-risk factors

Risk Groups and Factors	n=380	%
1. Low-risk Group		
Lack of good image of the fetal heart by US	80	21.05
Suspicion of CHD during 2nd trimester by US	41	10.78
Self-referral	13	3.43
Total	134	35.26
2. High-Risk Group		
2. a. Maternal Factors		
Gestational DM	50	13.16
In vitro fertilization	18	4.75
Multiple pregnancies	14	3.68
Maternal use of medicine	11	2.89
Advanced maternal age	13	3.43
Maternal CHD	7	1.84
Maternal rheumatologic diseases	5	1.32
Maternal TORCH infections	1	0.26
2. b. Fetal Factors		
Dysrhythmia	20	5.26
Polyhydramniosis, oligohydramniosis	13	3.43
Fetal extracardiac anomaly	12	3.16
Chromosomal anomaly	2	0.52
Increased nuchal translucency	3	0.79
2. c. Hereditary Factors		
Previous child or fetus with CHD	21	5.52
Previous child or fetus with extracardiac anomaly	32	8.42
Familial CHD (excluding parents and siblings)	24	6.31
Total	**246**	**64.74**

CHD: Congenital heart diseases, DM: Diabetes mellitus, TORCH: Toxoplasma, O (others), rubella, cytomegalovirus, herpes simplex virus, US: Ultrasound

The demographic data are summarized in Table 2. The comparison of the pregnant women included in the study according to their risk status revealed p=0.06. In the risk groups, the mean ages were 27.19±1.28 and 27.91±3.79 years, respectively and no statistically significant difference was found between the groups (p>0.05). The mean gestational week was 23.52±1.99 and 23.13±2.71 weeks in the study population, respectively. Similarly, no statistical difference was detected for this parameter between the groups (p>0.05). The percentages of primiparas in low- and high-risk groups were 64.93 and 58.94%, respectively. Additionally, two and four pregnancies were multiple in the low-risk and high-risk groups, respectively.

Table 2. The demographic data of the study population.

	Low-risk Group (n=134)	High-risk Group (n=246)	p
Age (years)	27.19±1.28 (19-44)	27.91±3.79 (21-44)	**>0.05**
Gestational week (weeks)	23.52±1.99 (17-36 weeks)	23.13±2.71 (17-36 weeks)	>0.05
Primipara (n/%)	87/64.93	145/58.94	>0.05
Multipara (n/%)	45/33.58	97/39.43	>0.05
Multiple pregnancy (n/%)	2/1.49	4/1.63	>0.05

ICEF was detected in a total of 77 (20.26%) cases, 68 (50.75%) cases were in the low-risk group and nine (3.66%) cases were in the high-risk group (Table 3). Left ventricular echogenic foci were detected in 59 (44.03%) fetuses in low-risk pregnancies and four (1.63%) fetuses in high-risk pregnancies, respectively and the statistical significance was achieved (p=0.001). Also, right ventricular echogenic foci were detected in seven (5.22%) fetuses in low-risk pregnancies and one (0.41%) fetus in high-risk pregnancies, respectively (p=0.03). It was observed that ICEF were single in 71 cases and multiple in six cases. In addition, ICEF was located in both ventricles in one (0.75%) and two (0.81%) cases in the risk groups, respectively (p=0.08). Also, multiple echogenic foci in one of the ventricles were detected in one (0.75%) case in the low-risk group and 2 (0.81%) cases in the high-risk group, respectively (p=0.07).

Table 3. Distribution of fetal cardiac echogenic foci detected in fetal echocardiography by pregnancy risk groups.

Fetal cardiac echogenic focus location	**Low-risk (n=134)**	**High-risk (n=246)**	*p*
Left ventricle	59 (44.03%)	4 (1.63%)	0.001
Right ventricle	7 (5.22%)	1 (0.41%)	0.03
Both ventricles	1 (0.75%)	2 (0.81%)	0.08
Multiple in one ventricle	1 (0.75%)	2 (0.81%)	0.07

In the low-risk group, ventricular septal defect was detected in four cases (2.98%) (Table 4). However, a ventricular septal defect was detected in two cases (0.81%), double outlet right ventricle in two cases (0.81%), hypoplastic left heart syndrome in three cases (1.22%), tricuspid atresia in two cases (0.81%), pulmonary atresia/hypoplasia in three cases (1.22%), tricuspid atresia and TGA in one case (0.41%), aortic coarctation/aortic arch hypoplasia in one case (0.41%), corrected TGA in one case (0.41%) and truncus arteriosus in one case (0.41%) were detected in the high-risk group (Table 4). Additionally, one fetus in a low-risk pregnancy and one fetus in a high-risk pregnancy had echogenic foci in one of the ventricles with congenital heart diseases.

Table 4. Distribution of congenital heart diseases by low-high risk groups.

Congenital Heart Disease	**Low-risk Group (n=134)**	**High-risk Group (n=246)**
Ventricular septal defects	4 (2.98%)	2 (0.81%)
Double outlet right ventricle	-	2 (0.81%)
Hypoplastic left heart syndrome	-	3 (1.22%)
Tricuspid atresia	-	2 (0.81%)
Pulmonary atresia/hypoplasia		3(1.22%)
Tricuspid atresia and TGA	-	1 (0.41%)
Aortic coarctation/aortic arch hypoplasia	-	1 (0.41%)
Corrected TGA	-	1 (0.41%)
Truncus arteriosus	-	1 (0.41%)
Total	**4 (2.98%)**	**16 (6.51%)**

TGA; Transposition of great arteries

Rhythm disturbances were also detected in our study. In this way, premature atrial extrasystoles were detected in three fetuses in the low-risk group while premature ventricular beats were detected in five pregnant women in the high-risk groups.

Discussion

ICEF are small structures typically located within the ventricles in the papillary muscle or chordae region. They have an echogenicity comparable to fetal bone. Also, ICEF usually moves synchronously with the mitral or tricuspid valve and they are not attached to the ventricular wall (1–4). Reducing the flow gain to ensure that the ribs do not disappear before their echogenicity is an important test to minimize false-positive results, as the papillary muscles can often be seen as echogenic dots (21). Although unclear, the etiology is likely a normal variant of papillary muscle development or increased mineralization of the papillary muscle or chordae within the ventricle (2). Some authors consider it to be a marker of disease in the fetus (5,6) while others believe it is a normal variant and a benign finding (2,3). In general, factors like technique, experience, and equipment influence the detection rate of ICEF. The prevalence of ICEF was reported between 0.5–20% of pregnancies in the literature (3,11,13). On the other hand, in the study by Shipp et al., the incidence of ICEF was as high as 30.4% in Asian mothers (22). This variation in the reported literature can be attributed to the operator's experience, the sophistication of the equipment, gestational age at the time of examination, maternal body habitus and the study population examined (3,11,13). The overall prevalence of ICEF in our study was 20.26% and it is comparable to that of other studies. The relatively higher prevalence of our result can be associated with ethnicity and different living spaces. Another reason why the prevalence of ICEF is higher in our study is that selected pregnant women are referred to our tertiary hospital. On the other hand, the prevalence of ICEF is significantly different between low- and high-risk pregnancies in the literature. The studies showed a prevalence of 0.5%-6.9% in low-risk pregnancies (8,13,14) while a prevalence of 2.7%-19.4% in high-risk pregnancies (2,8,10,13,14). During the same year, Simpson et al. published a prevalence of 6.9% for ICEF among a low-risk cohort out of the United Kingdom, while Merati et al. reported a prevalence of 3.2% in a low-risk Italian population (13,23). In our study, we found this prevalence as 50.75% in the low-risk group and 3.66% in the high-risk group, respectively. The high prevalence in the low-risk group in our study can be explained by the referral of selected pregnant women to our clinic, ethnicity, different living areas, and the low number of patients.

Intracardiac echogenic focus can be found in one or both ventricles, and they may be a single or multiple foci (23,24). The most frequent finding

is a single focus in the left ventricle (2,13,16). Similarly, in our study, single focus in the LV was mostly detected in both risk groups 44.03% in the low-risk and 1.63% in the high-risk group. Also, a single focus in the right ventricle was more often observed in the low-risk pregnancy group (5.22%) than in the high-risk pregnancy group (0.41%). Some researchers have suggested that right-sided or bilateral ICEF carries a higher risk of chromosomal abnormalities than left-sided ones (10,12,25). Also, some studies suggested that multiple ICEFs are associated with poor prognosis and should be analyzed in detail (17). However, most of these studies were based on small sample sizes and limited to fetal chromosomal abnormalities. Also, in our study, no similar correlation was found between right-sided or bilateral ICEF and congenital heart defects.

Barsoom et al. reported a very low (1.5%) sensitivity and 87.5% specificity for screening an isolated ICEF for congenital heart disease in a low-risk population (26). On the other hand, some studies showed that isolated echogenic focus is a risk factor for congenital heart disease in a low-risk population. Similarly, Shakoor et al. reported the prevalence of cardiac defects as 4.2% in fetuses with ICEF in their study (27). Additionally, Goncalves et al. reported a prevalence of 1.6% after excluding cases with chromosomal abnormalities, which is twice the prevalence in the overall study population (0.8%). (28). In addition, the study by Chiu et al. suggested that ICEF neither increased nor decreased the risk of cardiac structural defects, but fetuses with echogenic foci in the right ventricle showed a higher risk for cardiac structural defects (29). On the other hand, Didly et al. performed neonatal ECG on fetuses with the antenatal finding of ICEF and compared with the fetuses without such findings and they concluded that both antenatal and postnatal evaluation by fetal ECG is not indicated (30). Also, similar findings are observed by others (3,7,8,13,23-27). Similarly, our study supported these findings that we have found no correlation between the locations of ICEF and congenital heart diseases in low- and high-risk pregnancies.

Our study has some limitations. First, our hospital is a tertiary hospital, and patients with a suspected fetal cardiac anomaly are referred from all over the areas of our city, so the incidence of ICEF may be higher than that of the general population. Second, the number of pregnancies in each group was relatively low. Third, the identification of ICEF may be influenced by a variety of factors such as gestational age, fetal ECG image quality, and fetal position.

In conclusion, we reported a 20.26% prevalence of ICEF in our study population. Also, the prevalence of ICEF was 50.75% in low-risk pregnancies relatively higher than that of studies. However, this can be attributed to ethnicity, tertiary hospital referrals, a relatively low number of patients, and other associated factors. So, routine genetic analysis should not be required in low- and high-risk pregnancies with ICEF. Additionally, in our study, no correlation was found between congenital heart diseases and ICEF in both low-risk and high-risk pregnancies. In this way, larger controlled studies are needed to confirm the findings of this study.

Ethical Declarations

Ethics Committee Approval

The study was obtained from our University Medical Research Ethics Committee (Date: 26.09.2024, Decision No: 10-2024/01, Number: E-11095095-050.04-216359).

Informed Consent

Signed written informed consent was taken from all participants.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support. Author Contributions: Conception And Design: HA; Data Collection And/Or Processing: HA, GS, and FŞ; Supervision; HA and GS; Literature Review; HA and FŞ; Analysis and/or Interpretation: HA and GS: Writing; HA; Critical Review; GS and FŞ.

References

1.Schechter AG, Fakhry J, Shapiro LR, Gewitz MH. In utero thickening of the chordae tendinae. A cause of intracardiac echogenic foci. J Ultrasound Med 1987;6:691-5.

2.Petrikovsky B, Challenger M, Gross B. Unusual appearances of echogenic foci within the fetal heart: are they benign? Ultrasound Obstetric Gynecol 1996;8(4):229-31.

3.Levy DW, Mintz MC. The left ventricular echogenic focus: a normal finding. AJR Am J Roentgenol 1988;150:85-6.

4.Brown DL, Roberts DJ, Miller WA. Left ventricular echogenic focus in the fetal heart: pathologic correlation. J Ultrasound Med 1994;13:613-6.

5.Anderson N, Jyoti R. Relationship of isolated fetal intracardiac echogenic focus to trisomy 21 at the mid-trimester sonogram

in women younger than 35 years. Ultrasound Obstet Gynecol 2003;21:354-8.

6.Bradley KE, Santulli TS, Gregory KD, Herbert W, Carlson DE, Platt LD. An isolated intracardiac echogenic focus as a marker for aneuploidy. Am J Obstet Gynecol 2005;192:2021-6.

7.Rodriguez R, Herrero B, Bartha JL. The continuing enigma of the fetal echogenic intracardiac focus in prenatal ultrasound. Curr Opin Obstet Gynecol 2013;25(2):145-51.

8.Achiron R, Lipitz S, Gabbay U, Yagel S. Prenatal ultrasonographic diagnosis of fetal heart echogenic foci: no correlation with Down syndrome. Obstet Gynecol 1997;89(6):945-8.

9.Bromley B, Lieberman E, Laboda L, Benacerraf BR. Echogenic intracardiac focus: a sonographic sign for fetal Down syndrome. Obstet Gynecol 1995;86(6):998-1001.

10.Bromley B, Lieberman E, Shipp TD, Richardson M, Benacerraf BR. Significance of an echogenic intracardiac focus in fetuses at high and low risk for aneuploidy. J Ultrasound Med 1998;17(2):127-31.

11.How HY, Villafane J, Parihus RR, et al. Small hyperechoic foci of the fetal cardiac ventricle: a benign sonographic finding? Ultrasound Obstet Gynecol 1994;4:205.

12.Wax JR, Mather J, Steinfeld JD, et al. Fetal Intracardiac Echogenic Foci: current understanding and clinical significance. Obstet Gynecol Surv 2000;55:303.

13.Simpson JM, Cook A, Sharland G. The significance of echogenic foci in the fetal heart: a prospective study of 228 cases. Ultrasound Obstet Gynecol 1996;8:225–8.

14.Vibhakar NI, Budorick NE, Scioscia AL, Harby LD, Mullen ML, Sklansky MS. Prevalence of aneuploidy with a cardiac intraventricular echogenic focus in an at-risk patient population. J Ultrasound Med 1999;18:265–8.

15.Goncalves TR, Zamith MM, Murta CG, Bussamra LC, Torloni MR, Moron AF. Chromosomal and cardiac anomalies in fetuses with intracardiac echogenic foci. Int J Gynaecol Obstet 2006;95:132-7.

16.Wax JR, Philput C. Fetal intracardiac echogenic foci: does it matter which ventricle? J Ultrasound Med 1998;17:141-4.

17.Bronshtein M, Jakobi P, Ofir C. Multiple fetal intracardiac echogenic foci: not always a benign sonographic finding. Prenat Diagn 1996;16:131-5.

18.Donofrio MT, Moon-Grady AJ, Hornberger LK et al. American Heart Association Adults With Congenital Heart Disease Joint Committee of the Council on Cardiovascular Disease in the Young and Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and Council on Cardiovascular and Stroke Nursing. Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association. Circulation 2014;129(21):2183-242.

19.Wright L, Stauffer N, Samai C, Oster M. Who should be referred? An evaluation of referral indications for fetal echocardiography in the detection of structural congenital heart disease. Pediatr Cardiol 2014;35:928-33.

20.Özkutlu S, Ayabakan C, Karagöz T, et al. Prenatal echocardiographic diagnosis of congenital heart disease: comparison of past and current results. Turk J Pediatr 2005;47:232-8.

21.Bethune M. Management options for echogenic intracardiac focus and choroid plexus cysts: a review including Australian Association of Obstetrical and Gynaecological Ultrasonologists consensus statement. Australas Radiol 2007;51:324e9.

22.Shipp TD, Bromley B, Lieberman E, et al. The frequency of the detection of fetal echogenic intracardiac foci concerning maternal race. Ultrasound Obstet Gynecol 2000;15:460.

23.Merati R. Lovotti M, Norchi S et al. Prevalence of fetal left ventricular hyperechogenic foci in a low-risk population. Br J Obstet Gynaecol 1996;103:1102-4.

24.Guo Y, He Y, Gu X et al. Echogenic intracardiac foci and fetal cardiac anomalies: A review of cases from a tertiary care center in China. J Clin Ultrasound. 2017;1–5.

25.Carrico A, Matias A, Areias JC (2004) How important is a cardiac echogenic focus in a routine fetal examination? Rev Port Cardiol 23:459–61

26.Barsoom MJ, Feldman DM, Borgida AF, Esters D, Diana D, Egan JF. Is an isolated fetal cardiac echogenic focus an indication for fetal echocardiography? J Ultrasound Med 2001;20:1043-6.

27.Shakoor S, Ismail H, Munim S. Intracardiac echogenic focus and fetal outcome - review of cases from a tertiary care center in Karachi, Pakistan. J Matern Fetal Neonatal Med 2013;26:2-4.

28.Goncalves TR, Zamith MM, Murta CG, Bussamra LC, Torloni MR, Moron AF. Chromosomal and cardiac anomalies in fetuses with intracardiac echogenic foci. Int J Gynaecol Obstet 2006;95:132-7.

29.Chiu G, Zhao A, Zhang B, Zhang T. Intracardiac echogenic focus and its location: association with congenital heart defects. J Matern Fetal Neonatal Med 2019;32(18):3074-8.

30.Dildy GA, Judd VE, Clark SL. Prospective evaluation of the antenatal incidence and postnatal significance of the fetal echogenic cardiac focus: A case-control study. Am J Obstet Gynecol 1996;175:1008–12.

31.Wolman I, Jaffa A, Geva E, Diamant S, Strauss S, Lessing JB, Yaron Y. Intracardiac echogenic focus: no apparent association with structural cardiac abnormality. Fetal Diagn Ther 2000;15:216–8.

Received: 10 Nov 2024 | **Accepted:** 30 Jan 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 248-253
DOI: 10.54005/geneltip.1582495

ORIGINAL ARTICLE

Outcomes and Management of Pregnancies Complicated by Absent End-Diastolic Flow in the Umbilical Artery: A Retrospective Cohort Study

Umbilikal Arterde Diyastolik Akım Kaybı ile Komplike Gebeliklerin Sonuçları ve Yönetimi: Retrospektif Kohort Çalışması

[1]Nazan Vanlı Tonyalı, [1]Gizem Aktemur, [1]Gulsan Karabay, [1]Betul Tokgoz Cakir, [1]Ali Turhan Cağlar

[1]Department of Perinatology, Ankara Etlik City Hospital, Ankara, Türkiye

Correspondence

Nazan Vanlı Tonyalı,
Department of Perinatology, Ankara Etlik City Hospital, Ankara, Türkiye

E-Mail: nazanvanli@gmail.com

How to cite ?

Vanlı Tonyalı N, Aktemur G, Gulsan Karabay, Tokgoz Cakir B, Cağlar AT. Outcomes and Management of Pregnancies Complicated by Absent End-Diastolic Flow in the Umbilical Artery: A Retrospective Cohort Study. Genel Tıp Derg. 2025;35 (2): 248-253

ABSTRACT

Aim: This study aimed to evaluate perinatal outcomes in pregnancies complicated by absent end-diastolic flow (AEDF) in the umbilical artery.
Method: This retrospective cohort study was conducted in the Perinatology Clinic of Etlik City Hospital from November 2022 to June 2024. Eighty-five pregnant women diagnosed with AEDF in the umbilical artery Doppler were included. Key outcomes, including fetal birth weight, gestational age at delivery, Apgar scores, neonatal intensive care unit (NICU) admissions, and perinatal morbidity and mortality, were assessed.
Results: The mean gestational age at diagnosis and delivery was 28.86 ± 4.00 and 29.74±3.85 weeks, respectively, with a median interval from AEDF detection to delivery of two days. The mean birth weight was 1031.42±485.94 grams. A high cesarean delivery rate (89.4%) was observed, primarily due to fetal distress (63.2%). Fetal growth restriction (FGR) and preeclampsia were present in 80% and 38.8% of cases, respectively. The perinatal loss was 32.9%, with significant associations between higher hCG MoM levels and lower birth weight (r=-0.597, p=0.011). ROC analysis indicated gestational age at delivery as the strongest predictor of neonatal complications [Area under the curve (AUC): 0.804]. Admissions to NICU showed severe neonatal complications, including intracranial hemorrhage (ICH) and respiratory distress syndrome (RDS), aligning with the risk of poor outcomes in AEDF cases.
Conclusion: AEDF in the umbilical artery is a significant predictor of adverse perinatal outcomes, including high perinatal mortality and neonatal complications. Early detection and careful monitoring, alongside timely delivery, are critical in managing these high-risk pregnancies to improve neonatal outcomes. Further research should focus on optimizing intervention timing to balance fetal maturity with the risks of prematurity.

Keywords: Absent end-diastolic flow, fetal ultrasound, perinatal outcomes

ÖZ

Amaç: Bu çalışma, umbilikal arterde son diyastolik akım (AEDF) kaybıyla komplike olmuş gebeliklerde perinatal sonuçları değerlendirmeyi amaçlamıştır.
Yöntem: Bu retrospektif kohort çalışma, Kasım 2022 ile Haziran 2024 tarihleri arasında Etlik Şehir Hastanesi Perinatoloji Kliniği'nde yürütülmüştür. Umbilikal arter Doppler incelemesinde AEDF tanısı konulan 85 gebe çalışmaya dahil edilmiştir. Değerlendirilen temel sonuçlar arasında fetal doğum ağırlığı, doğum haftası, Apgar skorları, yenidoğan yoğun bakım (YYB) başvuruları ve perinatal morbidite ile mortalite yer almaktadır.
Bulgular: Tanı ve doğum sırasında ortalama gebelik haftası sırasıyla 28.86±4.00 ve 29.74±3.85 hafta olup, AEDF tespitinden doğuma kadar geçen sürenin medyan değeri iki gündü. Ortalama doğum ağırlığı 1031.42±485.94 gram olarak bulunmuştur. Yüksek sezaryen oranı (%89.4) gözlenmiş olup, ana neden fetal distres (%63.2) olarak belirlenmiştir. Olguların %80'inde fetal büyüme geriliği (FGR) ve %38.8'inde preeklampsi mevcut olup, perinatal kayıp oranı %32.9 olarak saptanmıştır. Yüksek hCG MoM seviyeleri ile düşük doğum ağırlığı arasında anlamlı bir ilişki bulunmuştur (r=-0.597, p=0.011). ROC analizinde, doğum haftasının neonatal komplikasyonlar için en güçlü öngörücü olduğu görülmüştür [Area under curve (AUC): 0.804]. YYB'ye alınan yenidoğanlarda, intrakraniyal kanama ve solunum sıkıntısı sendromu gibi ciddi neonatal komplikasyonlar gözlenmiş olup, AEDF olgularında kötü sonuç riskinin yüksek olduğu görülmüştür.
Sonuç: Umbilikal arterde AEDF varlığı, yüksek perinatal mortalite ve neonatal komplikasyonları içeren olumsuz perinatal sonuçların önemli bir belirleyicisidir. Erken tanı ve dikkatli izlem, yanı sıra zamanında doğum, bu yüksek riskli gebeliklerin yönetiminde neonatal sonuçları iyileştirmek için kritik önemdedir. İleri araştırmalar, prematürite riskleri ile fetal olgunluk arasındaki dengeyi optimize etmek için müdahale zamanlamasının iyileştirilmesine odaklanmalıdır.

Anahtar Kelimeler: Fetal ultrason, perinatal sonuçlar, son diyastolik akım kaybı

Introduction

The absence of end-diastolic flow (AEDF) as seen in the umbilical artery Doppler pattern or waveform data display is a crucial indication of fetal growth restriction (FGR) and placental insufficiency (1). A common finding in pregnancies was considered high-risk situations where complications are more likely to arise. FGR, especially when detected early in pregnancy, is associated with significant perinatal morbidity and mortality (2). Using Doppler ultrasonography of the umbilical artery provides very important information about the fetal-placental circulation. Being a key factor in monitoring fetal well-being during gestation, aberrant results like the lack of AEDF or reversal of end-diastolic flow (AREDF) have been associated with pregnancy outcomes including premature delivery and low birth weight. This can also lead to fetal demise according to studies (3).

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

Research has indicated that adverse outcomes like stillbirth and infant death occur frequently when there is a loss of end-diastolic flow detected before the 30th week of pregnancy (4). Deciding when to deliver a baby in the presence of this flow issue is a task as it involves balancing the well-being of the fetus with the risks associated with premature birth. In situations where FGR begins early in pregnancy the likelihood of fetal health problems and loss, during pregnancy rises if Doppler abnormalities are also present (3). The Trial of Randomized Umbilical and Fetal Flow in Europe (TRUFFLE) study examined cases with Doppler abnormalities in early (26-32 weeks) FGR cases. These abnormalities are linked to higher rates of perinatal health issues and mortality and pose an increased risk, for unfavorable outcomes. As highlighted by the study results close monitoring and making timely decisions regarding delivery play a crucial role in enhancing the well-being of both the fetus and newborn (5).

Our research focuses on assessing the pregnancy results of a group of individuals with no end diastolic flow in the artery who are receiving care at our clinic. Through analyzing these outcomes we aim to add to the increasing amount of research on the effective approaches for managing pregnancies, at high risk.

Materials And Methods

Study Design and Population: This was a retrospective cohort study conducted at Etlik Şehir Hastanesi Perinatoloji Kliniği between November 2022 and June 2024. Approval was received for this study from the Etlik Zübeyde Hanım Gynecology Training and Research Hospital Scientific Research Ethics Committee (Decision No: AEŞH-BADEK-2024-950, Date: 16/10/2024). The study included pregnant women diagnosed with absent end-diastolic flow (AEDF) in the umbilical artery during fetal Doppler ultrasound (US) screening. The inclusion criteria were singleton pregnancies, confirmed absent EDF on at least one Doppler US, and availability of comprehensive follow-up data through delivery. Patients with multiple gestations, major congenital anomalies, or incomplete medical records were excluded from the study.

A total of 85 pregnant women met the inclusion criteria and were followed for pregnancy outcomes, including fetal birth weight, gestational age at delivery, Apgar scores, neonatal intensive care unit (NICU) admission, perinatal morbidity, and mortality.

Data Collection: Data were extracted from the medical records of the patients, including demographic information (maternal age, parity, pre-existing medical conditions), obstetric history, and Doppler US findings. In this study, certain data points were unavailable due to logistical or clinical circumstances. For example, in some cases, specific tests or measurements were not ordered, or delivery occurred before the necessary data could be collected. To maintain the integrity of the statistical analysis, cases with missing data for key variables were excluded from the relevant analyses. This approach ensured that the results accurately reflect the available data and reduce the potential biases introduced by incomplete datasets.

Doppler US Protocol: Absent EDF was identified via Doppler ultrasonography, performed using the Voluson S10 Expert machine with a 3.5 MHz transducer. All Doppler US examinations were performed by experienced sonographers. The umbilical artery Doppler waveform was assessed at the free loop of the cord, and the angle of insonation was kept below 60 degrees. Doppler indices including the pulsatility index (PI), resistance index (RI), and the systolic-to-diastolic ratio (S/D ratio) were recorded. EDF was classified as normal, decreased, absent, or reversed based on the presence or absence of forward diastolic flow.

Statistical Analysis: Data were analyzed using [The Statistical Package for Social Sciences Software, e.g., SPSS, R]. Continuous variables were expressed as mean±standard deviation (SD), and categorical variables were reported as frequencies and percentages. The chi-square or Fisher's exact tests were used for categorical variables, and the student's t-test or Mann-Whitney U test was applied for continuous variables, as appropriate. A p-value of <0.05 was considered statistically significant.

Results

In this study involving 85 patients, 79 had singleton pregnancies and six had twin pregnancies. The average maternal age was 31.25 years with a standard deviation of 5.74 years. The mean body mass index (BMI) was 30.07, indicating an overweight status. The median gravidity was 2.0, with a range from one to nine pregnancies, while the median parity was 1.0, ranging from 0 to four live births. On average, patients had 1.0 living children, with a range from 0 to four. Six patients, representing 7.06%, conceived through in vitro fertilization (IVF). Among the 18 patients with available 24-hour urine protein levels, the median protein level was 1885 mg, with a range from 176 to 11519 mg. Antihypertensive medications were reported by 29 patients, accounting for 39.7% of the total. Additionally, 76 patients (89.4%) had cesarean deliveries (Table 1).

Table 1. Maternal Characteristics of Patients with Umbilical Absent End-Diastolic Flow

Variables	n	Values
Maternal Age (years)	85	31.25±5.74
BMI (kg/m²)	85	30.07±5.94
Gravidity	85	2.0 (2) (1-9)
Parity	85	1.0 (2) (0-4)

Living Children	85	1.0 (2) (0-4)
Abortions (min-max)	85	0.0 (0) (0-5)
IVF Pregnancies (%)	85	6 (7.06%)
24-Hour Urine Protein Level (mg)	18	1885 (176-11519)
Antihypertensive Medication Use (%)	85	29 (39.7)
Cesarean Delivery (%)	85	76 (89.4%)

BMI: Body mass index, kg: Kilograms, m²: Square meter, IVF: In vitro fertilization; mg: Milligram

Table 2 presents the maternal and neonatal characteristics of patients with umbilical AEDF. The gestational age at diagnosis was 28.86±4.00 weeks, while the gestational age at delivery was 29.74±3.85 weeks. The interval from the first detection of umbilical AREDV to delivery averaged two days, with a range of 0 to 62 days. The mean birth weight was 1031.42±485.94 grams. The perinatal loss occurred in 31 cases (38.9%), and abnormal ductus venosus waveform was noted in 6 patients.

Table 2. Maternal and Neonatal Characteristics of Patients with Umbilical Absent

End-Diastolic Flow

Gestational age at diagnosis (weeks)	**28. 86±4.00**
Gestational age at delivery (weeks)	29.74±3.85
The interval from 1st detection of umbilical AEDF to delivery (days)	2 (0-62)
Fetal gender	
Female	34 (40)
Male	51 (60)
Birth weight (grams)	1031.42±485.94
Betamethasone administration	76 (90.5)
MgSO4 administration	68 (80)
Apgar score at minute 1	5 (0-9)
Apgar score at minute 5	7 (0-10)
Perinatal Loss	28 (32.9)
Terminaiton of Pregnancy	5 (5.9)
Abnormal Ductus Venosus Waveform	6

AEDF: Absent End-Diastolic Flow, MgSO4: Magnesium Sulfate

FGR was the most prevalent condition, observed in 68 cases (80%). Additionally, Preeclampsia was noted in 33 cases (38.8%). Oligohydramnios was identified in 18 patients (21.2%), while Anhydramnios occurred in seven cases (8.2%) (Table 3).

Table 3. Accompanying Pathological Findings in Patients

Accompanying Pathological Findings	**n (%)**
FGR	68 (80)
GHT	9 (10.6)
Preeclampsia	33 (38.8)
Chronic Hypertension	5 (5.9)
DM or GDM	6 (7)
Oligohydramnios	18 (21.2)
Polyhydramnios	2 (2.4)
Anhydramnios	7 (8.2)

FGR: Fetal growth restriction, GHT: Gestational hypertension, DM: Diabetes mellitus, GDM: Gestational diabetes mellitus

The most common reason was fetal distress, accounting for 48 cases (63.2%). Other indications included severe preeclampsia (12 cases, 15.8%), HELLP syndrome (six cases, 7.9%), and 34 weeks of gestation, where we decided to deliver electively in cases of umbilical AEDF (Table 4).

Table 4. Cesarean Indications

Cesarean Indication	**n (%)**
Fetal distress	48 (63.2)
Severe preeclampsia	12 (15.8)
HELLP syndrome	6 (7.9)
Previous uterine scar in labor	1 (1.3)
34 weeks of gestation	8 (10.5)
Placental abruption	1 (1.3)

HELLP: Hemolysis, elevated liver enzymes, and low platelet count

Eighteen patients underwent first-trimester screening, seven patients underwent amniocentesis, among which one case of trisomy 21 was identified. In the correlation analysis, a statistically significant negative relationship was found between birth weight and hCG MoM (r=-0.597, p=0.011). This result indicates that as hCG MoM levels increase, birth weight decreases. No significant relationship was detected between PAPP-A MoM and birth weight (r=-0.098, p=0.708). Additionally, although a moderate positive correlation was observed between hCG MoM and PAPP-A MoM (r=0.449), this relationship did not reach statistical significance (p=0.070).

Among the 85 cases, four patients were diagnosed with AEDF and early-onset FGR at 22-23 weeks of gestation, for which poor prognosis information was provided. Following the request of the family, the termination of pregnancy was performed. Additionally, two cases subsequently resulted in intrauterine demise. The perinatal loss occurred in 28 (32.9). A total of 79 cases were admitted to NICU. During the follow-up at NICU, one or more complications were observed in 14 cases. Specifically, four cases of intracranial hemorrhage (ICH), two cases of sepsis, one case of bowel perforation, one case of portal vein thrombosis, one case of meningitis, and four cases of respiratory distress syndrome (RDS) were noted. Among the surviving neonates, cerebral palsy developed in one case, and retinopathy of prematurity (ROP) was diagnosed in three cases during follow-up. Additionally, one case was diagnosed with Down syndrome postnatally, and

one case was found to have aortic coarctation on postnatal echocardiography.

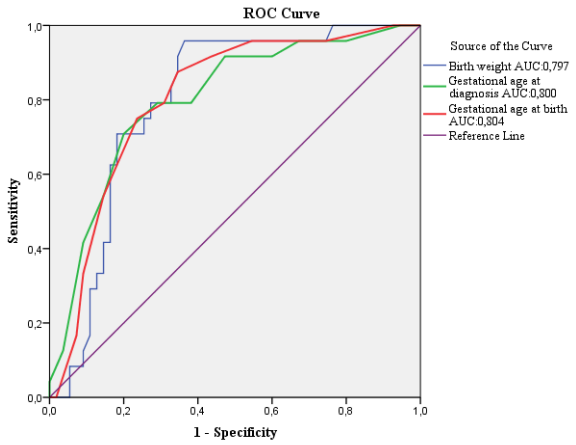
Table 5. Correlation Matrix of Birth Weight, hCG MoM, and PAPP-A MoM

Variables	Birth Weight	hCG MoM	PAPP-A MoM
Birth Weight	1	-0.597*	-0.098
hCG MoM	-0.597*	1	0.449
PAPP-A MoM	-0.098	0.449	1

*Correlation is significant at the 0.05 level (2-tailed). hCG MoM: Human chorionic gonadotropin multiple of the median; PAPP-A MoM: Pregnancy-associated plasma protein-A multiple of the median

In this study, birth weight, gestational age at diagnosis, and gestational age at birth were evaluated with the ROC curve to predict neonatal complications (Figure). The results showed that gestational age at birth (AUC: 0.804) was the strongest predictor. Gestational age at diagnosis (AUC: 0.800) was also an effective predictor but performed slightly less well than gestational age at birth. Birth weight (AUC: 0.797) had a lower predictive power than others; however, the weight was still found to be significant. All parameters showed significant predictive power compared to random guesses.

Figure. ROC Curve Analysis for Predicting Neonatal Complications Based on Birth Weight, Gestational Age at Diagnosis, and Gestational Age at Birth



Discussion

The study found that most patients experienced FGR (80%) and a significant number were diagnosed with preeclampsia (38/8%). The high rate of cesarean deliveries (89/4%) indicated the seriousness of the clinical situations with fetal distress being the main reason in 63/3. Among patients with first-trimester screening data, a significant negative correlation between hCG MoM levels and birth weight was detected.

In this study, we examined perinatal outcomes in pregnancies complicated by the loss of end-diastolic flow in the umbilical artery. AEDF was diagnosed at an average of 28.86 weeks and birth occurred at 29.74 weeks. The median time to birth with AEDF detection was two days. Our rate of antenatal steroid application for fetal neuroprotection was 90.5% and magnesium sulfate was 80%. The average birth weight was quite low at 1031.42 grams and the perinatal mortality rate was found to be high (32.9%). The study found that most patients experienced FGR (80%) and a significant number were diagnosed with preeclampsia (38/8%). The high rate of cesarean deliveries (89/4%) indicated the seriousness of the clinical situations with fetal distress being the main reason in 63/3. Among patients with first-trimester screening data, a significant negative correlation between hCG MoM levels and birth weight was detected.

Detection of end-diastolic flow in the umbilical artery using Doppler velocimetry serves as a crucial indicator of placental insufficiency in fetuses experiencing growth restriction. AEDF indicates higher vascular resistance in the placental region, which affects fetal blood flow during the diastolic phase of the heart (6). This condition is closely linked to adverse perinatal outcomes, such as higher rates of intrauterine mortality, neonatal health problems, and neonatal mortality. The presence of end-diastolic flow often precedes observable signs of fetal distress providing an opportunity, for early intervention to mitigate potential complications (7).

When maternal demographic data were examined, the mean maternal age was 31.25 (SD 5.74), the mean BMI was 30.07, and the mean gestational age was 28.86±4.00 weeks. In a similar study by Kinoshita et al., the average maternal age in pregnancies with AEDF was found to be 31 years (8). Gestational age at AEDF diagnosis varies between studies. In the study by Müller et al., the gestational age was similarly reported as 28.5 weeks (9).

Due to the high rate of fetal distress (63.2%), our cesarean section rate was 89.4% (n=76). Similarly, a high cesarean section rate was observed in the study by Kinoshita et al., and 154 out of 167 pregnancies (92.2%) ended in cesarean section (8). The underlying reason for these high cesarean section rates is due to the sudden change in fetal well-being in AEDF cases.

In many studies of AEDF cases, birth occurs in the early preterm period. In the study of Serdaroğlu et al., the average gestational age was reported as 32.63 weeks and the birth weight as 1196.84 grams (10). In the study by Deniz and Ulker, the birth weight was around 1604 grams at approximately 29 weeks of birth (11). Our data were also consistent with these studies, the birth week was 29.74±3.85 and the average birth weight was 1031.42±485.94 grams. The reason for the variability in birth weights and birth weeks is due

to the effects of conditions such as differences in clinical conditions causing AEDF and the presence of additional complications on birth weight and timing. In our study, the average time from the first detection of umbilical AEDF to birth was two days. Although the median interval from AEDF detection to delivery in our study was two days, the range was wide, from 0 to 62 days. This variation in timing is probably based on the severity of fetal compromise and maternal condition. In the study of Müller et al., the interval time was reported as 8.9 days (9). This shorter interval in our cohort likely reflects more urgent intervention due to severe fetal injury, whereas Müller's longer observation period suggests a more conservative approach allowing more time when fetal conditions permit. This difference shows that different clinical strategies can be followed to achieve the balance between placental insufficiency and the risk of premature birth.

Our perinatal loss rate was 32.9%, and two intrauterine deaths and four terminations occurred due to early-onset FGR. On the other hand, in another study, the intrauterine death rate within 30 days was reported as 15.8% and the postnatal death rate as 11.3% (8). The reason for our high perinatal loss rate may be that our facility is a tertiary reference center.

When the pathologies accompanying AEDF cases were examined, FGR was observed in 80% of the cases, preeclampsia in 38.8%, oligohydramnios in 21.2%, and anhydramnios in 8.2%. In the study of Caradeux et al., it was reported that preeclampsia and oligohydramnios are often accompanied by early-onset FGR cases and that this is associated with placental insufficiency (4). Similarly, In the study where Wang et al. investigated high FGR rates in cases with AEDF, the researchers emphasized the association between preeclampsia and negative perinatal outcomes (12). These studies emphasize the important role of placental dysfunction in the development of complications in cases with Doppler abnormalities.

The presence of AEDF brings about serious neonatal complications due to increased preterm birth as well as intrauterine complications. In our study, neonatal complications such as ICH, RDS, sepsis, and bowel perforation were observed in cases admitted to NICU. Ertan et al. demonstrated that neonates with absent or reversed end-diastolic flow in the umbilical artery were at high risk for severe neonatal morbidities, including cerebral hemorrhage and infections (3). Similarly, Madazli et al. found that gestational age at delivery plays a crucial role in determining perinatal outcomes in growth-restricted fetuses with AEDF (13). They reported high perinatal mortality rates, particularly in those delivered before 29 weeks of gestation. The findings from both Ertan and Madazli's studies align with our observations, suggesting that AEDF and AREDF are significant predictors of poor neonatal outcomes, necessitating timely intervention and careful perinatal management. The severity and range of complications underscore the importance of gestational age and fetal condition at the time of delivery in determining long-term neonatal health.

According to the ROC curve analysis, gestational age at birth stood out as the strongest indicator in predicting neonatal complications (AUC: 0.804). Birth weight (AUC: 0.797) and gestational age at diagnosis (AUC: 0.800) have lower predictive values. This finding emphasizes the importance of optimal birth time for neonatal outcomes. In the study of Madazlı et al., it was emphasized that the timing of birth is a determining factor in perinatal outcomes, especially in AEDF cases born before the 29th week of gestation (12).

The presence of AEDF in the umbilical artery is a critical indicator of placental insufficiency and fetal risk. In the presence of AEDF, close monitoring and timely intervention are critical. Our findings highlight the importance of integrating AEDF assessment into clinical decision-making, particularly to determine the optimal timing of birth. Early identification and monitoring of AEDF allows for balancing the complications that may occur due to preterm birth against the risks of long-term intrauterine exposure that may lead to worsening of the fetal condition. This information is particularly important in cases of severe FGR, where term delivery can significantly improve neonatal outcomes.

The retrospective design of this study limits the ability to determine causality and may affect the generalizability of findings to larger populations. Data were collected from a single tertiary care center and may not reflect changes in clinical practice and patient demographics in other settings. Future studies with prospective design and multicentric collaborations are needed to confirm these findings and increase their applicability to different populations.

Conclusions

This study highlights the critical impact of AEDF in the umbilical artery on perinatal outcomes, particularly in the context of FGR and placental insufficiency. The high rates of FGR (80%) and preeclampsia (38.8%), combined with severe neonatal complications and a significant perinatal loss rate (32.9%), emphasize the severity of the condition in pregnancies diagnosed with AEDF.

The findings of this study indicate that AEDF is a crucial predictor of poor neonatal outcomes, underscoring the need for early diagnosis and close monitoring to optimize perinatal care. As gestational age at delivery proved to be the strongest predictor of neonatal complications, careful timing of delivery is essential in balancing the risks associated with prematurity and the progression of placental insufficiency.

Conflict of Interest

No conflict of interest was declared by the authors.

Authorship Contribution

Idea/Hypothesis: NVT, GA; Design: NVT, GK; Data collection/Data processing: BTC, GA, and GK; Data Analysis: NVT, BYC; Preparation of the article: NVT, ATC

Financial Disclosure

No financial support

References

1.Bligard KH, Xu E, Raghuraman N, Dicke J, Odibo AO, Frolova AI. Significance of intermittent absent end-diastolic flow in the umbilical artery in predicting neonatal morbidity. Am J Obstet Gynecol. 2022;226(1):S184-5.

2.Kurkinen-Räty M, Kivelä A, Jouppila P. The clinical significance of an absent end-diastolic velocity in the umbilical artery detected before the 34th week of pregnancy. Acta Obstet Gynecol Scand. 1997;76(5):398-404.

3.Ertan AK, He JP, Tanriverdi HA, Hendrik J, Limbach HG, Schmidt W. Comparison of perinatal outcome in fetuses with reverse or absent end-diastolic flow in the umbilical artery and/or fetal descending aorta. J Perinat Med. 2003;31(4). Available from: https://www.degruyter.com/document/doi/10.1515/JPM.2003.043/html

4.Caradeux J, Martinez-Portilla RJ, Basuki TR, Kiserud T, Figueras F. Risk of fetal death in growth-restricted fetuses with umbilical and/or ductus venosus absent or reversed end-diastolic velocities before 34 weeks of gestation: a systematic review and meta-analysis. Am J Obstet Gynecol. 2018;218(2):S774-S782.e21.

5.Bilardo CM, Hecher K, Visser GH, Papageorghiou AT, Marlow N, Thilaganathan B, et al. Severe fetal growth restriction at 26–32 weeks: key messages from the TRUFFLE study. Ultrasound Obstet Gynecol. 2017;50(3):285-90.

6.Adedo AA, Arogundade RA, Okunowo AA, Idowu BM, Oduola-Owoo LT. Comparative study of the umbilical artery Doppler indices of healthy and growth-restricted fetuses in Lagos. J West Afr Coll Surg. 2022;12(2):63-9.

7.Gairabekova D, Van Rosmalen J, Duvekot JJ. The outcome of early□onset fetal growth restriction with or without abnormal umbilical artery Doppler flow. Acta Obstet Gynecol Scand. 2021;100(8):1430-8.

8.Kinoshita M, Thuring A, Morsing E, Maršál K. Extent of absent end□diastolic flow in the umbilical artery and outcome of pregnancy. Ultrasound Obstet Gynecol. 2021;58(3):369-76.

9.Müller T, Nanan R, Rehn M, Kristen P, Dietl J. Arterial and ductus venosus Doppler in fetuses with absent or reverse end□diastolic flow in the umbilical artery: correlation with short□term perinatal outcome. Acta Obstet Gynecol Scand. 2002;81(9):860-6.

10.Serdaroğlu Ö, Aldemir EY, Kavuncuoğlu S, Erbaş İM, Gedikbaşı A. Neurodevelopmental and somatic growth outcomes of premature IUGR newborns with absent or reversed end-diastolic flow on umbilical artery Doppler. İKSST. 2017. Available from: http://cms.galenos.com.tr/Uploads/Article_48028/%C4%B0KSSTD-9-121-En.pdf

11.Deniz A, Ulker K. Perinatal outcomes of pregnancies with intrauterine growth restriction and/or preeclampsia associated with reverse flow or absence of end-diastolic flow velocity in umbilical artery Doppler flowmetry. Kafkas J Med Sci. 2012;2(3):99-104.

12.Wang KG, Chen CY, Chen YY. The effects of absent or reversed end-diastolic umbilical artery Doppler flow velocity. Taiwan J Obstet Gynecol. 2009;48(3):225-31.

13.Madazli R. Prognostic factors for survival of growth-restricted fetuses with absent end-diastolic velocity in the umbilical artery. J Perinatol. 2002;22(4):286-90.

Received: 20 Aug 2024 | **Accepted:** 14 Nov 2024 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 254-262
DOI: 10.54005/geneltip.1536404

ORIGINAL ARTICLE

The Diagnostic Performance of Magnetic Resonance Texture Analysis in Histological Subtyping and Grading of the Renal Cell Carcinoma

Renal Hücreli Karsinomun Histolojik Alt Tiplendirilmesi ve Derecelendirilmesinde Manyetik Rezonans Doku Analizinin Tanısal Performansı

[1]Nusret Seher, [1]Mustafa Kolpay, [1]Abidin Kılıncer, [2]Lutfi Saltuk Demir, [3]Mehmet Kaynar, [3]Kadir Bocu, [3]Serdar Göktas

[1]Department of Radiology, Faculty of Medicine, Selcuk University, Konya, Türkiye
[2]Department of Public Health , Faculty of Medicine, Necmettin Erbakan University, Konya, Türkiye
[3]Department of Urology, Faculty of Medicine, Selcuk University, Konya, Türkiye

Correspondence

Nusret Seher M.D.
Selcuk University, Medical Faculty, Department of Radiology. The Central Campus, 42075, Konya, Türkiye

E-Mail: nusretseher@gmail.com

How to cite ?

Seher N, Kolpay M, Kılıncer A, Demir LS, Kaynar M, Bocu K, Göktas S. The Diagnostic Performance of Magnetic Resonance Texture Analysis in Histological Subtyping and Grading of the Renal Cell Carcinoma. Genel Tip Derg. 2025;35 (2): 254-262

ABSTRACT

Aim: Renal cell carcinoma (RCC) is the 6th most frequently diagnosed cancer worldwide in men and 10th in women, accounting for 5% of all oncological cases in men and 3% in women. RCC is usually detected incidentally but can be presented with symptoms such as lateral pain, hematuria, and a palpable mass. Therefore, we aimed to investigate and evaluate the efficiency of MRTA in distinguishing CC-RCC from NC-RCC, the three subtypes of RCC within each other, and high-grade and low-grade tumors.
Materials and Methods: Patients undergoing surgery for renal masses in our hospital between January 2015 and December 2019 and whose pathological diagnosis was RCC were determined and included in the study. Eighty-two patients with MR images in the Picture Archiving and Communication System (PACS) were retrospectively examined. The patient's age and gender were recorded. RCC subtypes and Fuhrman grades were determined according to histopathological results.
Results: Sixty-two patients were analyzed (34 males and 28 females). The average age of patients was 60.5 years (ranging between 24-81). Given the tumor localization, the tumors were located in the left kidney in 32 patients and the right kidney in 30 patients. Tumors were unilateral in all patients. Grouping according to RCC subtypes resulted in 40 CC-RCC (26 high-grade, 14 low-grade), 11 P-RCC (two high-grade, nine low-grade), and 11 CH-RCC.
Conclusion: MRTA revealed several parameters with satisfactory diagnostic performance in distinguishing CC-RCC from NC-RCC. Findings indicated that the texture analyses (TA) were the complements of the evaluation of multi-parametric magnetic resonance imaging (MRI) features. MRTA can be efficiently used as a noninvasive tool useful in subtyping and grading RCC. In routine practice, TA can be used in radiology departments as an adjunct modality to the findings of multiparametric MRI in patients with a preliminary diagnosis of RCC.

Keywords: Magnetic resonance texture analysis, renal cell carcinoma, tumor

ÖZ

Amaç: Renal hücreli karsinom (RCC), erkeklerde dünya çapında en sık teşhis edilen 6. ve kadınlarda 10. kanser olup, erkeklerde tüm onkolojik vakaların %5'ini ve kadınlarda %3'ünü oluşturmaktadır. RCC genellikle tesadüfen tespit edilir ancak lateral ağrı, hematüri ve elle hissedilen kitle gibi semptomlarla ortaya çıkabilir. Bu nedenle, MRTA'nın CC-RCC'yi NC-RCC'den, RCC'nin üç alt tipini birbiri içinde ve yüksek dereceli ve düşük dereceli tümörleri ayırt etmedeki etkinliğini araştırmayı ve değerlendirmeyi amaçladık.
Materyaller ve Yöntemler: Ocak 2015 ile Aralık 2019 arasında hastanemizde renal kitle nedeniyle ameliyat edilen ve patolojik tanısı RCC olan hastalar belirlendi ve çalışmaya dahil edildi. Resim Arşivleme ve İletişim Sisteminde (PACS) MR görüntüleri olan 82 hasta retrospektif olarak incelendi. Hastanın yaşı ve cinsiyeti kaydedildi. RCC alt tipleri ve Fuhrman dereceleri histopatolojik sonuçlara göre belirlendi.
Bulgular: Altmış iki hasta analiz edildi (34 erkek ve 28 kadın). Hastaların ortalama yaşı 60,5 yıldı (24-81 arasında değişiyordu). Tümör lokalizasyonuna bakıldığında, tümörler 32 hastada sol böbrekte ve 30 hastada sağ böbrekte yer alıyordu. Tümörler tüm hastalarda tek taraflıydı. RCC alt tiplerine göre gruplandırma sonucunda 40 CC-RCC (26 yüksek dereceli, 14 düşük dereceli), 11 P-RCC (iki yüksek dereceli, dokuz düşük dereceli) ve 11 CH-RCC ortaya çıktı.
Sonuç: MRTA, CC-RCC'yi NC-RCC'den ayırt etmede tatmin edici tanı performansına sahip birkaç parametre ortaya koydu. Bulgular, doku analizlerinin (TA) çok parametreli manyetik rezonans görüntüleme (MRI) özelliklerinin değerlendirilmesinin tamamlayıcısı olduğunu gösterdi. MRTA, RCC'nin alt tiplendirilmesi ve derecelendirilmesinde yararlı olan invaziv olmayan bir araç olarak etkili bir şekilde kullanılabilir. Rutin uygulamada, TA, RCC ön tanısı olan hastalarda multiparametrik MRI bulgularına ek bir modalite olarak radyoloji bölümlerinde kullanılabilir.

Anahtar kelimeler: Manyetik rezonans doku analizi, renal hücreli karsinom, tümör

Introduction

Worldwide, renal cell carcinoma (RCC) is the 6th most frequently diagnosed cancer in men and 10th diagnosed in women, accounting for 5% of all oncological cases in men and 3% in women(1, 2). Although it is usually detected incidentally, it can be presented with symptoms such as lateral pain, hematuria, and a palpable mass. Approximately 17% of patients with RCC have metastases at the time of diagnosis(3). Early diagnosis of RCC is important since it is a tumor that is generally detected incidentally and has nonspecific symptoms. More than 90% of RCC consist of three main sub-types (clear cell RCC

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

(CC-RCC) 75-80%, papillary RCC (P-RCC) 5-10%, and chromophobe RCC (CH-RCC) 5-10%). The histological subtype is one of the important prognostic factors. CC-RCC has higher mortality than non-clear (NC)-RCC(4, 5). The most important prognostic factor is the nuclear grading of the TNM stage and Fuhrman, consisting of four degrees (low-grade: 1 and 2; high-grade: 3 and 4) based on nuclear morphology and pleomorphism(6-9). Clear cell RCCs are more metastatic and mortal tumors, and it is estimated that 70%-90% of them show changes in the von Hippel-Landau gene by mutation or gene silencing (i.e. hypermethylation)(10, 11). Preoperative diagnosis is important for CC-RCC. Tyrosine kinase inhibitors such as sunitinib and mammalian target of rapamycin (mTOR) inhibitors such as everolimus are used for successful surgery in CC-RCCs (70-90% VHL gene mutation is present) as they decrease micrometastasis and increase surgical success (4). Therefore, the prognosis varies depending on anatomical, clinical, histological, and molecular factors. Thus, preoperative estimation of tumor subtype and grade is needed, and it can be done through the use of noninvasive tools such as imaging. Although rapid development in computed tomography (CT) and magnetic resonance imaging (MRI) has recently provided insight into anatomical and prognostic factors, it cannot provide sufficient data on the histological types of RCC and tumor behavior(12-15).

Texture analysis (TA) evaluates tumor heterogeneity at the pixel level through the distribution and spatial relationship of grayscale values and identifies the presence of small differences, potentially not perceptible to the human eye. It reflects areas such as tumor heterogeneity, necrosis, high cell density, and bleeding. Heterogeneity is also a known feature of malignancy as an essential prognostic factor because it is thought that high tumor heterogeneity may be associated with high tumor levels(16). Many studies have used TA for subtyping and grading RCC in contrast to enhanced CT images(17-22). In this study, we investigated MR texture analysis (MRTA) as a tool for subtyping and grading RCC. MRI provides multiple paradigms for the evaluation of morphology. Therefore, MRTA is more likely to provide more robust data than CT. This study aims to investigate and evaluate the efficiency of MRTA in distinguishing CC-RCC from NC-RCC, the three subtypes of RCC within each other, and high-grade and low-grade tumors.

Materials And Methods

Patient Selection

Following receipt of the ethics committee number 2020/189 from our university ethics committee, patients who underwent surgery for renal masses in our hospital between January 2015 and December 2019 and whose pathological diagnosis was RCC were determined. The study was conducted under the principles of the Declaration of Helsinki. 82 patients with MR images in the Picture Archiving and Communication System (PACS) were retrospectively examined. The age and gender of the patients were recorded. RCC subtypes and Fuhrman grades were determined according to histopathological results. Pathologically, tumors without uniform subtypes, tumors with sarcomatous features, tumors with rhabdoid features, and tumors without Fuhrman grading were excluded from the study. Patients with artifacts on MRI and non-optimal (such as the corticomedullary phase or nephrogram phase not being in the expected contrast staining phase) corticomedullary (CM) and nephrographic (NG) phases taken after the contrast were excluded from the study. Finally, a total of 62 RCC patients were analyzed.

The Magnetic Resonance Imaging (MRI) Protocol

All the MRI examinations were performed on a 1.5-T scanner (Aera, Siemens, Erlangen, Germany). From the pre-contrast sequences, axial T2-weighted (W) Half-Fourier Acquisition Single-shot Turbo Spin Echo (HASTE), axial T1W dual gradient echo in-phase (IP) and apparent diffusion coefficient (ADC) images were used. In the series taken after the contrast, images obtained in the CM (35-40 sec) and NG (90-100 sec) phases of the axial fat-saturated T1W Volume Interpolated Breath-hold Examination (VIBE) sequence were used. The use of contrast material included Gadovist (Bayer HealthCare) infusion at a dose of 0.1 mmol/kg followed by a 25 ml saline flush (administered at a rate of 3 mL /s using a power injector).

The Texture Analysis

Texture analysis was performed on 62 patients whose images were available. One radiologist with five years of experience in diagnostic imaging performed the texture analysis and he was blinded to the final histopathological diagnosis. For the analysis, axial T2W (Half Fourier Single-shot Turbo spin-Echo) HASTE images, axial T1W dual gradient echo IP images, ADC map, and the post-contrast (CM and NG phase) axial T1-VIBE images were used. The images were sent to the database of the TA program. MRTA was performed using software (Olea Medical, a Canon Group Company, Japan) by placing the freehand region of interest (ROI) in tumors to contain the entire tumor in all sequences. Axial T2W HASTE images were scanned to map the distribution of the tumor component that was initially traceable. Then, all the sequences to be measured were stacked side by side in the TA program, the only representative slice showing the entire tumor component was selected, and the ROI was plotted to cover almost all of the tumor in any sequence (Figure 1a-e).

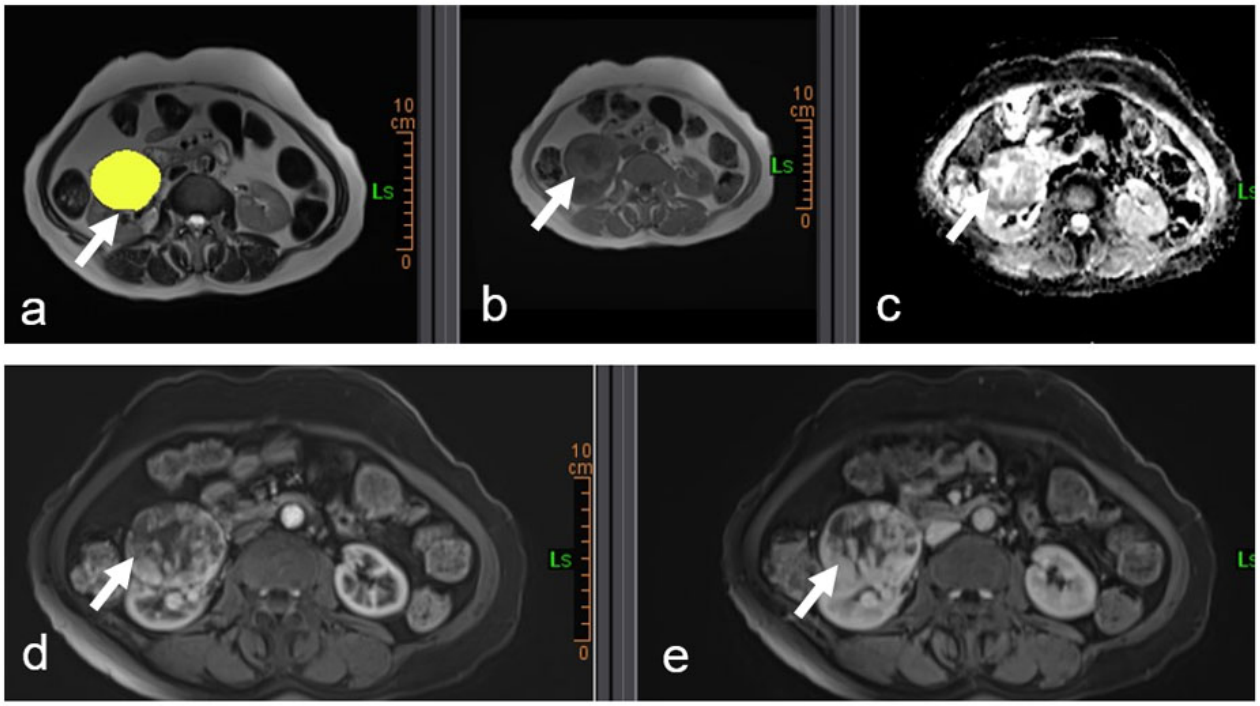


Figure 1. The sequences to be used in texture analysis were arranged side by side with the same sections (T2W (a), IP(b), ADC(c), CM phase(d), and NG phase (e)). Then, the ROI was drawn on one of the sequences to take up the entire tumor (arrow).

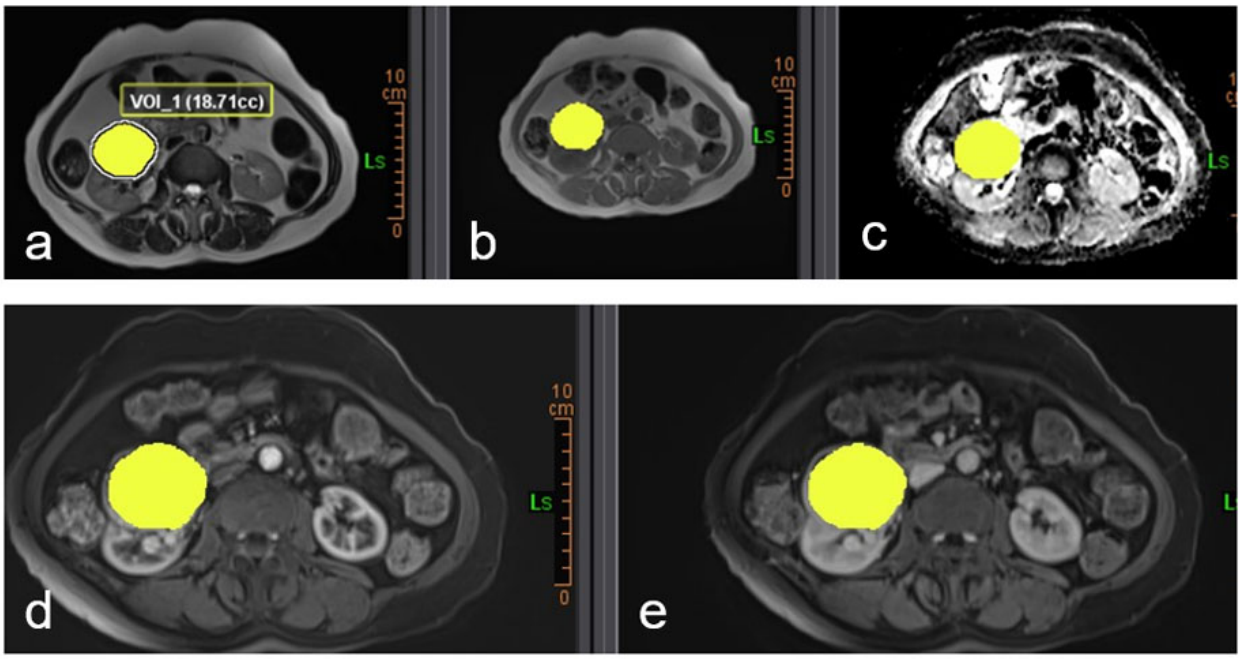


Figure 2. The ROI drawn on one of the sequences was copied to all sequences, in the same way, to avoid irregularities in the measurements (T2W (a), IP (b), ADC (c), CM phase (d), and NG phase (e)).

The ROI was then copied from the drawn sequence to other sequences (Figure 2a-e). Care was taken not to extend the ROI limits to peripheral 1-2 mm of the tumor to avoid possible errors. In tumors with a cystic or necrotic component weight, the ROI was plotted to include the solid part. After the ROIs were placed in the sequences, TA was performed in the Olea TA program using 7 separate parameters for each sequence. One of the most significant advantages of the Olea TA program was that it showed the analysis results in seconds (Figure 3). Parameters used for the TA included mean (average of the gray level intensity),

Features	ep2d_diff_FS_b50_400_800_p2_ADC_...	t1_fl2d_opp-in_t...	t1_vibe_fs_tra...	t1_vibe_fs_tra...	t2_haste_tra...
	VOI_3#1	VOI_2#1	VOI_4#1	VOI_5#1	VOI_1#1
Original First Order					
Entropy	5.560	4.783	5.527	5.595	5.429
Mean	1878.504	143.513	218.184	274.582	501.852
Median	1843.000	144.000	221.000	290.000	490.000
Skewness	0.082	-0.505	-0.027	-0.631	0.281
Kurtosis	2.457	5.252	2.216	2.714	2.631
Variance	83210.822	132.569	9130.391	8220.091	12380.816
Uniformity	0.024	0.042	0.024	0.024	0.027

Figure 3. Following the ROI drawing and selection of statistical parameters, a texture analysis results screen is shown.

median (value separating the higher half gray levels intensities within the ROI, from the lower half), entropy (the average amount of information required to encode the image values), skewness (asymmetry of the distribution of values about the mean value), kurtosis (peakedness of the histogram), variance (squared distances of each intensity value from the Mean value), uniformity (sum of the squares of each intensity value). Thus, 35 different measurements were made with 5 sequences and 7 different parameters for each patient.

Statistical Analysis

Statistical analysis was done using SPSS software (IBM Corp, Armonk, NY, USA) for Windows. The Kolmogorov–Smirnov test was used to determine the normal distribution of continuous variables. Quantitative variables were expressed as median with range (min □ max) since the MRTA parameters were not distributed normally. Comparisons between the groups were performed using Kruskal-Wallis or Mann-Whitney's U test for quantitative variables, as appropriate. A P value of <0.05 was considered significant. Then, the

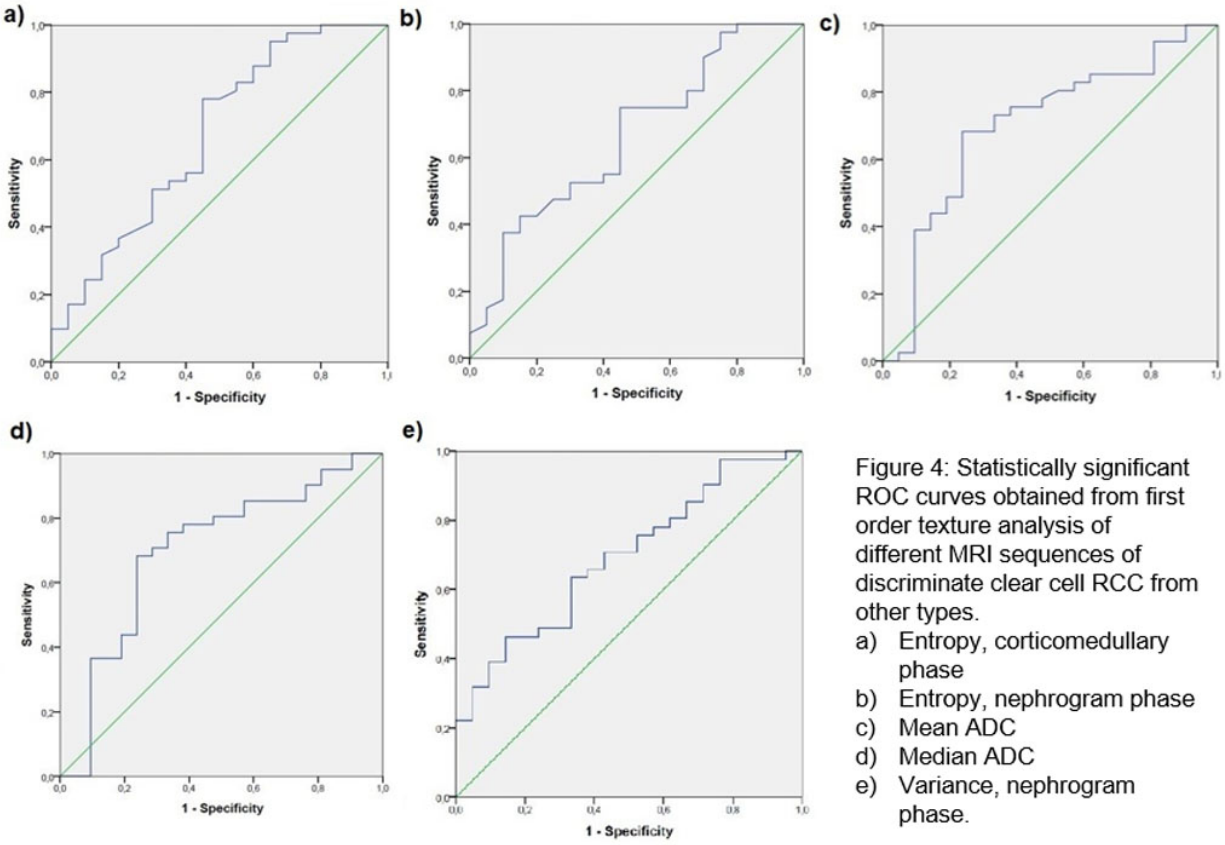


Figure 4: Statistically significant ROC curves obtained from first order texture analysis of different MRI sequences of discriminate clear cell RCC from other types.
a) Entropy, corticomedullary phase
b) Entropy, nephrogram phase
c) Mean ADC
d) Median ADC
e) Variance, nephrogram phase.

Figure 4. Statistically significant ROC curves obtained from first-order texture analysis of different MRI sequences of discriminate clear cell RCC from other types. a) Entropy, corticomedullary phase b) Entropy, nephrogram phase c) Mean ADC, d)Median ADC, e) Variance, nephrogram phase.

Receiver Operating Characteristic (ROC) analysis was performed on those with a significant P value in the data obtained. The area under the curve (AUC), cut-off values, sensitivity, and specificity values were determined.

Results

Sixty-two patients were analyzed (34 male, 28 female). The average age of patients was 60.5 (range, 24-81). When the tumor localization was examined, the tumor was located in the left kidney in 32 patients and the right kidney in 30 patients. Tumors were unilateral in all patients. Grouping according to RCC subtypes resulted in 40 CC-RCC (26 high-grade, 14 low-grade), 11 P-RCC (two high-grade, nine low-grade), and 11 CH-RCC.

Differentiation of CC-RCC from NC-RCC

After the Mann-Whitney U analysis was done, the P values of the 7 parameters used were calculated individually for each MR sequence and are shown in Table 1. In the statistical analysis, there were significant values in the differentiation of CC-RCC from NC-RCC in ADC, CM phase, and NG phase. In IP and T2W images, it was observed that the parameters used were not significant in distinguishing CC-RCC from NC-RCC. NG phase was observed to be the most significant sequence in distinguishing CC-RCC and NC-RCC. Significant values in the ROC analysis are shown in Table 2 and Figure 4.

Table 1. Mann-Whitney U test in distinguishing CC-RCC from NC-RCC

Sequences	Parameters	CC-RCC (n=40)	NC-RCC (n=22)	P (Mann-Whitney U) CC-NC RCC
ADC	Mean	1515 (649-2672)	1193 (271-2934)	0.011*
	Median	1528 (626-2714)	1166 (209-2933)	0.01*
	Skewness	-0.198 (-1.71-3.04)	0.34 (-1.36-2.28)	0.022*
	Kurtosis	3.77 (0.63-15.8)	3.72 (1.10-9.71)	0.87
	Variance	132400 (1562-980895)	63031 (6931-433098)	0.026*
	Uniformity	0.035 (0.02-0.17)	0.037 (0.02-0.10)	0.36
	Entropy	5.1 (3.78-5.64)	5.04 (4.06-5.57)	0.38
IP	Mean	188 (160-2705)	186(106-306)	0.17
	Median	185 (79-329)	175 (107-321)	0.19
	Skewness	0.55 (-1.87-2.88)	0.44 (-0.92-3.87)	0.25
	Kurtosis	4.7 (2.04-18.07)	3.27 (2.24-25.12)	0.09
	Variance	509 (65-9623)	461 (99-9319)	0.79
	Uniformity	0.039 (0.03-.07)	0.037 (0.03-0.09)	0.39
	Entropy	5.04 (4.07-5.68)	5.16 (3.97-5.53)	0.15
Corticomedullar phase	Mean	152 (54-604)	139 (80-685)	0.42
	Median	219 (51-626)	133(75-684)	0.48
	Skewness	0.1 (-42-.96)	-0.057 (-1.79-8.38)	0.48
	Kurtosis	3.24 (1.74-10.88)	4.30 (1.99-30.26)	0.017*
	Variance	2312 (224-35062)	1271 (82-8794)	0.066*
	Uniformity	0.032 (0.02-0.05)	0.037 (0.02-0.10)	0.009*
	Entropy	5.3 (4.72-5.70)	5.07 (3.76-5.58)	0.017*
Nephrogram phase	Mean	222 (65-526)	191 (104-333)	0.1
	Median	227 (64-551)	183 (88-354)	0.049*
	Skewness	-0.55 (-4.12-1.74)	0.12 (-2.01-3.58)	0.065
	Kurtosis	3.19 (0.48-8.95)	4.32 (2.28-23.41)	0.018*
	Variance	2975 (134-24368)	1876 (131-6401)	0.014*
	Uniformity	0.035 (0.02-0.06)	0.04 (0.03-0.09)	0.026*
	Entropy	5.27 (4.6-6.7)	4.95 (3.96-5.54)	0.017*
T2W	Mean	188 (105-604)	312 (148-845)	0.33
	Median	339 (156-596)	304 (144-851)	0.34
	Skewness	0.34 (-0.97-2.28)	0.34 (-0.97-2.28)	0.59
	Kurtosis	3.37 (1.58-16.5)	3.54 (1.69-9.62)	0.57
	Variance	4967 (180-32947)	2427 (370-47086)	0.36
	Uniformity	0.034 (.02-.07)	0.036 (0.02-0.07)	0.28
	Entropy	5.15 (4.17-5.71)	4.99 (4.27-5.62)	0.1

Median (Min-Max). Significant p-values are indicated with*. ADC: Apparent diffusion coefficient, CM: Corticomedullary, IP: In-phase, NG: Nephrogram, T2W: T2-weighted.

Table 2. Diagnostic performance of parameters and AUC values that are statistically significant.

Sequences	Parameters	AUC	Cut-off Value	Sensitivity	Specificity
ADC	Mean	0.75	1181	80	50
ADC	Median	0.76	1192.25	80.5	66.7
CM Phase	Entropy	0.67	5.01	82.9	45
NG Phase	Entropy	0.66	4.95	75	55
NG Phase	Variance	0.66	826.5	83.8	33.3

ADC: Apparent diffusion coefficient, AUC: Area under the curve, CM: Corticomedullary, NG: Nephrogram

Differentiation of Subtypes

A non-parametric Kruskal Wallis test was completed to compare the differences in texture parameters between the subtypes. The measured p values are shown in detail in Table 3. Non-parametric Mann-Whitney U test was used for the binary distinction of the subtypes. In separating CC-RCC from P-RCC; In the ADC sequence, the mean was significantly higher than P-RCC in CC-RCC (p=0.024). Median was significantly higher in CC-RCC than P-RCC (p=0.021). In the CM phase, uniformity was significantly lower in CC-RCC than in P-RCC (p = 0.048). In the NG phase, kurtosis was significantly lower than P-RCC in CC-RCC (p=0.048). Uniformity was significantly lower in CC-RCC than in P-RCC (p=0.003). In distinguishing CC-RCC from CH-RCC; and in the ADC sequence, the variance was significantly higher in CC-RCC than CH-RCC (p=0.03).

In the distinction between P-RCC and CH-RCC; in the NG phase, kurtosis was significantly higher than CH-RCC in P-RCC (p=0.021). Uniformity was significantly higher in P-RCC than in CH-RCC (p=0.024). There was no significant difference in parameters measured in IP and T2W sequences.

Table 3. Kruskal Wallis test in differentiating RCC subtypes

Sequences	Parameters	CC-RCC (n=40)	P-RCC (n=11)	CH-RCC (n=11)	P (Kruskal-Wallis)
ADC	Mean	1515 (649-2672)	1084 (271-2628)	1294 (703-2934)	0.019*
	Median	1528 (626-2714)	1046 (209-2771)	1240 (693-2933)	0.016*
	Skewness	-0.198 (-1.71-3.04)	0.34 (-1.36-2.28)	0.39 (-0.33-1.65)	0.067
	Kurtosis	3.77 (.63-15.8)	3.53 (2.30-9.71)	3.83 (1.10-6.99)	0.97
	Variance	132400 (1562-980895)	70813 (17412-433098)	34313 (6931-197276)	0.031*
	Uniformity	0.035 (0.02-0.17)	0.034 (0.02-0.10)	0.039 (0.03-0.07)	0.58
	Entropy	5.1 (3.78-5.64)	5.11 (4.38-5.57)	4.98 (4.06-5.31)	0.55
IP	Mean	188 (160-2705)	189 (106-306)	177 (126-286)	0.27
	Median	185 (79-329)	173 (107-321)	178 (125-281)	0.35
	Skewness	0.55 (-1.87-2.88)	0.43 (-0.92-0.90)	0.44 (-0.78-3.87)	0.44
	Kurtosis	4.7 (2.04-18.07)	3.15 (2.38-9.05)	3.62 (2.24-25.12)	0.22
	Variance	509 (65-9623)	1179 (246-9319)	240 (99-4764)	0.088
	Uniformity	0.039 (0.03-0.07)	0.037 (0.03-0.07)	0.036 (0.03-0.09)	0.637
	Entropy	5.04 (4.07-5.68)	5.15 (4.33-5.53)	5.18 (3.97-5.49)	0.31
CM Phase	Mean	152 (54-604)	139 (84-273)	145 (80-685)	0.61
	Median	219 (51-626)	126 (75-289)	147 (77-684)	0.55
	Skewness	0.1 (-0.42-0.96)	0.17 (-1.79-0.63)	-0.19 (-1.73-8.38)	0.68
	Kurtosis	3.241 (0.74-10.88)	4.3 (1.99-8.67)	3.88 (2.89-30.26)	0.056
	Variance	2312 (224-35062)	2357 (239-8794)	630 (82-5981)	0.13
	Uniformity	0.032 (0.02-0.05)	0.039 0.03-0.06)	0.035 (0.02-0.10)	0.033*
	Entropy	5.3 (4.72-5.70)	5.02 (4.61-5.58)	5.14 (3.76-5.54)	0.057
NG Phase	Mean	222 (65-526)	191 (104-333)	188 (105-280)	0.26
	Median	227(64-551)	190 (88-354)	183 (109-287)	0.13
	Skewness	-0.55 (-4.12-1.74)	0.21 (-1.96-3.58)	-0.07 (-2.01-3.12)	0.17
	Kurtosis	3.19 (.48-8.95)	6.66 (3.02-23.41)	3.22 (2.28-9.20)	0.003*
	Variance	2975 (134-24368)	1876 (292-6401)	1834 (131-4712)	0.048*
	Uniformity	0.035 (0.02-0.06)	0.049 (0.03-0.09)	0.031 (0.03-0.06)	0.003*
	Entropy	5.27 (4.6-6.7)	4.83 (3.96-5.40)	5.24 (4.64-5.54)	0.004*
T2W	Mean	188 (105-604)	292 (148-845)	354 (172-810)	0.27
	Median	339 (156-596)	274 (144-851)	351 (173-839)	0.21
	Skewness	0.34 (-0.97-2.28)	0.58 (0.15-2.23)	0.41 (-1.55-1.02)	0.42
	Kurtosis	3.37 (1.58-16.5)	3.74 (1.69-9.62)	3.54 (2.33-5.22)	0.83
	Variance	4967 (180-32947)	3177 (1073-47086)	2272 (370-44705)	0.51
	Uniformity	0.034 (0.02-0.07)	0.038 (0.03-0.07)	0.035 (0.02-0.04)	0.38
	Entropy	5.15 (4.17-5.71)	4.88 (4.27-5.46)	5.12 (4.88-5.62)	0.13

Median (Min-Max). Significant p-values are indicated with*. ADC: Apparent diffusion coefficient, CM: Corticomedullary, IP: In-phase, NG: Nephrogram, T2W: T2-weighted

Differentiation of Histologic Grade

A Mann-Whitney U test was completed to compare the differences in texture parameters between low-grade (1,2) and high-grade (3,4). In the IP sequence, the variance was significantly higher in the group with a low histologic grade than in the group with a high grade (p=0.024). In T2W images, the variance was significantly higher in the group with a low histologic grade than in the group with a high grade (p=0.0037). There was no significant difference in parameters measured in other sequences.

Discussion

Renal cell carcinoma is ranked as the 13th most common cause of death from cancer worldwide. More importantly, although most of the lesions detected are small in size, the locally advanced disease is present in a significant proportion of patients. In some patients, distant metastases can be seen at the time of diagnosis(2). The locally advanced disease, micrometastasis, and lymph node metastasis are more evident in CC-RCC(4, 5). Due to such situations, early diagnosis is vital in RCC. As known, the gold standard method is histopathological evaluation. Patients suspected of RCC may have a biopsy for early diagnosis and treatment, to determine the subtype and Fuhrman grade. However, a biopsy is an invasive procedure, and the sample tissue piece needs to contain a sufficient amount of tumoral tissue. Histological staging of RCC can be performed in

percutaneous biopsy, but it is generally not considered correct due to sampling problems, and the majority of tumors vary in histological grade compared to biopsy after nephrectomy(23). Also, the most important complications that can occur in a biopsy include the risk of bleeding (3.5%) and, most importantly, the risk of tumor seeding to the biopsy tract(24). So, the importance of the noninvasive diagnosis is gradually increasing. In the radiology literature, it is seen that the articles on noninvasive diagnosis of RCC have increased rapidly in recent years. In many of these articles, contrast enhancement patterns of tumors were emphasized with CT and MRI, subtype distinction, low-high-grade separation, and inferences were made more quantitatively(25-28). Vargas et al., in their multiparametric MRI study, showed that the percentage of signal intensity (SI) change in sequences taken after contrast in the distinction between subtypes could distinguish CC-RCC from other subtypes(27). To this date, there is ongoing research for noninvasive imaging techniques that can provide preoperative prognostic information for tumor subtype and grade and reduce the need for biopsy. TA articles related to RCC are limited in the literature. Many studies achieved satisfactory diagnostic performance in grading and subtyping RCC in contrast to enhanced CT images using the TA program(17-22).

Our study is an MRTA study with the largest patient population with RCC subtypes. In this study, we examined the performance of MRTA in three ways. First, we examined the performance of distinguishing CC-RCC from NC-RCC, second in distinguishing 3 subtypes between each other, and thirdly, differentiating low-grade (1-2) and high-grade (3-4) tumors according to the Fuhrman classification. MRI provides several advantages due to its high temporal resolution in the morphological and functional evaluation of tumors (T1W, T2W, post-contrast images, DWI), and the evaluation of their relationship with surrounding tissues. Therefore, it is more likely that MRTA can provide more robust and reliable data compared to the CT texture analysis. There are two MRTA studies on RCC in the literature. Vendrami et al. tried to distinguish two subtypes of P-RCC and showed that the combination of qualitative analysis and TA improves the prediction of type 2 tumors(2). Goyal et al., in a study of 34 patients, found significant results in distinguishing CC-RCC from NC-RCC with various texture parameters and in separating high-grade and low-grade CC-RCC(29). Our study showed a strong diagnostic performance in MRTA in the distinction of CC-RCC and NC-RCC with various texture parameters. Additionally, we obtained significant results in MRTA for distinguishing RCC subtypes and low-high-grade tumors.

Texture analysis measures heterogeneity by evaluating the background signal intensity and brightness differences according to the parameters used. Entropy and variance, dispersion and irregularity measurement tend to be higher at higher degrees of heterogeneity. Kurtosis, which is a measure of the histogram's peak, decreases with more heterogeneity. Mean and median, on the other hand, are associated with overall brightness, showing a positive correlation with higher signal intensity and amplification(16-20). Skewness defines the asymmetry of the mean value and shifts the tail of the histogram to the right (positive skewness) or left (negative skewness) depending on the increase and decrease in the number of bright pixels. Uniformity increases depending on the heterogeneity in the environment.

CC-RCC is more heterogeneous due to more necrosis than NC-RCC in terms of imaging properties, and CC-RCC is also more contrasted than P-RCC(18). In our study, according to the data, entropy, variance, and uniformity values were significantly higher in CC-RCC due to heterogeneity, especially in measurements performed in the post-contrast CM and NG phase.

In the literature, it was shown that P-RCC has more homogeneous diffusion restriction while CC-RCC has more heterogeneous diffusion restriction(25). In our study, when the parameters used in ADC were examined, the mean, median, and variance parameters were significantly higher in CC-RCC than in NC-RCC. Based on these values, it is understood that CC-RCC has a more heterogeneous ADC map.

When the low and high-grade tumors were compared, high-grade tumors were expected to show stronger contrast uptake and greater diffusion constraint. This suggests that ADC should show more positive skewness, and entropy in CM and NG phases. However, Cornelis et al. stated that the correlation of ADC and contrasted images with tumor grade remained weak(26). In our study, in the IP and T2W sequences, the variance parameter was significantly higher in low-grade tumors. These results caused us to think that as the tumor grade increases, the rate of microscopic and macroscopic fat decreases while necrosis increases. So, the standard deviation (SD) was higher since the fat component was more in lower grades; accordingly, the variance was significantly higher.

In the comparison of subtypes, the mean and median parameters in ADC were significantly higher in CC-RCC when compared with P-RCC, which showed that CC-RCC restricted more heterogeneous diffusion than expected. CC-RCC has a more heterogeneous pattern while P-RCC has a more homogeneous contrast pattern(27). Accordingly, in the CM and NG phases, uniformity was higher in P-RCC, while kurtosis in the NG phase was significantly lower in CC-RCC. In the comparison of CC-RCC and CH-RCC, the variance

in ADC was significantly higher in CC-RCC, which supported that CC-RCC is a more heterogeneous tumor. In the P-RCC/CH-RCC distinction, kurtosis and uniformity in the NG phase were higher in P-RCC than in CH-RCC, which indicates that P-RCC is contrasted less in the NG phase and more homogenous compared to CH-RCC(26).

Our study has yielded several texture parameters that perform well in differentiating CC-RCC from NC-RCC and high-grade low-grade CC-RCC and distinguishing subtypes from each other. TA has become an important topic that has been the focus of an increasing number of publications over the past decade. Tumor heterogeneity is an important prognostic factor, as well as one of the known essential features of malignancy because higher tumor heterogeneity is thought to be associated with higher tumor grades. TA uses a variety of mathematical methods that can be used to assess the gray level intensity and position of pixels in the image to extract texture features that can predict intralesional heterogeneity(28). In light of this information, TA is emerging as an essential tool in oncological imaging. However, in the future, if definitive evidence can be obtained, it can be used as a quantitative tool to assist in the morphological evaluation of renal tumors.

Our study had some limitations. First, our low-grade tumor count was lower than the high-grade tumor count. Second, we evaluated only the first order as statistical texture parameters. Advanced-level statistical parameters can provide more data size. Studies of the most advanced-level statistical parameters are not available in the literature, and the biological basis of these parameters is not yet known. Our study is a single-center study; multicenter studies for the diagnosis of RCC are also needed to support our findings.

In conclusion, the MRTA showed several parameters with satisfactory diagnostic performance (AUC> 0.75) in distinguishing CC-RCC from NC-RCC. Findings show that the TA complements the evaluation of multi-parametric MRI features. MRTA can be efficiently used as a noninvasive tool useful in subtyping and grading RCC. In routine practice, TA can be used in radiology centers as an adjunct to the findings of multiparametric MRI in patients with a preliminary diagnosis of RCC.

Conflict of Interest

The authors declare that they have no conflict of interest.

Financial Support

This study has received no funding.

References

1.Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2018. CA Cancer J Clin. 2018 Jan;68(1):7-30.

2.Capitanio U, Montorsi F. Renal Cancer. Lancet. 2016 Feb 27;387(10021):894-906.

3.Capitanio U, Bensalah K, Bex A, et al. Epidemiology of Renal Cell Carcinoma. Eur Urol. 2019 Jan;75(1):74-84.

4.Posadas EM, Limvorasak S, Figlin RA. Targeted Therapies for Renal Cell Carcinoma. Nat Rev Nephrol. 2017 Aug;13(8):496-511.

5.Shao Y, Xiong S, Sun G, et al. Prognostic Analysis of Postoperative Clinically Nonmetastatic Renal Cell Carcinoma. Cancer Med. 2020 Feb;9(3):959-970.

6.Ficarra V, Galfano A, Novara G, et al. Risk Stratification and Prognostication of Renal Cell Carcinoma. World J Urol. 2008 Apr;26(2):115-125.

7.Muglia VF, Prando A. Renal Cell Carcinoma: Histological Classification and Correlation with Imaging Findings. Radiol Bras. 2015 May-Jun;48(3):166-174.

8.Volpe A, Patard JJ. Prognostic Factors in Renal Cell Carcinoma. World J Urol. 2010 Jun;28(3):319-327.

9.Escudier B, Porta C, Schmidinger M, et al. Renal Cell Carcinoma: Esmo Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. Ann Oncol. 2016 Sep;27(suppl 5):v58-v68.

10.Moore LE, Nickerson ML, Brennan P, et al. Von Hippel-Lindau (Vhl) Inactivation in Sporadic Clear Cell Renal Cancer: Associations with Germline Vhl Polymorphisms and Etiologic Risk Factors. PLoS Genet. 2011 Oct;7(10):e1002312.

11.Sudarshan S, Karam JA, Brugarolas J, et al. Metabolism of Kidney Cancer: From the Lab to Clinical Practice. Eur Urol. 2013 Feb;63(2):244-251.

12.Kim JH, Bae JH, Lee KW, Kim ME, Park SJ, Park JY. Predicting the Histology of Small Renal Masses Using Preoperative Dynamic Contrast-Enhanced Magnetic Resonance Imaging. Urology. 2012 Oct;80(4):872-876.

13.Jung SC, Cho JY, Kim SH. Subtype Differentiation of Small Renal Cell Carcinomas on Three-Phase Mdct: Usefulness of the Measurement of Degree and Heterogeneity of Enhancement. Acta Radiol. 2012 Feb 1;53(1):112-118.

14.Young JR, Margolis D, Sauk S, Pantuck AJ, Sayre J, Raman SS. Clear Cell Renal Cell Carcinoma: Discrimination from Other Renal Cell Carcinoma Subtypes and Oncocytoma at Multiphasic Multidetector Ct. Radiology. 2013 May;267(2):444-453.

15.Sasaguri K, Takahashi N. Ct and Mr Imaging for Solid Renal Mass Characterization. Eur J Radiol. 2018 Feb;99:40-54.

16.Hodgdon T, McInnes MD, Schieda N, Flood TA, Lamb L, Thornhill RE. Can Quantitative Ct Texture Analysis Be Used to Differentiate Fat-Poor Renal Angiomyolipoma from Renal Cell Carcinoma on Unenhanced Ct Images? Radiology. 2015 Sep;276(3):787-796.

17.Lubner MG, Stabo N, Abel EJ, Del Rio AM, Pickhardt PJ. Ct Textural Analysis of Large Primary Renal Cell Carcinomas: Pretreatment Tumor Heterogeneity Correlates with Histologic Findings and Clinical Outcomes. AJR Am J Roentgenol. 2016 Jul;207(1):96-105.

18.Yu H, Scalera J, Khalid M, et al. Texture Analysis as a Radiomic Marker for Differentiating Renal Tumors. Abdom Radiol (NY). 2017 Oct;42(10):2470-2478.

19.Zhang GM, Shi B, Xue HD, Ganeshan B, Sun H, Jin ZY. Can Quantitative Ct Texture Analysis Be Used to Differentiate Subtypes of Renal Cell Carcinoma? Clin Radiol. 2019 Apr;74(4):287-294.

20.Bektas CT, Kocak B, Yardimci AH, et al. Clear Cell Renal Cell Carcinoma: Machine Learning-Based Quantitative Computed Tomography Texture Analysis for Prediction of Fuhrman Nuclear Grade. Eur Radiol. 2019 Mar;29(3):1153-1163.

21.Shu J, Tang Y, Cui J, et al. Clear Cell Renal Cell Carcinoma: Ct-Based Radiomics Features for the Prediction of Fuhrman Grade. Eur J Radiol. 2018 Dec;109:8-12.

22.Yaşar S, Voyvoda N, Voyvoda B, Özer T. Using Texture Analysis as a Predictive Factor of Subtype, Grade and Stage of Renal Cell Carcinoma. Abdom Radiol (NY). 2020 Nov;45(11):3821-3830.

23.Schieda N, Lim RS, Krishna S, McInnes MDF, Flood TA, Thornhill RE. Diagnostic Accuracy of Unenhanced Ct Analysis to Differentiate Low-Grade from High-Grade Chromophobe Renal Cell Carcinoma. AJR Am J Roentgenol. 2018 May;210(5):1079-1087.

24.Andersen MF, Norus TP. Tumor Seeding with Renal Cell Carcinoma after Renal Biopsy. Urol Case Rep. 2016 Nov;9:43-44.

25.Schieda N, Lim RS, McInnes MDF, et al. Characterization of Small (<4cm) Solid Renal Masses by Computed Tomography and Magnetic Resonance Imaging: Current Evidence and Further Development. Diagn Interv Imaging. 2018 Jul-Aug;99(7-8):443-455.

26.Cornelis F, Tricaud E, Lasserre AS, et al. Routinely Performed Multiparametric Magnetic Resonance Imaging Helps to Differentiate Common Subtypes of Renal Tumours. Eur Radiol. 2014 May;24(5):1068-1080.

27.Vargas HA, Chaim J, Lefkowitz RA, et al. Renal Cortical Tumors: Use of Multiphasic Contrast-Enhanced Mr Imaging to Differentiate Benign and Malignant Histologic Subtypes. Radiology. 2012 Sep;264(3):779-788.

28.Vendrami CL, Velichko YS, Miller FH, et al. Differentiation of Papillary Renal Cell Carcinoma Subtypes on Mri: Qualitative and Texture Analysis. AJR Am J Roentgenol. 2018 Dec;211(6):1234-1245.

29.Goyal A, Razik A, Kandasamy D, et al. Role of Mr Texture Analysis in Histological Subtyping and Grading of Renal Cell Carcinoma: A Preliminary Study. Abdom Radiol (NY). 2019 Oct;44(10):3336-3349.

Received:21 Nov 2024 | **Accepted:** 13 Jan 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 263-267
DOI: 10.54005/geneltip.1589500

ORIGINAL ARTICLE

Medicolegal Evaluation of Non-Fatal Occupational Accidents in the Province of Sanlıurfa, Türkiye

Şanlıurfa, Türkiye'deki Ölümcül Olmayan İş Kazalarının Medikolegal Değerlendirmesi

[1]Uğur Demir

[1]Department of Forensic Medicine, Medical Faculty of Harran University, Şanlıurfa, Türkiye

Correspondence

Assoc. Prof. Dr. Ugur DEMİR
Department of Forensic Medicine, Medical Faculty of Harran University, 63510, Şanlıurfa, Türkiye

E-Mail: ugurdmr81@gmail.com

How to cite ?

Demir U. Medicolegal Evaluation of Non-Fatal Occupational Accidents in the Province of Sanlıurfa, Türkiye. Genel Tıp Derg. 2025;35 (2): 263-267

ABSTRACT

Aim: This study aims to describe injuries resulting from occupational accidents treated at a university hospital in Şanlıurfa, Türkiye. The study provides information on age, gender, date of occupational accident, occupational accident sector, type of occupational accident, location of the wound, presence of brain/visceral lesion, type of wound, and discharge status.
Methods: In the study, hospital records for 10 years between 2014-2023 were retrospectively examined to determine occupational accident cases. Patient data were obtained from the hospital information management system. Occupational accident sectors were classified and injury locations were categorized.
Results: A total of 127 occupational accident cases were identified, with 92.9% being male and 7.1% female. The mean age was 35.3 ±11.03 years. The construction sector (32.3%) was found to have the highest case rate. The most common injury types were cuts/crushing/sharp/needle wounds (36.2%), fractures (27.8%), and blunt traumatic injuries (26.0%). Upper extremity trauma was the most frequent injury location (40.94%), followed by head trauma (14.96%) and lower extremity trauma (10.24%). Brain/internal organ lesions were present in seven cases.
Conclusion: Our study emphasizes the importance of understanding injury patterns to improve workplace safety. In our study, it is thought that work safety measures should be changed especially in the construction sector and protective measures for upper extremity injuries should be increased. Considering the regional and provincial differences in occupational accidents in our country, there is a need for multi-centered and larger dataset studies that include detailed statistical data on occupational accidents, sectors, and types of injuries.

Keywords: Accidents, injury, occupational, sector

ÖZ

Amaç: Bu çalışma, Şanlıurfa'da bir üniversite hastanesinde tedavi edilen iş kazası kaynaklı yaralanmaları tanımlamayı amaçlamaktadır. Çalışmamız yaş, cinsiyet, iş kazasının tarihi, iş kazasının gerçekleştiği sektör, iş kazası türü, yaranın lokalizasyonu, beyin/iç organ lezyonu varlığı, yara türü ve taburculuk durumu hakkında bilgi sağlamaktadır.
Gereç ve Yöntem: Çalışmada, 2014-2023 yılları arasındaki 10 yıllık döneme ait hastane kayıtları retrospektif olarak incelenerek iş kazası vakaları belirlenmiştir. Hasta verileri hastane bilgi yönetim sisteminden elde edilmiştir. İş kazası sektörleri sınıflandırılmış ve yaralanma lokalizasyonları kategorize edilmiştir.
Bulgular: Toplam 127 iş kazası vakası tespit edilmiş olup, vakaların %92,9'u erkek, %7,1'i kadındır. Ortalama yaş 35,3 ±11,03 yıldır. En yüksek vaka oranı inşaat sektöründe (%32,3) bulunmuştur. En sık görülen yaralanma türleri kesici/ezici/delici nitelikte yaralar (%36,2), kırıklar (%27,8) ve künt travmatik yaralanmalar (%26,0) olarak belirlenmiştir. Üst ekstremite travması en sık yaralanma lokalizasyonu (%40,94) olup, bunu kafa travması (%14,96) ve alt ekstremite travması (%10,24) izlemiştir. Beyin/iç organ lezyonu 7 vakada mevcuttur.
Sonuç: Çalışmamız, işyeri güvenliğini iyileştirmek için yaralanma modellerini anlamanın önemini vurgulamaktadır. Çalışmamızda özellikle inşaat sektöründe iş güvenliği önlemlerinin değiştirilmesi ve üst ekstremite yaralanmalarına yönelik koruyucu önlemlerin artırılması gerektiği düşünülmektedir. Ülkemizdeki iş kazalarının bölgesel ve il bazındaki farklılıkları göz önünde bulundurulduğunda, iş kazaları, sektörler ve yaralanma türleri hakkında detaylı istatistiksel verileri içeren çok merkezli ve daha geniş veri setli çalışmalara ihtiyaç duyulmaktadır.

Anahtar Sözcükler: İş, kaza, sektör, yaralanma

Introduction

Occupational accidents are defined in the Occupational Health and Safety Law as "an incident that occurs in the workplace or during the execution of work, causing death or rendering the body physically or mentally disabled" (1).

It has been stated that occupation-related injuries affect victims, their families, employers, and the whole society due to their occupational consequences (2), and it has been stated that a total of 374 million non-fatal occupational accidents occur worldwide every year, and this situation creates a significant economic impact (2,3).

Occupation-related accidents often result in serious injuries that require immediate medical attention, thus creating a significant additional burden on hospital emergency departments. Additionally, emergency departments serve as the first point of care for 78% of occupation-related injuries. This makes them important

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

both for emergency medical intervention and subsequent criminal investigation, while also being crucial for effective analysis of workplace accidents and hospital admissions, understanding underlying risk factors, and identifying occupational injury patterns that can inform workplace safety policies to develop effective occupational accident prevention strategies. The first steps to be taken to prevent occupational accidents are to measure the risk of death and injury by correctly identifying high-risk groups, to define whether there is a type of occupational accident frequently seen in certain sectors, and to define what types of injuries occur in a certain period and sector types (4,5).

Occupational accidents constitute a significant portion of forensic reports kept in emergency services due to reasons such as not giving enough importance to workplace safety, not taking the necessary precautions insufficiently or not paying any attention, expecting employees to work much more in less time for better results, personal inadequacies, incorrect behaviors, technical malfunctions (6,7). Injuries and deaths resulting from occupational accidents constitute an important part of forensic medicine practices, and since employees and employers have mutual responsibilities, any accident that occurs must be evaluated very carefully to see if it meets the definition of an occupational accident (7,8).

This study describes the injuries that occur after occupation-related accidents treated at Harran University Hospital and provides information about age, gender, date of occupational accident, sector of occupational accident, type of occupational accident, localization of wound, presence of brain/ internal organ lesion, type of wound and discharge status, where work-related injuries are most common and aims to improve our knowledge. The results of our study will be able to contribute to the literature on this subject.

Material and Methods

Patient data, including age, gender, date of work accident, sector of work accident, type of work accident, localization of wound, presence of brain/ internal organ lesion, type of wound, and discharge status, were obtained from Sanliurfa Harran University Hospital Information Management System (FONET). Hospital records for 10 years between 2014-2023 were retrospectively reviewed and work accident cases were identified and included in the study. Records with missing data and cases not meeting the definition of a work accident were removed.

Work accident sectors were classified as manufacturing sector, construction sector, transportation sector, service sector, other sectors, and cases where the sector was not defined in the medical document.

According to the location of the injury in the body during the work accident, it was classified as head trauma, face and neck trauma, eye injury, ear injury, upper extremity trauma, chest trauma, abdomen and pelvis trauma, lower extremity trauma, and spine trauma.

Ethical Approval

This retrospective study was carried out with the permission of the Clinical Research Ethics Committee of Harran University Rectorate (Decision number: E-76244175-050.04-371324, dated: September 9th, 2024).

Statistical analysis

Data were analyzed using SPSS for Windows version 21.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as mean and standard deviation (SD) values for continuous variables and as frequency (n) and percentage (%) for categorical variables. A Chi-squared test was used in the analysis of contingency tables when the sample size was > 5. A value of $p < 0.05$ was accepted as the level of statistical significance.

Results

In 10 years between 2014-2023, 127 patients were admitted to our hospital due to work accidents. Of the 127 patients, 118 (92.9%) were male, while nine (7.1%) were female. The mean age of men was 35.92±11.15 years and the mean age of women was 27.44±04.90 years (p=0.000). A significant difference was found in gender distribution, with the mean age of males being significantly higher than that of females. This demographic distribution shows that male employees are at higher risk for occupational accidents.

Of the patients admitted to the hospital as a result of an occupational accident, 57.5% (n=73) were between the ages of 18-35, 32.3% (n=41) were between the ages of 36-50, and 10.2% (n=13) were over the age of 50 (p=0.000). The mean age of all cases was 35.3 ±11.03, the youngest case was 18 years old, and the oldest case was 79 years old.

Cutters/crushing/cutting/penetration wounds were

the most common at 36.2% (n=46), followed by fractures at 27.8% (n=34), and Blunt traumatic injury (ecchymosis/bite wounds) at 26.0% (n = 33). Other types of injuries were significantly less frequent. Foreign bodies (eye/oral/anal/vaginal) were observed in 4.7% (n=6) of the cases, while undefined cases constituted 2.4% (n=3). Asphyxia findings and other injuries represented 1.6% (n=2) of cases each, while both burn and electrical burns/scalds and poisoning findings were the least common, occurring in 0.8% (n=1) of the cases (p=0,000). (Table 1).

Table 1. Types of Injuries, Occupational Accident Sector, and Body Localization after Occupational Accidents.

Type of Injuries	**Total n**	**Total %**	**P-value P=0.000**
Blunt traumatic injuries/ ecchymosis/aggravati-ons/bite wounds	33	26.0	
Fractures	34	27.8	
Cutters/cutters/crushing/ cutting/penetration wounds	46	36.2	
Burn and electrical bur-ns/scalds	1	0.8	
Foreign bodies (eye/ oral/anal/vaginal)	6	4.7	
Asphyctic findings	2	1.6	
Poisoning findings	1	0.8	
Other injuries	2	1.6	
Undefined	3	2.4	
Occupational Accident Sector	**Total n**	**Total %**	**P=0.000**
Construction sector	41	32.3	
Service sector	13	10.2	
Manufacturing sector	12	9.4	
Transportation sector	3	2.4	
Other sectors	18	14.2	
Undefined	40	31.5	
Body Localization	**Total n**	**Total %**	**P=0.000**
Upper Limb Trauma	52	40.9	
Head Trauma	19	15	
Face And Neck Trauma	9	7.1	
Lower Limb Trauma	13	10.2	
Ear Injury	4	3.1	
Eye Injury	10	7.9	
Chest Trauma	7	5.5	
Spine Trauma	7	5.5	
Abdominal/Pelvic trauma	6	4.7	

When the occupational accident sectors were evaluated, it was revealed that the construction sector constituted the largest proportion of cases, accounting for 32.3% (n=41) of the total. Other sectors represented the second most frequent category with 14.2% (n=18), followed by the service sector with 10.2% (n=13). The manufacturing sector constituted 9.4% (n=12) of the cases, while the transportation sector constituted the smallest proportion with 2.4% (n=3) (p=0,000) (Table 1). In our study, a significant relationship was found between the sectors and types of injuries (p=0,000).
In other sectors, the vast majority of them were animal (horse and cow) attacks. This situation is because the university hospital is located far from the city and there is a horse racing center and a private integrated cattle and meat facility close to the hospital, resulting in a total of 10 occupational accident cases from these two facilities.

When the distribution of occupational accidents according to the injury site on the body was examined, it was determined that upper extremity trauma constituted 40.94% (n=52) of all cases, head trauma constituted 14.96% (n=19), lower extremity trauma constituted 10.24% (n=13), eye injuries constituted 7.87% (n=10), face/neck trauma constituted 7.09% (n=9), chest trauma constituted 5.51% (n=7), spine trauma constituted 5.51% (n=7), abdominal/pelvic trauma constituted 4.72% (n=6), and ear injuries constituted 3.15% (n=4) (p=0,000). (Table 1).

In our study, three of seven cases had brain lesions, three had thoracal lesions, two had abdominal lesions, and no brain or internal organ lesions were detected in a total of 120 cases.

When the discharge status of the cases was examined according to the nature of the injury, 72.4% (n=92) of them were discharged after recovery and 27.6% (n=35) had an injury that could cause disability, such as a bone fracture (p=0.000).

Discussion

Recognizing the mechanism and regional characteristics of occupational accidents plays an important role in the prevention, medical management, and forensic evaluation of these injuries.

It has been stated that occupational accidents occur at a higher rate in men (98%) because they are employed in labor-intensive and high-risk sectors such as construction and manufacturing (3). Similarly, in South India, men were the most exposed to occupational accidents (86%) (9). It has been stated that the majority of the victims injured due to

occupational accidents in Turkey (73.10-97.50%) are men, and this situation is related to men being more involved in work and working in heavier jobs (10). Almeida et al. reported that the majority of victims are men (88.3%) (2). In our study, in line with the literature, 92.9% of occupational accidents occurred in men and the difference found was statistically significant.

It was reported that occupational accidents were most common in the 30-39 age group (42.5%) and in the construction sector (56.4%) (3). Sayhan et al. reported that the highest rate of injuries occurred in the 18-29 age group (75.7%) and in the construction sector (40.2%) (11). Some studies have indicated that occupational accidents occur most frequently in the machinery-automobile sector (22%) (12), the service sector (44%) (13) and the food sector (34.90%) (10). Almeida et al. reported that 62.1% of occupational accidents occur in the 25-45 age group (2). In the current study, it was determined that 57.5% of occupational accidents occurred in the 18-35 age group and most frequently in the construction sector (32.3%). The sectoral differences detected in the studies are due to the differences in the provinces where the studies were conducted, the distribution of the branches of work within the province, and the location of the hospital within the province. Our study and the literature show that workplace accidents mostly affect the young age group, that is, people in their most productive years. Therefore, it is necessary to give extra importance to preventing occupational accidents.

In a study conducted in Portugal by Almeida et al., it was stated that the most common main injury types among occupational accidents were falls from heights and traffic accidents (2). In a study conducted by Win et al. in Brunei, it was reported that the most common causes of occupational accidents were hitting objects/encountering falling objects (37.7%) and falling from heights (25%) (3). In Turkey, people are often exposed to sharp/needle injuries in workplaces (11,13,14). In some studies, it was reported that blunt object injuries (30.90%) and cutting tool injuries (15.60%) were detected (10). Sharp/needle injuries, which are reported to be the most common injury mechanism in Turkey in the literature, were also found to be the most common injury mechanism in our study and were seen in 36.2% of all cases.

In our study, it was determined that people are generally exposed to sharp/needle injuries in the construction sector frequently and that there is a significant difference between the sector and the type of injury. This situation shows that there is a need for advanced protective equipment and additional safety protocols specific to the sector, especially in high-risk activities such as the construction sector, which includes machinery and construction tools.

In a study conducted by Win et al., it was reported that upper extremity traumas were the most common, at a rate of 43.9% (3). In a study conducted by Hösükler et al., the most common was reported in the upper extremity at a rate of 54.9% (10). It has been reported in the literature that occupational accidents are most frequently seen in the upper extremities (3,10), and in our study, consistent with the literature, 40.94% of the cases had occupational accidents as a result of upper extremity trauma.

In a study conducted by Almeida et al. in Portugal, It was stated that among the permanent occupational damage parameters determined by the labor court, Permanent Absolute Disability for Any Work was seen at a rate of 35% (2). In the first and third months after the occupational accident, 21.6% and 61.2% of the patients returned to work, respectively, in other words, 38.8% of the participants stated that they could not return to work, mainly because they felt partial recovery (63.8%), took sick leave (25.7%) or lost their job (8.6%) (15). In our study, it was seen that 72.4% (n: 92) recovered and were discharged, while 27.6% (n: 35) had an injury that could cause disability, such as a bone fracture. This result reveals that one in every three to four people suffers a disability-causing injury after an accident at a workplace and that these work accidents can have permanent effects on the lives and productivity of employees due to their serious nature.

Study limitations

The biggest limitation of our study is the limited number of occupational accident cases. Secondly, our current study was retrospective and we could not extract more descriptive data. Finally, this study was conducted in a single tertiary hospital in the southeastern part of Turkey (18 km from the city center and residential areas) and large multicenter series are needed for useful results that broadly reflect national data.

Conclusion

Our study emphasizes the importance of understanding injury patterns to improve workplace safety.

In our study, it was determined that occupational

accidents occur most frequently in the construction sector (32.3%), cutting/crushing/piercing injuries (36.2%) are the most common type of occupational accident injury, and upper extremity traumas (40.9%) stand out as the most common body part. In light of the data, it is thought that work safety measures should be changed especially in the construction sector and protective measures for upper extremity injuries should be increased. Considering the regional and provincial differences in occupational accidents in our country, there is a need for multi-centered and larger dataset studies that include detailed statistical data on occupational accidents, sectors, and types of injuries. In this way, after determining the dimensions of the problem, it will be possible to obtain data that will contribute to the studies to be carried out to prevent accidents and reduce accident rates with measures to be taken in workplaces.

Conflict of Interest

The authors declared that they had no conflict of interest during the preparation and publication of this article.

Funding

The authors declared that they did not receive any financial support during the research and writing process of this article.

References

1.Occupational Health and Safety Law No. 28339, Official Gazette, 30/6/2012. Accessed 1 December 2024. https://www.mevzuat.gov.tr/MevzuatMetin/1.5.6331.pdf

2.Almeida I, Teixeira JM, Magalhães T. The impact of major occupational injuries on professional reintegration. A Portuguese medico-legal contribution. J Forensic Leg Med. 2022; 90:102391.

3.Win KN, Trivedi A, Lai A, Hasylin H, Abdul-Mumin K. Non-fatal occupational accidents in Brunei Darussalam. Ind Health. 2021; 17;59(3):193-200.

4.Zakeri H, Jahed Taherani H, Afshari Saleh L. A survey on occupational injuries and related factors among emergency patients of Mashhad teaching hospitals over a year. J Inj Violence Res. 2024 May 11;16(1).

5.Demir U, Asirdizer M, Kartal E, Etli Y, Hekimoglu Y. An investigation of the effect of the COVID-19 (SARS-CoV-2) pandemic on occupational accidents (Tokat-Turkey). Arch Environ Occup Health. 2023;78(1):28-37.

6.Hakkoymaz H, Öztürk C, Okyay RA, Gedik MS, Kilci Aİ, Güler Ö, Yaman FN, Koşargelir M. Evaluation of Occupational Accidents in a Tertiary Emergency Department Introduction. Eurasian J Emerg Med. 2020;19(2):121-6

7.Bütün C, Beyaztaş F, Yaman S, Artar A, Öğüt O. Death due to Occupational Accident A Report of Two Cases. Bull Leg Med. 2015;20.116-119.

8.Asıldağ K, Akbaba M, Annaç M. Forensic medical evaluation of patients admitted to the emergency department due to occupational accidents. Eur J Ther. 2017; 23(2): 49-54.

9.Regina DL, Kanagalakshmi V, Alex RG. Profile, risk factors, and outcome of occupational injuries reported to the emergency department in a tertiary care hospital in South India. J Family Med Prim Care. 2020; 9:5684-8.

10.Hösükler E, Turan T, Erkol ZZ. Analysis of injuries and deaths by trauma scores due to occupational accidents. Ulus Travma Acil Cerrahi Derg. 2022; 28(9):1258-1269.

11.Sayhan MB, Sayhan ES, Yemenici S, Oguz S. Occupational injuries admitted to the emergency department. J Pak Med Assoc. 2013; 63(2):179-84.

12.Satar S, Kekec Z, Sebe A, Sari A. Analysis of occupational ınjuries admitted To Cukurova University, School of Medicine Department of Emergency. Cukurova Med J. 2004; 29:118-27.

13.Erdemli H, Kavalci C, Erdemli DS, Kocalar UG. Analysis of work-related injuries admitted patient to the emergency department. J Surg Arts. 2017; 2:26-33.

14.Celik K, Yilmaz F, Kavalci C, Ozlem M, Demir A, Durdu T, Sonmez BM, Yilmaz MS, Karakilic ME, Arslan ED, Yel C. Occupational injury patterns of Turkey. World J Emerg Surg. 2013; 28;8(1):57.

15.Abedzadeh-Kalahroudi M, Razi E, Sehat M, Asadi-Lari M. Return to work after trauma: A survival analysis. Chin J Traumatol. 2017;20(2):67-74.

Received: 09 Oct 2024 | **Accepted:** 17 Jan 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 268-274
DOI: 10.54005/geneltip.1563740

ORIGINAL ARTICLE

Women's Experiences of Vaginal Birth: A Qualitative Study

Kadınların Vajinal Doğum Deneyimleri: Nitel Bir Çalışma

[1]Havva Yeşildere Sağlam, [2]Atike Kaya, [3]Elif Gürsoy

[1]Kütahya Health Sciences University, Faculty of Health Sciences, Department of Nursing, Kütahya, Türkiye
[2]Eskisehir Osmangazi University, Health Sciences Institute, Department of Nursing, Eskisehir, Türkiye
[3]Eskisehir Osmangazi University, Faculty of Health Sciences, Department of Nursing, Eskisehir, Türkiye

Correspondence

Atike KAYA
Eskisehir Osmangazi University, Health Sciences Institute, Department of Nursing, Eskisehir, Türkiye

E-Mail: atike20102011@gmail.com

How to cite ?

Yeşildere Sağlam H, Kaya A, Gürsoy E. Women's experiences of vaginal birth: A qualitative Study. Genel Tip Derg. 2025;35 (2): 268-274

ABSTRACT

Aim: Women gain important experiences during the birth process that they will remember throughout their lives. This study aims to examine women's traumatic birth experiences.
Methods: A qualitative descriptive approach was used in this study. Data were collected using a Personal Information Form and a Semi-structured Interview Form. Interviews continued until data saturation was reached and the study was completed with 16 women. The thematic analysis method was used in data analysis.
Results: Women's experiences were analyzed under four main themes: situations that leave a mark, physical environment, obstetric violence and expectations.
Conclusion: It was determined that women had traumatic experiences related to the birth process. It was determined that women experienced complex emotions during the birth process and were exposed to obstetric violence. Women characterized birth as salvation and beginning. For women to have a positive birth experience, their care should be planned in a respectful, supportive, and holistic manner and their decisions should be respected.

Keywords: vaginal birth, birth experience, qualitative research

ÖZ

Amaç: Kadınlar doğum sürecinde yaşam boyunca hatırlayacakları önemli deneyimler kazanırlar. Bu çalışmanın amacı kadınların travmatik doğum deneyimlerini incelemektir.
Yöntem: Bu çalışmada nitel tanımlayıcı bir yaklaşım kullanıldı. Veriler; Kişisel Bilgi Formu ve Yarı Yapılandırılmış Görüşme Formu kullanılarak toplandı. Görüşmeler veri doygunluğuna ulaşılana kadar devam etti ve çalışma 16 kadınla tamamlandı. Veri analizinde tematik analiz yöntemi kullanıldı.
Bulgular: Kadınların deneyimleri dört ana tema altında analiz edildi. Bu temalar; iz bırakan durumlar, fiziksel çevre, obstetrik şiddet ve beklentilerdi.
Sonuç: Kadınların doğum süreciyle ilgili travmatik deneyimler yaşadıkları belirlendi. Kadınların doğum süreci boyunca karmaşık duygular yaşadıkları ve obstetrik şiddete maruz kaldıkları belirlendi. Kadınlar doğumu kurtuluş ve başlangıç olarak nitelendirdiler. Kadınların olumlu bir doğum deneyimi yaşamaları için bakımlarının saygılı, destekleyici ve bütüncül bir şekilde planlanması ve kadınların kararlarına saygı gösterilmesi gerekir.

Anahtar Kelimeler: vajinal doğum, doğum deneyimi, nitel araştırma

Introduction

Women gain important experiences during the birth process that they will remember for the rest of their lives (1, 2). Birth experiences are women's personal feelings and interpretations of the birth process (3). Every woman dreams of having a positive birth experience in birth at the end of pregnancy (4). However, women's experiences and expectations of childbirth inherently involve negative emotions as well as positive emotions, including joys and beliefs as well as worries and fears (5). Women's negative birth experiences, negative attitudes, and expectations towards childbirth affect their choice of birth method and increase cesarean section rates (6). In the literature, it is stated that negative birth experiences are associated with posttraumatic stress, fear of childbirth, negative effects on the baby, breastfeeding problems, inability to accept the maternal role, and emotional disorders in women. On the other hand, it is stated that mothers with positive experiences increase their self-confidence with a sense of success, adapt better to motherhood and the bond between mother and baby is stronger (3, 7). Birth, which is a meaningful event for the pregnant woman and her family, is usually embedded in a woman's memory and remembered in detail. Women's birth experiences are shared and spread among women through intergenerational transmission and can affect the perception and experiences of birth in society. Therefore, understanding women's birth experiences and their meanings is crucial in providing individualized and culturally sensitive care during and after birth. Considering that women's experiences in all societies will be influenced by cultural, economic, and

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

social factors, this study focuses on the experiences of women. In this context, the study was conducted to determine women's traumatic experiences of vaginal birth.

Materials And Methods

Study design and Participants

In this study, a qualitative descriptive approach based on in-depth interviews was used to obtain rich data on women's experiences. Women's experiences were explored through individual, semi-structured interviews. The study process followed the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist (8).

The purposive sampling method was used to determine the research group. Criterion sampling sampling method among purposive sampling methods was used to determine the participants of this study. The study sample consisted of women giving birth vaginally living in Central Anatolia Region in Turkey. The study sample consisted of 16 women. Inclusion criteria were; 1) having a vaginal birth; 2) volunteering to participate in the study; 3) being 18 years of age or older, and 4) not having a history of risky pregnancy. In qualitative research, it is not possible to determine the sample size before the research, and the sample size can be determined according to data saturation (9). In this study, it was determined that the data was repeated after the interview with the 12th woman, and the data collection process was terminated for the 16th woman.

Data collection

Data were collected between April 2023 and September 2023 using a personal information form and a semi-structured interview form. The personal information form included questions about women's sociodemographic and obstetric characteristics. The semi-structured interview form consisted of five questions about the participants' birth experiences (Table 1). The first two authors contacted the participants, invited them to the study, and scheduled the appointments. Interviews were conducted by two researchers in a quiet and safe environment. While one of the researchers continued the interview, the other researcher made observations and took notes. The in-depth face-to-face interviews with the participants lasted approximately 35-60 minutes. Data were collected using a voice recorder. Three pilot interviews were conducted to test the interview questions. No changes were made to the interview questions in the pilot study.

Table 1. Research questions

Research questions
•Can tell us about your birth story? •Can you share your experiences about your most recent birth? •Please share with us what you felt during the birth process. •Did you receive any support during your birth process? Can you tell us about the support you received during this process? •Based on your experiences during your birth process, what are your expectations in this process?

Data analysis

The thematic analysis method was used to analyze the qualitative data obtained from the research. Participants were given code names such as P1, P2, etc. to protect the confidentiality of their identity information. A separate Word document was created for each participant. Braun & Clark's (10) six-stage method was used to manually analyze the data. In the first stage of data analysis, the statements were read several times to obtain information about women's experiences during the birth process. Initial codes were given to the data independently by the researchers. The coding made by the research team was discussed and a consensus was reached. Then, the codes were analyzed and main themes and sub-themes were formed. The themes were examined according to the codes and participants' statements, and the comprehensibility of the themes was evaluated. The authors reached a consensus on the themes. The themes were then named and participants' experiences and perceptions were reported.

Rigour and trustworthiness

To ensure scientific and methodological rigor, Lincoln and Guba's recommendation (Credibility, Consistency, Conformability, and Transferability) was applied (11). For reliability, the data collection process was recorded with a voice recorder and transcribed verbatim. The data were analyzed independently by three researchers and a consensus was reached on themes/subthemes. The relationships between themes and sub-themes were checked for integrity. In addition to interviews, different data collection methods such as observations and note-taking were used to ensure consistency and data triangulation. For consistency, the research process and the analysis process were reviewed by the research team. For verifiability, all stages of the study were accurately recorded and presented. Participant statements were included in the results. For transferability, the explanation of the methodology of the study was given in detail.

Ethical statement

Ethics committee permission was obtained from the ethics committee of a university (E-25403353-050.99-313327). The study was conducted under the principles of the Declaration of Helsinki. Participants were informed about the purpose of the study and how it would be conducted and informed written consent for participation in the study and permission to record the interviews were obtained.

Results

The ages of the participants ranged between 24 and 65. The majority of the participants are university graduates and have nuclear families. The educational level of the participants varied between primary school, high school, and university (Table 2).

Table 2. Socio-demographic characteristics of the participants

Number of Partici-pants	Age (years)	Educational level	Employment Status	Gravida	Parity
P1	29	High school	Housewife	2	2
P2	42	High school	Employee	1	1
P3	33	High school	Employee	3	2
P4	65	Primary school	Housewife	5	5
P5	30	University	Employee	2	2
P6	50	University	Teacher	2	2
P7	44	University	Teacher	2	1
P8	54	University	Housewife	2	2
P9	32	University	Teacher	3	2
P10	40	University	Teacher	2	2
P11	35	University	Teacher	1	1
P12	60	Primary school	Housewife	2	2
P13	55	High school	Employee	4	4
P14	46	Primary school	Housewife	5	3
P15	25	University	Nurse	1	1
P16	24	University	Nurse	1	1

P: Participants

The findings of the research were collected under four main themes and 11 sub-themes (Table 3).

Table 3. Themes and sub-themes

Themes	Sub-themes
Situations leaving a mark	Salvation and beginning Social support Coping with pain
	Fear
Physical Environment	Violation of privacy Traumatic obstetric table
Obstetric Violence	Maltreatment Care without consent Restriction of movement
Expectations	Humanistic care Support from healthcare professionals

Situations leaving a mark

Women can recall and describe their birth-related memories in long-term detail. This theme was analyzed under four themes: "Salvation and beginning", "Social support", "Coping with pain" and "Fear".

Salvation and beginning

Women stated that they see the act of giving birth as a liberation-ending and that birth is a new beginning for the transition to motherhood. Women stated that they wanted to finish the birth as soon as possible, get rid of the baby, which was a part of their body, and hold their baby in their arms in a healthy way.

"I saw the birth as salvation, I wanted it to end as soon as possible, I wanted to go home. Alhamdulillah, my daughter and I survived safely. People are happy to be saved, and to hold their baby in good health. It is as if you forget what you went through in an instant..." (P1)

Social support

Women expressed social support in this process in different dimensions as support from family, spouse, and health personnel. They frequently emphasized that they wanted their husbands and mothers to be with them and that the support of health personnel was necessary.

"You're kind of in a life-and-death situation. You are in an unfamiliar environment with people you don't know. When I was in pain, I wish there was someone there to support me, to hold my hand, to tell me that I can do it, that I can succeed, to tell me to hold on, to support me..."(P1)

Coping with pain

Some of the women stated that they experienced uncontrollable severe pain during the birth process and some of them stated that they could endure this pain during this process. While individuals used various methods for coping, some individuals stated that they were relieved by the support and practices of health personnel.

"My midwife was with me. As the pain came, she opened her legs and told me to squat. She was patting my back and massaging my waist. Because the pain was coming from my back. I was relaxing..." (P6)

Fear

Women stated that they did not know what the process would be like and what they would encounter during

the birth process. They stated that they experienced feelings such as fear of something happening to their baby and fear of losing their own life.

"When birth begins, I thought I wouldn't be able to leave the delivery room. I had the fear that I would die. At that moment you think about nothing but death and if you left a child behind you always think about the child… "(P2)

Physical environment

Under the physical environment theme, two sub-themes were examined: "Violation of privacy" and "Traumatic obstetric table".

Violation of privacy

The fact that the delivery rooms were not single rooms and were separated only by a screen caused women's lack of privacy. Women could not protect their privacy physically and also witnessed the birth of other pregnant women. They described this situation as a negative experience.

"At the hospital, different people come every time and do vaginal examinations. They never ask for permission. I felt so bad... The rooms were not separate, I stayed in the same room with different pregnant women. There were other patients in the room, two or three beds were in one room. There was only a curtain between us. It was as if privacy was not important at all..." (P9)

Traumatic obstetric table

Women stated that when they think of the birth environment, the most memorable thing is the obstetric table. They reported feeling uncomfortable and unwell during their stay on the obstetric table. Being naked in the lithotomy position in a crowded environment with no attention to privacy was very uncomfortable for women.

"I don't remember much of the surroundings. The obstetric table in the delivery room already scares me. I only remember the obstetric table, I was wearing only a gown. I had no clothes underneath, I was left naked. I had my feet up. I stayed like that for a long time..." (P8)

Obstetric violence

This theme was analyzed under three themes: "Maltreatment", "Care without consent" and "Restriction of movement".

Maltreatment

Some of the women stated that the healthcare workers did not communicate with them sufficiently, did not behave tolerantly, did not consider their requests, and that they were neglected. They even stated that they were insulted, yelled at, scolded, and physically intervened when they did not do what the health personnel wanted.

"I couldn't push, I couldn't do it. This time they said the baby's heartbeat was slow. I was panicking. The medical staff kept pressing her elbows on me. She shouts, pushes, yells at you to push, and pinches you on top of that..." (P3)

Care without consent

Women stated that midwives, nurses, and physicians did not obtain their consent in any way during vaginal examinations, episiotomy, or induction practices, and even when they asked questions about the practice, they did not receive an answer.

"Midwives were coming and going in the room. They were constantly checking the opening with vaginal examination. A lot of vaginal examinations were done without my consent. None of them asked or asked permission." (P15)

The women said that the information they were given was misleading and that they felt unsafe in their environment and were unaware of what to expect.

"They put in intravenous serum to make the birth easier. If I had known it was oxytocin, I wouldn't have had it installed. While examining him, he burst the sac. I couldn't understand what was happening, she didn't say anything, it just happened..." (P7)

Restriction of movement

Some of the women stated that they could not move as they wanted during the birth process and that they had to lie down and were constantly connected to the non-stress test (NST) device. This situation disturbed them and caused them to have a negative experience.

"They gave oxytocin intravenously and put me to bed. They connected me to NST. I never moved until the birth took place. I never got out of bed. They did not allow me to walk. Maybe if they had let me walk, the pain would have eased and I could have had a comfortable birth. Even walking around would have been a great luxury for me there." (P4)

Expectations

The theme of expectations was analyzed in two sub-themes: "Humanistic care" and "Support from healthcare professionals".

Humanistic care

During the birth process, women expressed that they wanted to be shown a smile, that communication was important, and that they wanted to be treated humanly. They stated that even a kind word and attention make people happy and affect their psychology positively.

"A little attention can put a smile on people's faces. It can accelerate their struggle with life. But with a small negative word, women completely collapse emotionally." (P1)

Support from healthcare professionals

The presence and support of the health care team during labor was stated as an important factor that made women feel safe. Women stated that neither physician, nurse nor midwife support alone was sufficient and that a team approach was necessary.

"Thanks to the positive approach of the staff in the delivery room, I did not feel anything like anxiety or fear. I completely left myself to them. If I get pregnant again, I would like to have a vaginal birth with the same team." (P7)

"The midwife told me what to do. She taught me how to breathe deeply. She also gave me information about pushing. I did what she said and it was not much of a problem. It hurt like this, but the process went well and the information she gave was sufficient for me." (P16)

Discussion

This study aimed to examine the birth experiences of women during vaginal birth. Women's experiences were examined under four main themes: situations leaving a mark, physical environment, obstetric violence and expectations. While birth is experienced positively for some women, it may cause negative experiences for others (4, 5). The pain experienced by women during labor and their coping with this pain also has an important place in their minds. In studies conducted in the literature, labor pain has been described as an experience that affects the birth process and leaves a mark (1, 3, 12, 13). In this study, women stated that although they experienced severe pain and there were challenging factors, all the negativities were forgotten when they had their babies as soon as the birth occurred. During this period, women saw birth as a salvation because they were afraid that something would happen to them, and they stated that they had a new beginning when they held their babies in their arms. Similarly, this situation is among the vaginal birth experiences of women in other studies (2, 4). In this study, it was observed that women's social support had an especially important place in their memories. Support given during times of stress has positive effects on women giving birth (14). It is stated in the literature that adequate social support is important for mothers to have positive experiences, makes mothers feel safe, and gives courage and hope (2-4, 15, 16). Women's birth experiences are extremely important because they leave positive or negative traces in their memories. For this reason, it would be beneficial to alleviate women's fears about childbirth and provide adequate support during this process. While the birth was the happiest moment because it was the beginning of motherhood, on the other hand, the fear that something would happen to both the baby and herself caused emotional turmoil during this process. Similarly, in a meta-synthesis study examining women's vaginal birth experiences, women expressed their fear of harming themselves or their babies (12).

When a safe birth environment is provided for women, the birth process proceeds normally and a positive experience is experienced (17). In our study, the physical environment appears as an important factor that is remembered. Women stated that they were uncomfortable because they stayed in an unwanted position on the obstetric table for a long time, and that their privacy was not ensured sufficiently during the labor and birth process. Abuya et al. (18) study, women stated that their privacy was not ensured during the birth process. In the literature, the design of birth environments that meet the needs of women will be extremely important (17, 19, 20) due to the direct impact of the characteristics of the birth environment on birth physiology and women's experiences.

Obstetric violence, this invisible form of violence, is a complex problem that negatively affects women during the birth process (21). Violence during birth can occur in many ways, including mistreatment, medicalization of birth, and poor communication. Each of these can affect women's experiences during birth (22). Martínez-Galiano et al. (23) state in their study that more than two-thirds of women are exposed to any type of obstetric violence. It is a remarkable finding that experiences of obstetric violence were

expressed by a large number of women in our study. Women stated that they encountered ill-treatment during the birth process, that they were not given adequate information, and that some interventions were performed without their consent. Women stated that they were scolded, insulted, and even physically intervened (fundal pressure). Additionally, women stated that the procedure was started directly without informing them or obtaining their consent. Studies in the literature indicate that women are not adequately informed about care, treatment and practices and their consent is not obtained (24, 25). Similarly, in the study of Annborn et al. (21), women stated that they were given incomplete or no information during the birth process and that they were ignored. Meyer et al. (26) study states that the two most common types of maltreatment are ineffective communication and lack of informed consent. It is stated in the literature that women experience many events during the birth process, such as hitting, using force, applying fundal pressure, frequent vaginal examination, routine episiotomy, cesarean section, and oxytocin application (23, 24, 27, 28). Obstetric violence is experienced by many women, and these experiences have the potential to remain in their memories and affect their later lives (21, 22). While women's experiences with the care and support they receive from healthcare workers in health facilities may be positive for some mothers, they may be negative for others (3). In our study, women expressed that they wanted to receive humane care and that the approach of the medical staff was important in this process. Additionally, women expressed the need for nurses, midwives, and physicians to continue their care with a team approach. Namujji et al. (3) stated in their study that women receiving attention, good care, and support went through the birth process more comfortably and safely and were satisfied. Good communication is one of the most important prerequisites for good and safe care (21). When healthcare professionals encourage women to take an active role in their health and well-being, women feel part of the process. Health professionals communicating effectively with women, approaching them with respect and empathy, and providing care and support by considering women's rights with a humane approach during the action process will be very effective in improving the birth experience that will not be erased from women's memories.

Limitations

Due to the nature of the qualitative research method, the data obtained are specific to the participants. The data is limited to the region where the research was conducted and includes the experiences of 16 participants. For this reason, the results of the study cannot be generalized to all women. The reliability of the data is limited to the accuracy of the information provided by the participants during the interview. In addition, the lack of a limitation on the time elapsed since vaginal birth in the study may have caused recall bias.

Conclusion

Women's experiences were examined under four main themes: situations leaving a mark, physical environment, obstetric violence and expectations. It was determined that women experienced complex emotions during the birth process and were exposed to obstetric violence. As a result of the study, for women to have a positive birth experience, their care should be planned in a respectful, supportive, and holistic manner, and their decisions should be respected. Women's care should be continued, taking into account their need for information and the need to obtain their consent. During the birth process, health professionals should provide care and support to women by taking into account not only the physiological dimension but also the psychological and social dimensions.

Acknowledgments

We would like to thank all the participants in our study for spending the time sharing their experiences.

Conflict of Interest

The authors report no actual or potential conflicts of interest.

Funding

No institutions or organizations supported and financed the study.

References

1.Dahlberg U, Persen J, Skogås A-K, Selboe S-T, Torvik HM, Aune I. How can midwives promote a normal birth and a positive birth experience? The experience of first-time Norwegian mothers. Sex Reprod Healthc. 2016;7:2-7.

2.Hosseini Tabaghdehi M, Keramat A, Kolahdozan S, Shah Hosseini Z, Moosazadeh M, Motaghi Z. Positive childbirth experience: A qualitative study. Nurs Open. 2020;7(4):1233-8.

3.Namujju J, Muhindo R, Mselle LT, Waiswa P, Nankumbi J, Muwanguzi P. Childbirth experiences and their derived

meaning: a qualitative study among postnatal mothers in Mbale regional referral hospital, Uganda. Reprod Health. 2018;15:1-11.

4.Çetin Avcı S, Işık G, Çetişli Egelioğlu N. Doğum Korkusu Yaşayan Annelerin Doğum Deneyimleri: Fenomenolojik Bir Çalışma. Journal of Nursology. 2023;26(1):34-42.

5.Aktaş Reyhan F, Dağlı E. Doğum Anılarının Üç Kuşak-Kuşaklararası Aktarımı ve Üçüncü Kuşaktaki Doğum Algısına Etkisi. Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi. 2022;11(3):1143-50.

6.Bal MD, Yılmaz S, Beji NK. Kadınların sezaryen doğum tercihleri. Florence Nightingale Hemşirelik Dergisi. 2013;21(2):139-46.

7.Yanıkkerem E, Göker A, Piro N. Sezaryen doğum yapan kadınların doğum yöntemleri hakkında düşünceleri ve aldıkları bakım memnuniyeti. Selçuk Tıp Dergisi. 2013;29(2):75-81.

8.Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. International journal for quality in health care. 2007;19(6):349-57.

9.Yıldırım A, Şimşek H. Sosyal bilimlerde nitel araştırma yöntemleri: Seçkin yayıncılık; 2013.

10.Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3(2):77-101.

11.Schwandt TA, Lincoln YS, Guba EG. Judging interpretations: But is it rigorous? Trustworthiness and authenticity in naturalistic evaluation. New Dir Eval.2007;2007(114):11-25.

12.Wigert H, Nilsson C, Dencker A, Begley C, Jangsten E, Sparud-Lundin C, et al. Women's experiences of fear of childbirth: a meta-synthesis of qualitative studies. Int J Qual Stud Health Well-being. 2020;15(1):1704484.

13.Aktaş S, Aydın R. The analysis of negative birth experiences of mothers: a qualitative study. J Reprod Infant Psychol. 2019;37(2):176-92.

14.Mirghafourvand M, Meedya S, Mohammadi E, Mohammad-Alizadeh-Charandabi S, Jafarabadi MA, Ghanbari-Homaie S. Iranian women's perception on the determinants of birth experience: a qualitative study. BMC Pregnancy Childbirth. 2022;22(1):751.

15.Deliktaş Demirci A, Kabukcuglu K, Haugan G, Aune I. "I want a birth without interventions": Women's childbirth experiences from Turkey. Women Birth. 2019;32(6):e515-e22.

16.Parry DC. "We wanted a birth experience, not a medical experience": exploring Canadian women's use of midwifery. Health Care Women Int.2008;29(8-9):784-806.

17.Aune I, Torvik HM, Selboe S-T, Skogås A-K, Persen J, Dahlberg U. Promoting a normal birth and a positive birth experience—Norwegian women s perspectives. Midwifery. 2015;31(7):721-7.

18.Abuya T, Sripad P, Ritter J, Ndwiga C, Warren CE. Measuring mistreatment of women throughout the birthing process: implications for quality of care assessments. Reprod Health Matters. 2018;26(53):48-61.

19.Aktas Reyhan FA, Sayiner FD, Ozen H. A mixed-design study on the development of birth unit assessment scale. Midwifery. 2023;123:103708.

20.Foureur M, Davis D, Fenwick J, Leap N, Iedema R, Forbes I, et al. The relationship between birth unit design and safe, satisfying birth: Developing a hypothetical model. Midwifery. 2010;26(5):520-5.

21.Annborn A, Finnbogadóttir HR. Obstetric violence a qualitative interview study. Midwifery. 2022;105:103212.

22.Schoene BE, Oblasser C, Stoll K, Gross MM. Midwifery students witnessing violence during labor and birth and their attitudes towards supporting normal labor: a cross-sectional survey. Midwifery. 2023;119:103626.

23.Martínez-Galiano JM, Martinez-Vazquez S, Rodríguez-Almagro J, Hernández-Martinez A. The magnitude of the problem of obstetric violence and its associated factors: A cross-sectional study. WomenBirth. 2021;34(5):e526-e36.

24.Meijer M, Brandão T, Cañadas S, Falcon K. Components of obstetric violence in health facilities in Quito, Ecuador: A descriptive study on information, accompaniment, and position during childbirth. Int J Gynaecol Obstet.. 2020;148(3):355-60.

25.Coates R, Cupples G, Scamell A, McCourt C. Women's experiences of induction of labor: qualitative systematic review and thematic synthesis. Midwifery. 2019;69:17-28.

26.Meyer S, Cignacco E, Monteverde S, Trachsel M, Raio L, Oelhafen S. 'We felt like part of a production system': A qualitative study on women's experiences of mistreatment during childbirth in Switzerland. PloS one. 2022;17(2):e0264119.

27.Avcı N, Kaydırak MM. A qualitative study of women's experiences with obstetric violence during childbirth in Turkey. Midwifery. 2023;121:103658.

28.Bohren MA, Mehrtash H, Fawole B, Maung TM, Balde MD, Maya E, et al. How women are treated during facility-based childbirth in four countries: a cross-sectional study with labor observations and community-based surveys. The Lancet. 2019;394(10210):1750-63.

Received: 15 Nov 2024 | **Accepted:** 20 Jan 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 275-283
DOI: 10.54005/geneltip.1586166

ORIGINAL ARTICLE

Investigation of Causing Microorganisms and Antimicrobial Sensitivity Patterns in Diabetic Foot Wounds

Diyabetik Ayak Yaralarında Etken Mikroorganizmaların ve Antimikrobiyal Duyarlılık Paternlerinin Araştırılması

[1]Aynur Ismayıl, [2]Bayram Colak, [2]Serdar Yormaz, [1]Hatice Turk Dagi, [1]Salih Macin

[1]Department of Microbiology , Faculty of Medicine, Selcuk University, Konya, Türkiye
[2]Department of General Surgery, Faculty of Medicine, Bakırçay University, İzmir, Türkiye

Correspondence

Assoc. Prof. Dr. Salih Maçin
Selcuk University, Faculty of Medicine, Department of Microbiology, Konya, Türkiye

E-Mail: salihmacin@hotmail.com

How to cite ?

Ismayıl A, Colakc B, Yormaz S, Turk Dagi H, Macin S. Investigation of Causing Microorganisms and Antimicrobial Sensitivity Patterns in Diabetic Foot Wounds. 2025;35 (2): 275-283

ABSTRACT

Aim: Diabetic foot is the clinical term describing a series of diabetes-related lower extremity complications, such as ulceration, infection, and gangrene. This study aimed to prospectively investigate the causative aerobic bacteria in diabetic foot ulcer samples, as well as anaerobic bacteria and fungi, which are thought to play an important role in diabetic foot infections. Additionally, the antimicrobial susceptibility of the causative microorganisms obtained from the cultures will be investigated.
Methods: Fifty-nine samples were collected from 50 patients with type 2 diabetes mellitus (DM). The BD Phoenix TM automated system was used for species-level identification of microorganisms and antimicrobial susceptibility testing. The antimicrobial susceptibility of anaerobic microorganisms was tested using the gradient test method.
Results: Gram-negative aerobic bacteria were found to be the most common agents (65%) in diabetic foot infections, with 65% being multidrug-resistant. Staphylococcus aureus was identified as the most common cause of monomicrobial infections, with a methicillin-resistant rate (MRSA) of 27%. Vancomycin, teicoplanin, and linezolid were the most effective antibiotics against Gram-positive agents, while ceftolozane/tazobactam, piperacillin/tazobactam, meropenem, ertapenem, colistin, and amikacin were the most effective against Gram-negative agents.
Conclusions: The high prevalence of multidrug-resistant Gram-negative agents highlights the importance of prudent antibiotic use. Considering DM is 80% preventable through lifestyle changes, increasing public awareness about healthy living is crucial.

Keywords: Antibiotic susceptibility, diabetic foot, diabetic foot ulcer, microorganism

ÖZ

Amaç: Diyabetik ayak (DA), ülserasyon, enfeksiyon ve gangren gibi diyabete bağlı bir dizi alt ekstremite komplikasyonlarını tanımlayan klinik terimdir. Bu çalışmadaki amaç diyabetik ayak enfeksiyonu (DAE)'nda etken aerob, anaerop bakteriler ve mantarların prospektif olarak araştırılmasıdır. Aynı zamanda kültürlerden elde edilen etken mikroorganizmaların antimikrobiyal duyarlılıkları araştırılacaktır.
Gereç ve Yöntemler: Tip 2 diabetes mellitus'u olan 50 hastadan alınan 59 örnek çalışmaya dahil edilmiştir. Mikroorganizmaların tür düzeyinde tanımlanması ve antimikrobiyal duyarlılık testleri için BD Phoenix TM otomatize sistem kullanılmıştır. Anaerob mikroorganizmaların antimikrobiyal duyarlılığı gradyan E- test yöntemiyle test edilmiştir.
Bulgular: Çalışma sonucuna göre DAE'de en sık (%65) etken Gram-negatif aerob bakteriler olup, bunların büyük çoğunluğu (%65) çoklu ilaca dirençli olarak saptanmıştır. Monomikrobiyal enfeksiyon nedeni olarak en sık Staphylococcus aureus izole edilmiş ve MRSA oranı % 27 olarak bulunmuştur. Çalışmanın sonuçları Gram-pozitif etkenlere vankomisin, teikoplanin ve linezolidin en etkili antibiyotikler olduğunu göstermiştir. Gram-negatif etkenlere karşı en etkili antibiyotikler ise seftolozan/tazobaktam, piperasilin/tazobaktam, meropenem, ertapenem, kolistin ve amikasin olarak bulunmuştur.
Sonuçlar: Gram-negatif etkenlerin büyük çoğunluğunun çok ilaca dirençli olduğu dikkate alındığında akılcı antibiyotik kullanımının önemi bir kez daha ortaya çıkmaktadır. Diyabetin yaşam tarzı değişikliklerine bağlı %80 önlenebilir bir hastalık olduğu dikkate alınmalı ve sağlıklı hayat tarzı konusunda toplumsal bilinçlendirmenin önemi vurgulanmalıdır.

Anahtar Kelimeler: Antibiyotik duyarlılığı, diyabetik ayak, diyabetik ayak ülseri, mikroorganizma

Introduction

Diabetes mellitus (DM) is a widespread social disease that reduces individual quality of life and causes lifelong acute and chronic complications. It is reaching pandemic proportions, affecting people across various socioeconomic groups (1). Diabetic foot (DF) refers to a range of diabetes-related lower extremity complications, including ulceration, infection, and gangrene. It is the most common typical complication of DM after cardiovascular disease (2). Diabetic foot ulcers (DFUs) often result from poor glycemic control, neuropathy, peripheral vascular disease, or inadequate foot care. DFUs are one of the leading causes of foot osteomyelitis and lower extremity amputations (3).

The lifetime risk of DFUs ranges between 19% and 34%, with a reported amputation incidence of 20% and a 5-year mortality rate of 50-70%. Early detection and multidisciplinary care are critical for reducing associated morbidity (4). The financial burden of treating diabetic foot disease in the United States is substantial, costing an estimated $9 to $13 billion annually, in addition to

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

DM treatment costs (5).

Studies from 2010 to 2019 show that Staphylococcus aureus is the most frequently isolated Gram-positive agent in diabetic foot infections (DFIs), followed by Pseudomonas aeruginosa, the most common Gram-negative pathogen. Methicillin resistance rates of Staphylococcus aureus vary between 16% and 44%. The prevalence of monomicrobial infections has increased due to the widespread use of broad-spectrum antibiotics, which has also led to rising multidrug resistance patterns in Pseudomonas aeruginosa. A large analysis of patients in Turkey found high levels of drug resistance, including the production of extended-spectrum beta-lactamases (ESBLs), in 38% of E. coli and Klebsiella isolates (6).

In a study investigating DFI agents using a next-generation sequencing method, the most frequently detected anaerobes in new ulcers were Peptoniphilus, Anaerococcus, Finegoldia, Porphyromonas, and Prevotella and in recurrent ulcers, Finegoldia, Peptoniphilus, Anaerococcus, Porphyromonas, and Actinomyces were detected (7). The most frequently detected fungal pathogens in DFI are Candida parapsilosis, Candida albicans, Candida glabrata, and Candida tropicalis, respectively (8).

The causative aerobic bacteria in DFU samples, as well as anaerobic bacteria and fungi, which are thought to have an important place in DFI, were investigated prospectively. At the same time, to investigate the antimicrobial susceptibility of causative microorganisms obtained from DFU samples by culture method, to contribute to treatment, reducing patient care costs and preventing serious complications such as amputation.

Materials and Methods

Between March 1, 2022, and April 1, 2023, swab or tissue biopsy samples were collected from 50 patients diagnosed with type 2 DM, aged 18 years or older, with no history of pregnancy. These patients were admitted to Selçuk University Hospital for wound care or debridement. The type and antimicrobial susceptibility of the microorganisms were determined using automated methods. Debridement procedures were performed aseptically in an operating room environment, with tendon or deep tissue samples collected and sent to the microbiology laboratory in sterile, dry containers.

The samples were cultured using the following media:

Eosin Methylene Blue (EMB) agar (Oxoid, UK)

5% sheep blood agar (Biomerieux, France)

Chocolate agar (Biomerieux, France)

Sabouraud Dextrose Agar (SDA) (Oxoid, UK)

Schaedler agar (GBL, Turkey)

The inoculated plates were incubated at 36–37°C under aerobic and anaerobic conditions until visible growth occurred. Incubation periods were 24–48 hours for aerobic bacteria, 48–72 hours for anaerobic bacteria, and 24–96 hours for fungi.

Samples with any visible growth on at least one of the inoculated plates were considered culture-positive. Bacterial and fungal colonies were stained using the Gram staining method. Microorganism species identification and antibiotic susceptibility testing (AST) were performed using the BD Phoenix™ automated system. For AST, isolates from non-selective, antibiotic-free media were used, as selective media can inhibit certain bacteria types. The gradient test method was employed for anaerobic microorganisms to interpret minimum inhibitory concentration (MIC) values and classify them as susceptible, intermediately susceptible, or resistant (SIR).

Patients were evaluated after approval was obtained Ethics Committee of Selçuk University (Decision No: 2022/64, Date: 02/03/2022). The study was conducted under the principles of the Declaration of Helsinki.

Results

A total of 59 samples were collected from 50 patients with type 2 DM, with the majority being from male patients (62%). The ages of the patients ranged from 34 to 78 years, with a mean age of 58.5 years. The most common pathogens isolated from the samples were Gram-negative bacteria (65%), followed by Gram-positive bacteria (35%). Among the Gram-negative isolates, Pseudomonas aeruginosa was the most frequent pathogen (25%), followed by Escherichia coli (19%). Among the Gram-positive isolates, Staphylococcus aureus was the most prevalent (15%), with 27% of these isolates being methicillin-resistant (MRSA)

Growth was observed in 45 out of the 59 samples (76.3%). A total of 57 microorganisms were isolated, of which 52 were aerobic bacteria, three were yeasts, and two were anaerobic bacteria. The microorganism-to-sample ratio was 1.3. Polymicrobial growth was observed in nine patient samples (20.5%).

Yeast was present in three samples, and anaerobic microorganisms were found in 2 samples. The most frequently detected pathogens across all samples were Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa (Table 1).

When the isolated microorganisms were analyzed according to gender, differences were noted between male and female patients. In women, the most common pathogens were Klebsiella pneumoniae (20%), P. aeruginosa (20%), and Morganella morganii (13%). In contrast, among men, the most frequently isolated pathogens were S. aureus (27%), E. coli (22%), Proteus mirabilis (11%), and P. aeruginosa (11%).

A total of 15 Gram-positive microorganisms were isolated. Of these, 13 (87%) were detected as monomicrobial agents, while the remaining two isolates were found in conjunction with anaerobic or Gram-negative microorganisms. The number and percentage of each microorganism isolated from all samples are detailed in Table 1.

Table 1. Distribution of causative microorganisms

Microorganisms	Number	Percentage %
Gram-positive bacteria	**15**	**26.32**
Staphylococcus aureus	11	19.30
Enterococcus faecalis	3	5.26
Streptococcus pyogenes	1	1.75
Gram-negative bacteria	**37**	**64.91**
Escherichia coli	9	15.79
Pseudomonas aeruginosa	7	12.28
Proteus mirabilis	5	8.77
Enterobacter cloacae	3	5.26
Klebsiella pneumoniae	3	5.26
Morganella morganii	3	5.26
Acinetobacter baumannii	2	3.51
Serratia marcescens	2	3.51
Stenotrophomonas maltophilia	1	1.75
Klebsiella aerogenes	1	1.75
Klebsiella oxytoca	1	1.75
Anaerobic bacteria	**2**	**3.51**
Actinomyces spp.	1	1.75
Leptotrichia buccalis	1	1.75
Candida species	**3**	**5.26**
Candida tropicalis	2	1.75
Candida parapsilosis	1	3.51
TOTAL	**57**	**100**

Antibiotic Susceptibility Results of Microorganisms

Of the 11 Staphylococcus aureus isolates, 27% were identified as methicillin-resistant S. aureus (MRSA), while 73% were methicillin-sensitive S. aureus (MSSA). Ten (91%) of the S. aureus isolates grew as monomicrobial agents, while one isolate was found in combination with an anaerobic microorganism. All S. aureus isolates were resistant to penicillin but were sensitive to daptomycin, linezolid, vancomycin, and teicoplanin. Additionally, 66.7% of the isolates were susceptible to amikacin, trimethoprim/sulfamethoxazole, and quinolones. According to EUCAST guidelines, all S. aureus isolates were considered intermediately susceptible to levofloxacin and ciprofloxacin.

Enterococcus faecalis was isolated from three samples. Antimicrobial susceptibility testing (AST) results showed that all isolates were susceptible to vancomycin, teicoplanin, linezolid, ampicillin, and amoxicillin/clavulanic acid. Streptococcus pyogenes was isolated from one sample and was found to be resistant only to tetracycline, but sensitive to quinolones, penicillins, cephalosporins, daptomycin, erythromycin, linezolid, and teicoplanin. According to EUCAST guidelines, S. pyogenes was considered intermediately susceptible to levofloxacin. The most effective antibiotics against Gram-positive agents were determined to be vancomycin, teicoplanin, and linezolid.

Acinetobacter baumannii was isolated from two wound cultures. The AST results for both isolates were identical: they were sensitive to colistin but resistant to imipenem, levofloxacin, amikacin, gentamicin, meropenem, ciprofloxacin, and trimethoprim/sulfamethoxazole. Two Stenotrophomonas maltophilia isolates were also obtained. Both isolates were found to be sensitive to trimethoprim/sulfamethoxazole, which is recommended by EUCAST for the treatment of S. maltophilia infections.

A total of nine Escherichia coli isolates were obtained. All E. coli isolates were found to be sensitive to colistin, with eight also sensitive to carbapenems and ceftolozane/tazobactam. The lowest sensitivity was observed against ampicillin, amoxicillin/clavulanic acid, and ciprofloxacin. Five of the isolates were identified as ESBL (Extended Spectrum Beta-Lactamase) producers, and one was considered a potential carbapenemase producer (indicated by the presence of carbapenemase, overproduction of AmpC, or due to ESBL production).

A total of five Proteus mirabilis isolates were obtained. All of them were resistant to ampicillin but sensitive to amikacin, ceftolozane/tazobactam, piperacillin/tazobactam, ertapenem, and meropenem.

All Klebsiella species were found to be resistant to ampicillin and cefazolin. Klebsiella aerogenes and Klebsiella oxytoca were sensitive to third- and fourth-generation cephalosporins and carbapenems, and no ESBL production was detected. However, Klebsiella pneumoniae isolates were identified as ESBL-positive and potential carbapenemase producers.

Three Enterobacter cloacae isolates were obtained. Of these, 66.7% were determined to be potential carbapenemase producers. All isolates were found to be sensitive to colistin but resistant to piperacillin/tazobactam.

Serratia marcescens was isolated from a wound culture. It was found to be resistant to ampicillin, amoxicillin/clavulanic acid, cefazolin, cefuroxime, and tested negative for ESBL production. Morganella morganii was isolated from three wound samples. Two of these isolates were identified as potential carbapenemase producers.

Both S. marcescens and M. morganii are naturally resistant to colistin. All isolates were susceptible to amikacin, ceftolozane/tazobactam, ceftriaxone, cefepime, piperacillin/tazobactam, and meropenem. According to EUCAST guidelines, cefotaxime, ceftriaxone, or ceftazidime should not be used to treat infections caused by Serratia and Morganella species, even if these bacteria are susceptible in vitro.

A total of seven P. aeruginosa isolates were obtained. P. aeruginosa is naturally resistant to ampicillin,

Table 2. Antibiotic susceptibility rates in Gram-negative bacteria

	Escheri-chia coli n=9 (%)	*Proteus mirabilis* n=5 (%)	*Klebsiella spp.* n=5 (%)	*Entero-bacter cloacae* n=3 (%)	*Morga-nella morganii* n=3 (%)	*Serratia mar-ces-cens* n=2 (%)
Amikacin	9 (100)	4 (80)	2 (40)	2 (40)	3 (100)	1 (100)
Ampicillin	1 (11.1)	0	0	0	0	0
Amoxicillin/Clavulanic acid	2 (22.2)	4 (80)	1 (20)	0	0	0
Ceftolozane/Tazobactam	8 (88.8)	5 (100)	2 (40)	2 (66.7)	3 (100)	1 (100)
Ciprofloxacin	1 (11.1)	2 (40)	1 (20)	2 (66.7)	0	1 (100)
Ceftriaxone	4 (44.4)	2 (40)	2 (40)	1 (33.3)	3 (100)	1 (100)
Cefuroxime	3 (33.3)	2 (40)	1 (20)	0	0	0
Colistin	9 (100)	-	4 (80)	3 (100)	-	-
Ertapenem	8 (88.8)	5 (100)	2 (40)	1 (33.3)	3 (100)	1 (100)
Cefepim	4 (44.4)	2 (40)	1 (20)	1 (33.3)	3 (100)	1 (100)
Gentamicin	3 (33.3)	2 (40)	3 (60)	2 (66.7)	2 (66.7)	1 (100)
Imipenem	8 (88.8)	-	4 (80)	2 (66.7)	1 (33.3)	1 (100)
Levofloxacin	5 (55.5)	2 (40)	1 (20)	2 (66.7)	1 (33.3)	1 (100)
Meropenem	8 (88.8)	5 (100)	4 (80)	2 (66.7)	3 (100)	1 (100)
Trimethoprim/Sulfamethox-azole	3 (33.3)	1 (20)	2 (40)	2 (66.7)	0	1 (100)
Piperacillin/Tazobactam	7 (77.7)	5 (100)	1 (20)	0	3 (100)	1 (100)

- susceptibility testing has not been studied.

amoxicillin, amoxicillin/clavulanic acid, ampicillin/sulbactam, cefazolin, cephalothin, cephalexin, cefadroxil, cefotaxime, ceftriaxone, ertapenem, chloramphenicol, trimethoprim, tetracycline, and tigecycline.

The MIC values of antibiotics used in the treatment of P. aeruginosa were as follows:

•Ciprofloxacin: 0.001-0.5 µg/mL

•Levofloxacin: 0.001-2 µg/mL

•Imipenem: 0.001-4 µg/mL

•Cefepime and Ceftazidime: 0.001-8 µg/mL

•Piperacillin/tazobactam: 0.001-16 µg/mL

In our study, since the MIC value for all P. aeruginosa isolates was >0.001 µg/mL, they were found to be moderately sensitive to these antibiotics. According to EUCAST 2023 data, MIC values ≤0.001 µg/mL for ciprofloxacin, ceftazidime, cefepime, imipenem, levofloxacin, and piperacillin/tazobactam should be interpreted as sensitive. Since the MIC values for these antibiotics in our study were >0.001 µg/mL, all P. aeruginosa isolates were reported as moderately sensitive. The most effective antibiotics against P. aeruginosa were determined to be amikacin, ceftolozane/tazobactam, and imipenem.

The gradient test method was used for the anaerobic microorganisms isolated in our study. Actinomyces spp., a Gram-positive bacillus, was isolated as a monomicrobial infection agent. The patient had a history of repeated debridement and first-toe amputation. The gradient test revealed the following MIC values:

•Ertapenem: <0.25 µg/mL (susceptible)

•Meropenem: <0.25 µg/mL (susceptible)

•Vancomycin: <1 µg/mL (susceptible)

•Penicillin-G: <0.25 µg/mL (susceptible)

•Ampicillin/sulbactam: <1 µg/mL (susceptible)

•Ticarcillin/clavulanic acid: <0.5 µg/mL (susceptible)

Since metronidazole and aminoglycosides were not sensitive in vitro, testing was not performed with these antibiotics.

Another anaerobic microorganism isolated was identified as Leptotrichia buccalis. L. buccalis is a Gram-negative bacterium and was found to be sensitive to the following antibiotics, as determined by the AST using the gradient test method: metronidazole, ticarcillin/clavulanic acid, ampicillin/sulbactam, doripenem, and chloramphenicol.

Discussion

Tissue samples collected by curettage or biopsy should be preferred for identifying pathogens that cause diabetic foot infections and for obtaining AST results. Bone cultures are recommended if osteomyelitis is present. Blood cultures should only be obtained from patients with sepsis (9). Studies using molecular microbiological techniques have identified significantly more microorganisms from a broader range of species (10). Microorganisms that are difficult to grow in traditional culture media (anaerobes and Gram-positive bacilli) have been identified more frequently by gene sequencing (6). The roles of Corynebacterium spp. and obligate anaerobes, which are isolated more frequently with these methods, in pathogenicity are unclear (11). There is generally good agreement between these two methods regarding the most common pathogens identified (12). The small number of patients in the molecular sequencing method may increase the systematic error rate. Additionally, this method identifies both live and dead microorganisms and does not assess the antibiotic susceptibility of isolates. It may also be more expensive and require longer processing times compared to standard culture techniques (13). Considering these factors, the traditional cud was used in our study.

Because DFIs can progress rapidly, empiric antibiotic therapy should be initiated before culture results are available. The choice of antibiotics should take into account the clinical features and severity of the infection, recent culture results, history of recent antibiotic use, and information on local antibiotic resistance patterns. In European countries, the most common pathogens are aerobic Gram-positive cocci, particularly Staphylococcus aureus. If there are no risk factors for Gram-negative or obligate anaerobic infections, narrow-spectrum therapy targeting staphylococci and streptococci is usually sufficient. Risk factors for Gram-negative infections include previous antibiotic therapy or hospitalization, while ischemia or gangrene are associated with anaerobic infections. In severe infections, a broader-spectrum regimen should be chosen (14).

Patients' clinical responses to treatment, along with culture and antibiotic sensitivity results, should be evaluated to determine the need for adjustments

to the empirical treatment regimen. According to antimicrobial stewardship principles, the most appropriate and narrowest-spectrum regimen should be selected for the shortest duration necessary (15). Since bone necrosis occurs in cases of diabetic foot osteomyelitis (DFOM), surgical resection is usually preferred. In approximately one-third of patients, bone infection may recur months after seemingly successful treatment. Clinicians should assume that osteomyelitis is in remission within one year after treatment, and only then should they consider the infection to be completely resolved.

In addition to bone involvement in DFI, infection with antibiotic-resistant pathogens (especially MRSA, Pseudomonas aeruginosa, and Gram-negative bacilli with ESBL) and the presence of severe peripheral artery disease or end-stage renal disease reduce the likelihood of successful treatment. Patients with these risk factors require particularly careful monitoring. In patients who do not respond to treatment, imaging and repeat cultures with appropriate samples may be performed to detect deep tissue involvement.

Patients with DFI require appropriate wound care, including wound cleaning and debridement, revascularization of ischemic limbs, and optimizing glycemic control. Clinicians should carefully monitor patients with a previous history of DFI and educate them and their caregivers on the most effective prevention techniques (9).

In a similar study conducted by Kow et al., which aimed to detect factors in DFU, most of the patients included (n = 77, 59.2%) were men, and the male-to-female ratio was found to be 1.45 (17). In Palomo et al.'s study, the rate of male patients was reported as 69.7% (18). Similarly, in the study conducted by Li et al. at a diabetic foot center in China, the majority of patients (75%) were male (19). In our study, male patients also constituted the majority (78%), and the male-to-female ratio was found to be 3.55. The higher prevalence of diabetic foot disease and DFU in men suggests that male patients may have poorer foot care practices. Ismail et al detected a total of 178 (124 aerobic, and 54 anaerobic) pathogens from DFI patients and determined the isolate/sample ratio to be 1.82 on average (20). Kow et al. isolated 142 agents from 130 tissue samples and reported the isolate/sample ratio as 1.09 (17). Hatipoğlu et al. included 343 samples (isolate/sample ratio 1.2) taken from 287 patients in Turkey (21). The number of microorganisms isolated in our study was 57 and the isolate/sample ratio was 1.3, and this value was found to be compatible with studies conducted in Turkey. In their study with 146 swabs and 179 tissue samples, Jouhar et al. showed that there was a polymicrobial infection in 54% of the cases (16). Ismail et al. detected polymicrobial infection in 42 (42.9%) of 98 cases (20). In Kow et al.'s study, 130 tissue samples were examined and the majority of them (n = 69, 53.1%) grew a single pathogen, followed by samples with no growth (n = 34, 26.2%) and polymicrobial infections (n = 27, 20.8%). (17). In our study, the non-growth sample rate was found to be 25.42% and the polymicrobial infection rate was 20.5%. The lower polymicrobial infection rate compared to some studies may be because the majority of the samples in our study were tissue biopsy samples.

Kow et al. showed that the majority of the pathogens (52.8%) were Gram-negative bacteria (17). Jouhar et al. isolated Gram-negative microorganisms in 55% of tissue cultures (16). Ismail et al. found Gram-negative bacteria to be dominant among aerobic pathogens (98/124; 79%) and also demonstrated that the rate of Gram-negative bacteria and anaerobes isolated from DFUs increased with the severity of diabetic foot infections (20). In our study, aerobic Gram-negative bacteria constituted 71% of aerobic pathogens and 65% of all pathogens. Although the severity of DFU was not classified, the high prevalence of Gram-negative bacteria suggests that the DFUs in our study may be at a more advanced stage.

Macdonald et al. reported that 8,418 pathogens were detected from 6,736 samples in their meta-analysis, which included 57 studies. Among these isolates, the most frequently detected pathogens were Staphylococcus aureus, Pseudomonas spp., and Escherichia coli (22). Gram-positive aerobes have been reported in 66% to 84% of diabetic foot infections in developed countries. In Kalan et al.'s study, which investigated all chronic wounds, including DFU, S. aureus was found to be the most common species (>50% of all wounds), followed by coagulase-negative staphylococci and streptococci (23). In our study, the most common causative microorganisms were S. aureus (19.3%), E. coli, and P. aeruginosa. Gram-positive aerobic bacteria made up 26.32% of the total isolates. Although the Gram-positive isolation rate is lower compared to developed countries, the fact that they constitute more than one-quarter of the total isolates highlights the importance of empiric treatment that includes antibiotics effective against

Gram-positive bacteria.

In a study conducted in Egypt, Ismail et al. found that more than 50% of Gram-positive pathogens were MRSA (20). The frequency of MRSA in diabetic foot infections has increased significantly worldwide in recent years, now accounting for 50% of all S. aureus isolates. In Algeria, this rate reaches 85%. However, in Jouhar et al.'s study, MRSA accounted for only 4% of the total isolates (16). In our study, MRSA constituted 20% of all Gram-positive bacteria. While S. aureus was the most frequently isolated bacterium in many DFIs, Jouhar et al. showed that Escherichia coli was the most common isolate, accounting for 15% of cases. Ismail et al. identified Pseudomonas spp. and Proteus spp. as the most common pathogens.

In a study conducted in Turkey, a systematic analysis of articles published over 20 years compared two time frames (1989–2007 and 2007–2011). The total percentage of Gram-negative and Gram-positive aerobic bacteria was similar in each period. However, in the second period, it was observed that the isolation rate of S. aureus decreased from 23.8% to 19.1%, and the MRSA rate decreased from 7.8% to 5.7% (24). In our study, the frequency of S. aureus isolation (19.3%) and MRSA isolation (5.27%) was consistent with the trends observed in Turkey. The decrease in the MRSA rate suggests that empiric antibiotic therapy may not need to cover MRSA.

In a study conducted at a diabetic foot center in China, Li et al. found the fungal infection rate to be 7.5% (19). In Jouhar et al.'s study, yeast fungi represented 5% of the total isolates (16). According to the results of our study, fungal growth was observed in 5% of the samples. The most frequently detected fungal pathogens in diabetic foot infections are Candida albicans, Candida glabrata, and Candida tropicalis, after Candida parapsilosis. In our study, C. tropicalis and C. parapsilosis were isolated (8). The results of our study were consistent with similar studies in terms of the isolation rate and types of yeast fungi. Treatment of fungal infections typically takes longer than bacterial infections, and this should be considered when determining the treatment plan.

Studies conducted at different times and in different countries show significant variability in the rate of anaerobic bacterial isolation in diabetic foot infections (DFI). In our study, anaerobic microorganisms constituted 4% of the isolates. The sharp differences between studies may be attributed to nonstandardized culture methods, including variations in sample types, handling conditions, and laboratory techniques.

Charles et al. showed that Peptostreptococcus and Bacteroides species are common anaerobic agents in DFI (25). However, Barshes et al., using 10 years of hospital data, were unable to detect Bacteroides and Corynebacterium species (26). These microorganisms were not isolated in our study either. Instead, we isolated Actinomyces spp. and Leptotrichia buccalis, which differ from the most commonly reported anaerobic agents. Leptotrichia species are nonmotile anaerobic bacteria predominantly found in the oral cavity and other parts of the body (27). Actinomyces spp. are part of the normal microflora of the oral and gastrointestinal tracts, and a case of foot infection caused by Actinomyces was reported by Bettesworth et al (28). Further studies may be needed to investigate anaerobic microorganisms that cause DFI, as the diversity of these pathogens and their role in infection is not fully understood.

In a systematic review of studies conducted in Turkey, Hatipoğlu et al. showed that the most effective antibiotics against Gram-positive bacteria were vancomycin, teicoplanin, and linezolid (24). The results of our study are consistent with previous studies, demonstrating that the most effective antibiotics against Gram-positive bacteria are vancomycin, teicoplanin, and linezolid. This suggests that there has been no significant change in the empirical treatment of diabetic foot infections with agents that target Gram-positive bacteria.

The fact that diabetic foot is most commonly detected in the elderly highlights the importance of regular monitoring of blood sugar levels and existing comorbidities, especially in men. Early diagnosis and appropriate treatment are crucial, as they can prevent permanent sequelae. It is important to recognize that DM is an 80% preventable disease through lifestyle changes, and raising social awareness about the benefits of a healthy lifestyle is essential. Regular training for healthcare personnel and efforts to increase public awareness can help reduce the devastating effects of diabetes-related complications.

Among DM complications, DF is the most common cause of hospitalization and may require long-term treatment. Beyond the high healthcare costs, DF has significant economic and social implications due to its potential for leading to amputation and even mortality. Therefore, it requires careful monitoring,

just as much as the management of DM itself. A multidisciplinary approach is essential for successful treatment of diabetic foot ulcers and for reducing treatment costs.

Once a diagnosis of diabetic foot is made, scheduling regular check-ups for patients, along with consistent dressing and wound care, will reduce the risk of developing advanced wounds. Additionally, patients should be reminded of the importance of foot care, as it plays a crucial role in preventing the progression of DF disease. In cases of progressive tissue loss due to infection, hospitalization is necessary. For diabetic foot ulcers, early referral, prompt initiation of antibiotic therapy, and, if needed, early vascular intervention should be planned to prevent disease progression and tissue loss.

Conclusion

In this study, high microorganism isolation rates and antibiotic resistance rates were found in patients with DM. Antibiotic susceptibility tests (AST) provide an important contribution to the rational use of antibiotics. Two standard guidelines are commonly used for the application of test results worldwide (29). Considering that the majority of Gram-negative agents consist of MDROs, the importance of rational antibiotic use comes to the fore once again. In light of all these findings, it is of great importance to increase the number of diabetic foot centers in our country and provide foot care training.

Authors' Contribution

Conception: AI, SM, HTD. Design: AI, SM. Data collection and processing: AI, SM, BÇ, SY. Data analysis and interpretation: AI, SM, BÇ, SY, HTD. Writing: AI, SM, BÇ, SY, HTD. Critical review: AI, SM, BÇ, SY, HTD.

Conflict of interest

The author declares that they have no conflict of interest.

Financial support

The study was funded by the Selcuk University Scientific Research Project (BAP) during the design of the research, data collection, analysis, interpretation, and writing of the article (Project no: 22122023).

References

1.Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9(th) edition. Diabetes Res Clin Pract 2019; 157, 107843.

2.Rodrigues BT, Vangaveti VN, Urkude R, Biros E, Malabu UH. (. Prevalence and risk factors of lower limb amputations in patients with diabetic foot ulcers: A systematic review and meta-analysis. Diabetes Metab Syndr 2022; 16(2), 102397.

3.Singer AJ, Tassiopoulos A, Kirsner RS. Evaluation and Management of Lower-Extremity Ulcers. N Engl J Med 2018; 378(3), 302-303.

4.McDermott K, Fang M, Boulton AJ, Selvin E, Hicks CW. Etiology, Epidemiology, and Disparities in the Burden of Diabetic Foot Ulcers. Diabetes Care 2023; 46(1), 209-221.

5.Rice JB, Desai U, Cummings AK, Birnbaum HG, Skornicki M, Parsons NB. The burden of diabetic foot ulcers for Medicare and private insurers. Diabetes Care 2014; 37(3), 651-658.

6.Hawkins BK, Barnard M, Barber KE, et al. Diabetic foot infections: A microbiologic review. Foot (Edinb) 2022; 51, 101877.

7.Smith K, Collier A, Townsend EM, et al. One step closer to understanding the role of bacteria in diabetic foot ulcers: characterizing the microbiome of ulcers. BMC Microbiol 2016; 16, 54.

8.Saeed K, Esposito S, Akram A, et al. Hot topics in diabetic foot infection. Int J Antimic Agents 2020; 55(6), 105942.

9.Boulton AJM, Armstrong DG, Hardman MJ, et al. Diagnosis and Management of Diabetic Foot Infections. Arlington (VA): American Diabetes Association 2020; Jan, 1-24.

10.Pereira SG, Moura J, Carvalho E, Empadinhas N. Microbiota of Chronic Diabetic Wounds: Ecology, Impact, and Potential for Innovative Treatment Strategies. Front Microbiol 2017; 8, 1791.

11.Johani K, Fritz BG, Bjarnsholt T, et al. Understanding the microbiome of diabetic foot osteomyelitis: insights from molecular and microscopic approaches. Clin Microbiol Infect 2019; 25(3), 332-339.

12.Malone M, Gosbell IB, Dickson HG, Vickery K, Espedido BA, Jensen SO. Can molecular DNA-based techniques unravel the truth about diabetic foot infections? Diabetes Metab Res Rev 2017; 33(1).

13.Lipsky BA, Senneville É, Abbas ZG, et al. Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF 2019 update). Diabetes Metab Res Rev 2020; 36 Suppl 1, e3280.

14.Peters EJG, Lipsky BA, Senneville É, et al. Interventions in the management of infection in the foot in diabetes: a systematic review. Diabetes Metab Res Rev 2020; 36 Suppl 1, e3282.

15.Uçkay I, Berli M, Sendi P, Lipsky BA. Principles and practice of antibiotic stewardship in the management of diabetic foot infections. Curr Opin Infect Dis 2019; 32(2), 95-101.

16.Jouhar L, Jaafar RF, Nasreddine R, et al. Microbiological

profile and antimicrobial resistance among diabetic foot infections in Lebanon. Int Wound J 2020; 17(6), 1764-1773.

17.Kow R, Low C, Ayeop M, Che-Ahmad A, Awang M. Characteristics and Microbiological Profile of Patients with Diabetic Foot Infections in Kuantan, Pahang. Malays Orthop J 2022; 16(1), 11.

18.Palomo AT, Pires APM, Matielo MF, et al. Microbiology of Diabetic Foot Infections in a Tertiary Care Hospital in São Paulo, Brazil. Antibiotics 2022; 11(8), 1125.

19.Li X, Cheng Q, Du Z, Zhu S, Cheng C. Microbiological concordance in the management of diabetic foot ulcer infections with osteomyelitis, on the basis of cultures of different specimens at a diabetic foot center in China. Diabetes Metab Syndr Obes: Targets Therapy 2021; 14, 1493

20.Ismail AA, Meheissen MA, Elaaty TAA, Abd-Allatif NE, Kassab HS. Microbial profile, antimicrobial resistance, and molecular characterization of diabetic foot infections in a university hospital. Germs 2021; 11(1), 39-51.

21.Hatipoglu M, Mutluoglu M, Turhan V, et al. Causative pathogens and antibiotic resistance in diabetic foot infections: A prospective multi-center study. J Diabetes Complicat 2016; 30(5), 910-916.

22.Macdonald KE, Boeckh, Stacey, HJ, Jones JD. The microbiology of diabetic foot infections: a meta-analysis. BMC Infect Dis 2021; 21(1), 1-10.

23.Kalan LR, Brennan MB. The role of the microbiome in nonhealing diabetic wounds. Ann N Y Acad Sci 2019; 1435(1), 79-92.

24.Hatipoglu M, Mutluogl M., Uzun G, Karabacak E, Turhan V, Lipsky B. The microbiologic profile of diabetic foot infections in Turkey: a 20-year systematic review: diabetic foot infections in Turkey. Eur J Clin Microbiol infect dis 2014; 33, 871-878

25.Charles PG, Uçkay I, Kressmann B, Emonet S, Lipsky BA. The role of anaerobes in diabetic foot infections. Anaerobe 2015; 34, 8-13.

26.Barshes NR, Clark NJ, Bidare D, Dudenhoeffer JH, Mindru C, Rodriguez-Barradas MC. Polymicrobial Foot Infection Patterns Are Common and Associated With Treatment Failure. Open Forum Infect Dis 2022; 9(10), ofac475.

27.Eribe ERK, Olsen I. Leptotrichia species in human infections II. J Oral Microbiol, 2017;9(1), 1368848.

28.Bettesworth J, Gill K, Shah J. Primary actinomycosis of the foot: a case report and literature review. J Am Col Certif Wound Spec 2009; 1(3), 95-100.

29.Maçin S, Akyön Yılmaz, Y, Özden Ö, Gür D. (2017). Interpretation of Antibiotic Susceptibility Test Results of Pseudomonas aeruginosa, Acinetobacter baumannii and Escherichia coli Isolates According to EUCAST and CLSI: Hacettepe Experience. Türk Mikrobiyol Cem Derg 2017; 47(1):21-25.

Received: 12 Dec 2024 | **Accepted:** 21 Feb 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 284-291
DOI: 10.54005/geneltip.1600277

ORIGINAL ARTICLE

Impact of Prognostic Nutritional Index on Clinical Outcomes in Hereditary Angioedema: A single-center experience

Herediter Anjiyoödemde Prognostik Nutrisyonel İndeksin Klinik Sonuçlar Üzerine Etkisi: Tek Merkez Deneyimi

[1]Merhmet Emin Gerek, [1]Fatih Çölkesen, [1]Tuğba Önalan, [1]Fatma Arzu Akkuş, [2]Recep Evcen, [3]Mehmet Kılınç, [1]Selim Karaman, [1]Şevket Arslan

[1]Department of Internal Medicine, Division of Clinical Immunology and Allergy, Necmettin Erbakan University, Faculty of Medicine, Konya, Türkiye
[2]Division of Clinical Immunology and Allergy, Rize Training and Research Hospital, Rize, Türkiye
[3]Division of Clinical Immunology and Allergy, Batman Training and Research Hospital, Batman, Türkiye

Correspondence

Dr. Mehmet Emin Gerek
Hocacihan Mah. Abdulhamid Han Cad. No:3 42080 Selçuklu, Konya, Türkiye

E-Mail: drmegerek@gmail.com

How to cite ?

Gerek ME, Çölkesen FÖnalan T, Akkuş FA, Evcen R, Kılınç M, Kahraman S, Arslan Ş. Impact of Prognostic Nutritional Index on Clinical Outcomes in Hereditary Angioedema: A single-center experience. Genel Tıp Derg. 2025;35 (2): 284-291

ABSTRACT

Background/Aim: This study aims to evaluate the impact of the Prognostic Nutritional Index (PNI) on clinical outcomes in hereditary angioedema (HAE) patients. HAE is a rare genetic disorder (prevalence approximately 1:50,000) marked by recurrent episodes of severe swelling due to a deficiency in the C1 inhibitor (C1-INH) protein, affecting the complement and contact systems. PNI, a measure of nutritional and immune status, has been used to predict clinical outcomes in various chronic diseases, but its role in HAE remains unclear.
Methods: A single-center retrospective cohort of 60 patients was analyzed. Clinical characteristics and PNI were assessed and calculated using the formula: [Serum Albumin (g/L)] + [5 × Peripheral Blood Lymphocyte Count (×10□/L)]. Patients were stratified into low and high PNI groups based on a cut-off value of 51.725, derived from receiver operating characteristic (ROC) curve analysis (AUC = 0.902, $p < 0.001$). Statistical significance was set at $p < 0.05$.
Results: Low PNI was significantly associated with increased attack frequency ($p < 0.001$), extended diagnostic delays ($p = 0.022$), and greater laryngeal ($p = 0.003$) and gastrointestinal involvement ($p = 0.005$). Furthermore, low PNI was negatively correlated with monthly attack frequency (Spearman's rho = -0.653, $p < 0.001$) and positively correlated with the C1-INH function (Spearman's rho = 0.408, $p = 0.001$).
Conclusion: These findings underscore the importance of incorporating nutritional evaluations into HAE management, as poor nutritional status may exacerbate disease severity. Further prospective studies are needed to validate these associations and explore nutritional interventions as a complementary strategy in HAE treatment.

Keywords: C1 inhibitor protein, hereditary angioedema, immune system diseases, nutritional status, prognostic nutritional index

ÖZ

Giriş/Amaç: Bu çalışmanın amacı, Prognostik Nutrisyonel İndeksin (PNI), HAE hastalarındaki klinik sonuçlar üzerindeki etkisini değerlendirmektir. Herediter anjiyoödem (HAE), C1 inhibitör (C1-INH) protein eksikliğine bağlı olarak kompleman ve kontakt sistemlerini etkileyen, yaklaşık 1:50.000 prevalans ile seyreden nadir bir genetik hastalıktır. Hastalık, tekrarlayan ciddi şişlik atakları ile karakterizedir. Prognostik Nutrisyonel İndeks (PNI), beslenme ve immün durumun bir göstergesi olarak çeşitli kronik hastalıklarda klinik sonuçları öngörmek amacıyla kullanılmaktadır; ancak, HAE üzerindeki etkisi henüz netlik kazanmamıştır.
Yöntem: Tek merkezli retrospektif bir kohort çalışması kapsamında 60 hasta analiz edilmiştir. Hastaların klinik özellikleri ve PNI değerleri incelenmiş, PNI şu formülle hesaplanmıştır: [Serum Albümini (g/L)] + [5 × Periferik Kan Lenfosit Sayısı (×10□/L)]. Alıcı çalıştırma özellik (ROC) eğrisi analiziyle belirlenen 51.725 kesim değeri esas alınarak hastalar düşük ve yüksek PNI gruplarına ayrılmıştır (AUC = 0.902, $p < 0.001$). İstatistiksel anlamlılık seviyesi $p < 0.05$ olarak kabul edilmiştir.
Bulgular: Düşük PNI, artmış atak sıklığı ($p < 0.001$), uzamış tanı gecikmesi ($p = 0.022$), ve daha sık larinks ($p = 0.003$) ve gastrointestinal tutulum ($p = 0.005$) ile anlamlı olarak ilişkilendirilmiştir. Ayrıca, düşük PNI ile aylık atak sıklığı arasında negatif bir korelasyon (Spearman rho = -0.653, $p < 0.001$) ve C1-INH fonksiyonu ile pozitif bir korelasyon (Spearman rho = 0.408, $p = 0.001$) bulunmuştur.
Sonuç: Bu bulgular, HAE yönetiminde beslenme değerlendirmelerinin önemini vurgulamaktadır. Zayıf beslenme durumu, hastalık şiddetini artırabilir. Bu ilişkilerin doğrulanması ve HAE tedavisinde tamamlayıcı bir strateji olarak beslenme müdahalelerinin etkilerinin araştırılması için ileriye dönük çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Beslenme durumu, C1 inhibitör protein, herediter anjiyoödem, immün sistem hastalıkları, prognostik nutrisyonel indeks

Introduction

Hereditary angioedema (HAE) is a rare genetic disorder characterized by recurrent episodes of severe swelling, primarily due to a deficiency or dysfunction of the C1 inhibitor (C1-INH) protein, playing a crucial role in regulating the complement and contact systems of the immune response (1). The clinical manifestations of HAE can lead to significant morbidity, affecting various tissues including the skin, gastrointestinal (GI) tract, and respiratory airways, and can result in life-threatening complications, if not managed appropriately (2).

The pathophysiology of HAE is primarily linked to mutations in the SERPING1 gene, which encodes the C1-INH protein, resulting in decreased plasma levels of functional C1-INH and subsequent dysregulation of bradykinin production (1, 3). This dysregulation is responsible for the characteristic swelling episodes, which can occur spontaneously or be triggered by

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

various factors, including trauma, stress, and certain medications (2).

The management of HAE has evolved significantly over recent years, with the introduction of targeted therapies, such as bradykinin B2-receptor antagonists (e.g., icatibant) and C1-INH concentrates, which have shown to improve treatment outcomes for patients experiencing acute attacks (4, 5). Current guidelines recommend a tailored approach to treatment, considering the frequency and severity of attacks, with options for on-demand therapy and long-term prophylaxis (6, 7).

Despite these advancements, challenges remain in the clinical management of HAE, particularly in accurately diagnosing acute attacks, as there are currently no specific laboratory markers for HAE episodes (8). Recent studies propose that increased levels of prothrombin fragment F1+2 and D-dimer could serve as diagnostic tools for acute attacks, pointing to the need for further validation through rigorous research (8). Moreover, the quality of life (QoL) for patients with HAE is significantly impacted by the unpredictability and severity of attacks, necessitating the development of patient-reported outcome measures to better assess the burden of the disease and the effectiveness of treatment strategies (9). As the understanding of HAE continues to evolve, ongoing research is essential to refine treatment protocols and improve clinical outcomes for affected individuals.

The Prognostic Nutritional Index (PNI) has emerged as a significant tool in assessing the nutritional status of patients, particularly in the context of chronic diseases. Originally developed to predict surgical outcomes, PNI has been correlated with disease severity and immune function in various chronic inflammatory and autoimmune disorders (10, 11).

However, its relevance in HAE remains largely unexplored, with limited data on how nutritional status may influence the clinical manifestations of this condition. Nutritional deficiencies can exacerbate the severity of chronic diseases, potentially leading to increased frequency and severity of HAE attacks (6).

Given that HAE is characterized by recurrent episodes of swelling, understanding the interplay between nutritional status and immune response could provide insights into disease management (12). Patients with HAE may experience nutritional deficiencies due to recurrent GI attacks, leading to impaired nutrient absorption and reduced dietary intake. Additionally, chronic inflammation and increased metabolic demand may further contribute to malnutrition, exacerbating disease severity and attack frequency. Recent studies suggest that nutritional assessments, including PNI, may offer valuable prognostic information for patients with chronic conditions, indicating a need for further exploration in the context of HAE (11).

This study aims to investigate the potential impact of nutritional status, as measured by PNI, on clinical outcomes in patients with HAE, thereby highlighting an under-researched area that could enhance patient care strategies. Understanding the relationship between nutritional status and disease activity in HAE could offer novel perspectives for patient management, potentially guiding more personalized therapeutic strategies incorporating nutritional assessments as part of routine care.

Materials and Methods

Study design and patient selection

This study is a single-center, retrospective cohort analysis. The study cohort comprised HAE patients followed at the immunology outpatient clinic from 2019 to 2023. Patients were included in the study if they had a confirmed diagnosis of HAE based on clinical and laboratory findings, had complete clinical and biochemical data, and were 18 years or older at the time of evaluation. The exclusion criteria for this study included chronic liver disease, malignancy, severe renal impairment (estimated glomerular filtration rate <30 mL/min/1.73 m^2), or any chronic inflammatory or autoimmune disorder that could potentially influence nutritional status and immune function. Additionally, patients with incomplete medical records were excluded.

Data collection and assessments

Assessment of patients' data

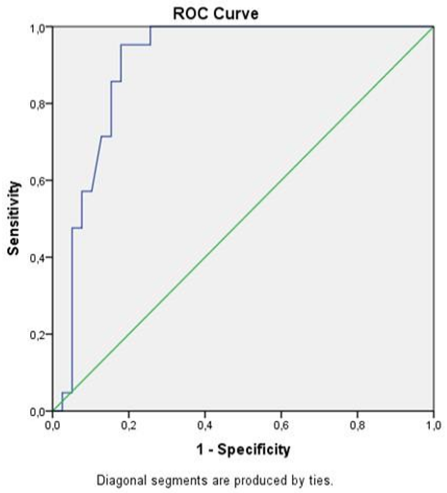
Demographic data collected for the patients encompassed age, gender, type of HAE, age of symptom onset related to HAE, and age at diagnosis. The diagnostic delay was determined by subtracting the age of symptom onset from the age at diagnosis. Data regarding the functional level of the C1 esterase inhibitor at the time of diagnosis was documented. Supplementary laboratory parameters comprised white blood cell (WBC) count, neutrophil count, lymphocyte count, hemoglobin concentration,

platelet count, creatinine concentration, aspartate aminotransferase (AST) level, alanine aminotransferase (ALT) level, albumin concentration, and C-reactive protein (CRP) level. These laboratory values were acquired from patients during asymptomatic intervals.

Calculation of the optimal cut-off for the prognostic nutritional index

PNI was determined using the formula: serum albumin concentration (g/L) + 5 × peripheral blood lymphocyte count (×10□/L) (13). The ROC curve analysis revealed that the area under the curve (AUC) for the PNI level's capacity to differentiate clinical conditions was 0.902. The AUC value obtained was statistically significant ($p < 0.001$), with a 95% confidence interval of 0.822 to 0.982 (Figure 1). As a result, the patients were categorized into two groups according to a PNI threshold of 51.725.

Figure 1. ROC curve for determining the optimal cut-off value of the prognostic nutritional index.



Statistical analysis

Statistical analysis was conducted using IBM SPSS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as median (interquartile range) for numerical variables and as numbers and percentages for categorical variables. The Mann–Whitney U test was employed to analyze differences between variables according to their distribution patterns. The chi-squared ($\chi 2$) and Fisher's exact tests were used for comparing percentages. Receiver Operating Characteristic (ROC) curve analysis was used to ascertain the optimal cut-off value for the PNI. The ROC curve visually represents the correlation between the sensitivity and specificity of the test, facilitating the assessment of the model's discriminative capability. Youden's Index was calculated to determine the optimal cut-off value derived from the ROC analysis. Spearman correlation analysis was conducted to assess the relationship between PNI levels and the annual frequency of attacks. $p<0.05$ was considered statistically significant.

Ethical Approval

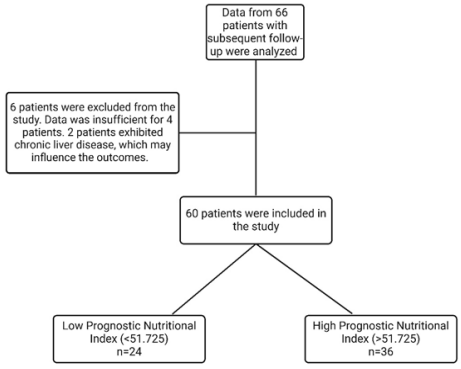
This study was approved by the Ethics Committee of Necmettin Erbakan University (Approval Number: 2024/5336). All data collection and analysis were conducted in compliance with ethical standards and the Declaration of Helsinki.

Results

Study population

Of the 66 patients initially monitored, two were excluded from the study due to chronic liver disease, which could potentially influence the outcomes, and four others were excluded due to incomplete data. A study cohort of 60 patients was established, excluding these six individuals. The low PNI group comprised 24 patients, while the high PNI group included 36 patients. The clinical and demographic data of these two patient groups were compared and analyzed (Figure 2).

Figure 2. Flowchart of patient selection and categorization based on prognostic nutritional index threshold.



The median age of the patients was 41 years, and 36 of the patients were female. In the comparison between patients with low (<51.725) and high (>51.725) PNI levels, no significant difference was found between the two groups in terms of age ($p = 0.774$). Gender distribution analysis revealed a significantly higher proportion of males in the high PNI group compared to the low PNI group, with this difference being statistically significant ($p = 0.013$). No significant difference was observed between the groups concerning the type of

HAE. However, the diagnostic delay was found to be significantly longer in the low PNI group (Table 1).

Table 1. Comparison of demographic and clinical characteristics between low and high prognostic nutritional index groups in patients with hereditary angioedema

	PNI Low (<51.725) (n=24)	PNI High (>51.725) (n=36)	p
Age (years) (median, IQR)	41.5 (30.25-49)	40.5 (28-51)	0.774*
Gender			
Female (n) (%)	19 (79.2)	17 (47.2)	**0.013****
Male (n) (%)	5 (20.8)	19 (52.8)	
Hereditary Angioedema Type			
Type 1 (n) (%)	15 (62.5)	22 (61.1)	0.914**
Type 2 (n) (%)	9 (37.5)	14 (38.9)	
Diagnostic delay (years) (median, IQR)	16.5 (5.5-21.8)	8.5 (4.3-14.5)	**0.022***

*Mann–Whitney U test (data are shown as median with IQR). **χ^2 test (data are shown as numbers and percentages). IQR: Interquartile range,

PNI: Prognostic nutritional index

Evaluation of attack frequency, involvement patterns, and clinical parameters concerning PNI levels

In the comparison between groups with low and high PNI levels, the frequency of attacks was significantly higher in the low PNI group (30.0% vs. 5.0%; p < 0.001). No significant differences were observed between the groups regarding mucocutaneous involvement (40.0% vs. 58.3%; p = 0.410). However, laryngeal involvement was significantly more prevalent in the low PNI group compared to the high PNI group (26.7% vs. 16.7%; p = 0.003). Additionally, GI involvement was significantly more frequent in the low PNI group (35.0% vs. 31.7%; p = 0.005). Furthermore, the median number of attacks per month was notably higher in the low PNI group (5 [IQR: 3.25-8]) compared to the high PNI group (1 [IQR: 0.4-2]; p < 0.001) (Table 2).

Table-2. Clinical outcomes, attack frequency, and involvement patterns in hereditary angioedema patients categorized by prognostic nutritional index levels

	PNI Low (<51.725) (n=24)	PNI High (>51.725) (n=36)	p
Presence of Frequent Attacks (n) (%)	18 (75.0)	3 (8.3)	**<0.001***
Mucocutaneous Involvement (n) (%)	24 (100.0)	35 (97.2)	**1***
Gastrointestinal Involvement (n) (%)	21 (87.5)	21 (58.3)	**0.005***
Laryngeal Involvement (n) (%)	16 (66.7)	10 (27.8)	**0.003***
Number of Attacks per Month (median, IQR)	5 (3.25-8)	1 (0.4-2)	**<0.001****

*χ^2 test (data are shown as numbers and percentages). **Mann–Whitney U test (data are shown as median with IQR). IQR: Interquartile range, PNI: Prognostic nutritional index **Mann–Whitney U test (data are shown as median with IQR)

Biochemical and hematological differences based on PNI levels

In the comparison between the groups with low (<51.725) and high (>51.725) PNI levels, significant differences were observed in several biochemical and hematological parameters. The C1-INH function was significantly lower in the low PNI group (p=0.001). There was no statistically significant difference in WBC count and neutrophil count between the two groups (p = 0.940 and p = 0.357, respectively). The lymphocyte count was significantly lower in the low PNI group compared to the high PNI group (p=0.001). No significant differences were found between the two groups in terms of hemoglobin levels, platelet count, creatinine, AST, and ALT levels (p > 0.05 for all). However, albumin levels were significantly lower in the low PNI group compared to the high PNI group (p<0.001) No statistically significant difference was observed in CRP levels between the groups (p = 0.561) (Table 3).

Table-3. Comparison of biochemical and hematological parameters in hereditary angioedema patients stratified by prognostic nutritional index levels

	PNI Low (<51.725) (n=24)	PNI High (>51.725) (n=36)	p*
C1 inhibitor function (%) (median, IQR)	8.85 (5.25-12)	11.4 (10-19.55)	**0.001**
White Blood Cell count (10^3/μL) (median, IQR)	7.39 (6.99-8.57)	7.61 (6.60-9.02)	0.940
Neutrophil count (10^3/μL) (median, IQR)	4.52 (4.19-5.51)	4.41 (3.59-5.80)	0.357
Lymphocyte count (x10^3/mL) (median, IQR)	1.86 (1.38-2.16)	2.22 (1.99-2.41)	**0.001**
Hemoglobin (g/dL) (median, IQR)	13.7 (12.9-15.0)	14.3 (13.2-15.4)	0.287
Platelet count (10^3/μL) (median, IQR)	276 (226-323)	264 (231-308)	0.597
Creatinine (mg/dL) (median, IQR)	0.75 (0.66-0.88)	0.77 (0.68-0.91)	0.602
Aspartate Aminotransferase (U/L) (median, IQR)	15.9 (13.3-19.8)	17.1 (13.0-21.8)	0.551
Alanine Aminotransferase (U/L) (median, IQR)	13.1 (10.8-22.6)	16.7 (12.2-24.9)	0.216
Albumin (g/L) (median, IQR)	39 (36-40)	44 (42-47)	**<0.001**
C-reactive protein (mg/L) (median, IQR)	2.24 (1.48-3.60)	2.45 (1.18-4.48)	0.561

*Mann–Whitney U test (data are shown as median with IQR). IQR: Interquartile range,

PNI: Prognostic nutritional index

Correlation analysis between PNI levels and attack frequency, clinical and laboratory parameters

Spearman correlation analyses were performed to assess the relationships between PNI levels and various clinical parameters, including monthly attack

frequency, disease duration, the C1-INH function, and age at symptom onset (complaint age). The analysis showed a significant negative correlation between PNI levels and monthly attack frequency (Spearman's rho = -0.653, p < 0.001), associating lower PNI levels with more frequent attacks. By contrast, the relationship between PNI levels and disease duration was weak and not statistically significant (Spearman's rho = -0.155, p = 0.237), indicating a lack of meaningful association. A moderate positive correlation was found between PNI levels and the C1-INH function (Spearman's rho = 0.408, p = 0.001), indicating that higher PNI levels were associated with the improved C1-INH function. There was not a statistically significant correlation between PNI levels and age at symptom onset (Spearman's rho = 0.141, p = 0.284) (Table 4).

Table-4. Spearman correlation analysis between prognostic nutritional index levels and clinical and laboratory parameters in hereditary angioedema patients

Clinical Parameter	Spearman's rho	p	Interpretation
Monthly attack frequency	-0.653	< 0.001	Significant negative correlation
Duration of disease	-0.155	0.237	Weak negative, not statistically significant
Age at the onset of symptoms	0.141	0.284	Weak positive, not statistically significant
C1 inhibitor function	0.408	0.001	Moderate positive correlation, significant

Discussion

This study is one of the initial investigations to thoroughly assess the influence of prognostic nutritional index (PNI) levels on clinical outcomes in individuals with HAE. Our findings indicate that diminished PNI levels correlate with elevated attack frequencies, heightened laryngeal and GI involvement, and prolonged diagnostic delays. These findings offer a novel viewpoint on the impact of HAE and the role of nutritional status.

The observation of elevated monthly attack frequencies in patients with diminished PNI levels highlights the significance of nutritional status in affecting disease progression. This corresponds with the guideline established by Maurer et al. which underscores the essential influence of nutritional factors in the pathogenesis of chronic inflammatory diseases (14).

Research on prognostic nutritional indices in alternative conditions offers supplementary context. Jiang et al. discovered that diminished PNI levels in gastric cancer patients were significantly correlated with postoperative complications and reduced long-term survival (15). This highlights the essential connection between malnutrition and clinical decline. Zhang et al. similarly indicated that PNI is a reliable predictor of diabetic nephropathy progression (16). Lower PNI was associated with heightened renal dysfunction and inflammation. Nergiz et al. demonstrated that in patients with acute ischemic stroke, a lower PNI predicted increased infection rates (17). This underscores its value as an indicator of immune competence and systemic susceptibility.

The heightened incidence of laryngeal involvement in patients with diminished PNI levels emphasizes the necessity of vigilant monitoring of nutritional status to avert potentially fatal respiratory complications. Laryngeal edema presents a considerable threat of airway obstruction. Our results corroborate those of Zanichelli et al. who underscored the necessity of prompt identification and assertive treatment of high-risk individuals with C1-INH deficiency (18).

Moreover, research conducted by Wiednig et al. indicates that nutritional interventions may directly mitigate the severity of mucosal edema by enhancing systemic inflammatory regulation (5). This suggests that targeted dietary modifications may play a role in reducing the risk of laryngeal attacks in HAE patients.

This study identifies a significant association between low PNI levels and GI involvement in patients with HAE, underscoring the interplay between nutritional status and disease severity. GI symptoms, including recurrent abdominal pain, vomiting, and diarrhea, may contribute to a detrimental cycle of malabsorption, protein depletion, and heightened inflammatory responses (19). Increased vascular permeability and mucosal edema in the GI tract may further impair nutrient absorption, exacerbate weight loss, and disrupt metabolic homeostasis (20). Lumry et al. reported that persistent GI symptoms in HAE significantly reduce dietary intake, exacerbating malnutrition and inflammation (21). Similarly, Santos et al. demonstrated that targeted nutritional interventions, including specialized dietary modifications and supplementation, alleviated symptom severity and improved overall health outcomes in HAE patients (22). These findings suggest that nutritional deficiencies are not merely a consequence of HAE but may actively contribute to disease progression and symptom

exacerbation.

Given these observations, routine nutritional assessments and proactive interventions are imperative in the clinical management of HAE. Longhurst et al. highlighted the benefits of personalized dietary strategies in mitigating GI distress, enhancing patient resilience to acute episodes, and improving QoL (23). Specifically, monitoring PNI levels and addressing deficiencies through targeted supplementation, particularly of proteins, vitamins, and essential micronutrients, may play a crucial role in optimizing disease management (24). Our findings underscore the necessity of integrating nutritional monitoring into the standard clinical approach for HAE, considering its potential impact on disease severity and treatment outcomes.

The correlation between diminished PNI levels and GI involvement underscores the complex effects of nutritional deficiencies in HAE. GI symptoms, including abdominal pain, vomiting, and diarrhea, diminish QoL and may aggravate nutritional deficiencies in a detrimental cycle.

Lumry et al. highlighted that recurrent GI symptoms in patients with HAE substantially diminish their nutritional intake, exacerbating malnutrition and inflammatory responses (21). Santos et al. observed that GI-focused nutritional interventions, including targeted supplementation and dietary alterations, diminished symptom severity and enhanced overall health in their cohort of HAE patients (22). Longhurst et al. emphasized the significance of personalized nutritional care in mitigating GI distress (23). Their findings indicated enhanced resilience to acute episodes and improved patient-reported outcomes post-intervention. These studies collectively emphasize the imperative to tackle GI-related nutritional challenges in the management of HAE.

The noted decline in the C1-INH function linked to inadequate nutritional status reinforces the hypothesis that PNI may intensify complement system dysfunction. The activity of the complement system is influenced by systemic inflammation, which is exacerbated in malnourished conditions (14). This interaction may elucidate the heightened severity and frequency of attacks noted in patients with a low PNI.

Additionally, Ishiguro et al. emphasized the significance of lymphocyte count within the PNI framework, suggesting its potential as a dependable biomarker for immune competence (25). These findings suggest that improving nutritional status could positively impact complement regulation and immune function in HAE patients.

These findings indicate that nutritional status must be prioritized as a critical factor in the management of HAE patients. Nutritional interventions aimed at sustaining elevated PNI levels may decrease attack frequency, enhance the C1-INH functionality, and improve overall patient outcomes. Wiednig et al. established that nutrition-oriented therapeutic strategies improve long-term patient satisfaction and adherence to treatment (5).

Routine evaluation of PNI should be incorporated into clinical practice to enable the prompt identification of at-risk patients. Customized nutritional approaches, encompassing dietary guidance and supplementation, may alleviate the disease burden. Santos et al. emphasized the beneficial impact of nutritional education in managing chronic diseases (22). This could be tailored for HAE patients to improve adherence and results.

Moreover, interdisciplinary cooperation among immunologists, dietitians, and psychologists is essential for formulating a comprehensive strategy for patient care. This strategy could tackle the physical dimensions of nutritional deficiencies and the psychosocial obstacles encountered by HAE patients. Research by Bonner et al. has highlighted the significance of patient-reported outcomes in informing treatment strategies (9). This could potentially facilitate the implementation of customized nutritional interventions.

Utilizing technological innovations like digital health tools and mobile applications may enable real-time tracking of nutritional status and patient compliance with dietary plans. These tools have demonstrated the potential to improve patient engagement and outcomes in various chronic diseases. They may be modified for HAE management (23). Shi et al. demonstrated the prognostic significance of integrated nutritional indices and digital monitoring in chronic disease management, which may be beneficial for HAE patients (26).

Ultimately, catering to the distinct requirements of subpopulations, such as pediatric or geriatric patients with HAE, may enhance treatment strategies. Farkas et al. emphasized the unique challenges encountered by pediatric HAE patients, wherein nutritional deficiencies may negatively affect growth and development (27). Customizing nutritional interventions for these at-risk

populations may avert long-term complications and enhance overall disease outcomes.

The retrospective design of this study limits the ability to establish causal relationships between nutritional status and clinical outcomes in HAE. Future studies with expanded sample sizes and longitudinal designs are necessary to validate these findings. Additionally, research evaluating targeted dietary and nutritional interventions in HAE patients could address critical gaps in knowledge. For instance, investigating the effects of protein-rich diets on the C1-INH function—a hypothesis grounded in the role of albumin (a key component of PNI) in maintaining immune and inflammatory balance—may provide mechanistic insights. While no direct studies have yet explored protein intake's impact on C1-INH activity in HAE, the rationale stems from the observation that hypoalbuminemia, often linked to malnutrition, correlates with systemic inflammation and complement dysregulation (14, 22). Similarly, micronutrient supplementation trials (e.g., vitamin D, zinc) could assess their potential to reduce attack frequency, given emerging evidence of their immunomodulatory roles in other inflammatory conditions (16, 24). Such investigations would clarify whether nutritional optimization directly modulates disease pathophysiology or simply reflects broader systemic health.

In addition to PNI and C1-INH levels, investigating the roles of additional biomarkers (such as albumin, cytokines, and inflammatory mediators) in forecasting clinical outcomes may yield a more thorough comprehension of disease mechanisms. Maurer et al. emphasize that the relationship between bradykinin-induced inflammation and nutritional status requires additional examination (14).

Ultimately, investigating the psychosocial aspects of nutritional deficiencies in HAE is essential. Lumry et al. underscored that inadequate nutritional status and frequent episodes substantially contribute to depression and diminished productivity in HAE patients (21). This highlights the necessity for comprehensive management strategies. Moreover, incorporating patient-reported outcomes into forthcoming studies may yield an enhanced understanding of the effects of nutritional interventions on QoL (9).

This study highlights the substantial influence of nutritional status, as evaluated by PNI, on the clinical outcomes of HAE patients. Regular PNI monitoring and focused nutritional interventions may significantly decrease the attack frequency and disease burden while enhancing QoL. Prospective studies are crucial to validate these findings and discover new therapeutic targets. Healthcare providers can formulate more tailored and effective management strategies to enhance patient outcomes and long-term health by addressing the complex relationship between nutrition and HAE.

Key Findings of the Study

Reduced PNI levels were significantly correlated with elevated attack frequency, extended diagnostic delays, and increased laryngeal and GI involvement in patients with HAE.

Low PNI levels exhibited a negative correlation with monthly attack frequency (Spearman's rho = -0.653, $p < 0.001$) and a positive correlation with the C1-INH function (Spearman's rho = 0.408, $p = 0.001$).

Laryngeal involvement was significantly more common in the low PNI group than in the high PNI group (66.7% vs. 27.8%; $p = 0.003$), suggesting an increased risk of potentially fatal airway obstruction.

GI involvement occurred more frequently in the low PNI group (87.5% vs. 58.3%; $p = 0.005$), significantly affecting patients' QoL.

The findings underscore the essential importance of nutritional status in HAE management. Consistent assessment of PNI levels may enhance clinical outcomes and guide individualized treatment approaches.

Authors' Contributions

Study design, supervision of work and task distribution, interpretation of results: Dr. MEG; ehmet Emin Gerek:Statistical analysis and data interpretation: Associate Professor Dr. Fatih CÇ;ölkesen: Data collection and initial data processing: Dr. TO;uğba Önalan: Data collection and statistical validation: Dr. FAA;atma Arzu Akkuş: Data curation and quality control: Dr. RE;ecep Evcen: Data collection and manuscript drafting support: Dr. MK;ehmet Kılınç: Data curation and literature review: Dr. SK;elim Kahraman: Supervision of work, critical revision of the manuscript, and interpretation of results: SAProfessor Dr. Şevket Arslan:

References

1.Zuraw BL. The pathophysiology of hereditary angioedema. World Allergy Organ J. 2010;3(9 Suppl): S25-S28.

2.Vuzitas A, Sarafoleanu C. Hereditary angioedema - an

otolaryngologist's perspective. Rom J Rhinol. 2016;6(23):133-138.

3.Lima H, Zheng J, Wong D, Waserman S, Sussman GL. Pathophysiology of bradykinin and histamine-mediated angioedema. Front Allergy. 2023;4:1263432.

4.Chalise R, Poudel S, Bist M, Regmi A, Ghimire A, Khanal K. Role of tranexamic acid in NSAIDs induced angioedema. Nepal Respir J. 2023;2(1):31-33.

5.Wiednig M. Successful treatment of acute hereditary angioedema attacks with self-administered icatibant in patients with venous access problems. BMJ Case Rep. 2013:bcr2013009320.

6.Weller K, Groffik A, Magerl M, Tohme N, Martus P, Krause K, et al. Development and construct validation of the Angioedema Quality of Life Questionnaire. Allergy. 2012;67(10):1289-1298.

7.Bowen T, Cicardi M, Farkas H, Bork K, Longhurst H, Zuraw BL, et al. 2010 International consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. Allergy Asthma Clin Immunol. 2010;6(1):24.

8.Kesim BE, Uyguner ZO, Gelincik A, Gökmen NM, Sin A, Karakaya G, et al. The Turkish Hereditary Angioedema Pilot Study (TURHAPS): the first Turkish series of hereditary angioedema. Int Arch Allergy Immunol. 2011;156(4):443-450.

9.Bonner N, Abetz-Webb L, Renault L, Caballero T, Longhurst H, Maurer M, et al. Icatibant Outcome Survey (IOS) International Executive Committee and the Hereditary Angioedema Association (HAEA) Medical Advisory Board. Development and content validity testing of a patient-reported outcomes questionnaire for the assessment of hereditary angioedema in observational studies. Health Qual Life Outcomes. 2015;13(1):92.

10.Mori S, Usami N, Fukumoto K, Mizuno T, Kuroda H, Sakakura N, et al. The significance of the prognostic nutritional index in patients with completely resected non-small cell lung cancer. PLoS One. 2015;10(9):e0136897.

11.Demir A, Çelik Ö, Uygur B, Somuncu MU, Bayram M, Yılmaz E, et al. Malnutrition provides important long-term prognostic information in patients undergoing endovascular abdominal aortic aneurysm repair. Vascular. 2020;29(3):330-339.

12.Wu K, Vadakara J. Rituximab in the treatment of acquired angioedema secondary to marginal zone lymphoma of the spleen. Cureus. 2023;15(3):e36790.

13.Onodera T, Goseki N, Kosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. Nihon Geka Gakkai zasshi. 1984;85(9):1001-1005.

14.Maurer M, Magerl M, Betschel S, Aberer W, Ansotegui IJ, Aygören-Pürsün E, et al. The international WAO/EAACI guideline for the management of hereditary angioedema—the 2021 revision and update. Allergy. 2022;77(7):1961-1990.

15.Jiang N, Deng JY, Ding XW, Ke B, Liu N, Zhang RP, et al. The prognostic nutritional index predicts postoperative complications and long-term outcomes of gastric cancer. World J Gastroenterol. 2014;20(30):10537-10544.

16.Zhang J, Xiao X, Wu Y, Yang J, Zou Y, Zhao Y, et al. Prognostic nutritional index as a predictor of diabetic nephropathy progression. Nutrients. 2022;14(17):3634.

17.Nergiz S, Ozturk U. The effect of the prognostic nutritional index on infection in acute ischemic stroke patients. Medicina (Kaunas). 2023;59(4):679.

18.Zanichelli A, Arcoleo F, Barca MP, Borrelli P, Bova M, Cancian M, et al. A nationwide survey of hereditary angioedema due to C1 inhibitor deficiency in Italy. Orphanet J Rare Dis. 2015;10(1):11.

19.Sharma J, Jindal AK, Banday AZ, Kaur A, Rawat A, Singh S, et al. Pathophysiology of hereditary angioedema (HAE) beyond the SERPING1 gene. Clin Rev Allergy Immunol. 2021;60(3):305-315.

20.Abe A, Kurita K, Hayashi H, Ishihama T, Ueda A. Correlation between the prognostic nutritional index and occlusal status in gastric cancer. Oral Dis. 2020;26(2):465-472.

21.Lumry WR, Settipane RA. Hereditary angioedema: epidemiology and burden of disease. Allergy Asthma Proc. 2020;41:S08-S13.

22.Santos GM, Andrade FM, Marrana C, Gouveia S. The importance of patient empowerment: a clinical case of hereditary angioedema. Cureus. 2023;15(10):e47644.

23.Longhurst H, Bork K. Hereditary angioedema: an update on causes, manifestations and treatment. Br J Hosp Med. 2019;80(7):391-398.

24.Pandey G, Patel B, Dave PS, Patel S, Arora R, Parekh C. Prognostic nutrition index and its significance in advanced ovarian cancer. Indian J Gynecol Oncol. 2020;18(3):85.

25.Ishiguro T, Aoyama T, Ju M, Kazama K, Fukuda M, Kanai H, et al. Prognostic nutritional index as a predictor of prognosis in postoperative patients with gastric cancer. In Vivo. 2023;37(3):1290-1296.

26.Shi J, Liu T, Ge Y, Liu C, Zhang Q, Xie H, et al. Cholesterol-modified prognostic nutritional index (CPNI) as an effective tool for assessing the nutrition status and predicting survival in patients with breast cancer. BMC Med. 2023;21(1):512.

27.Farkas H. Pediatric hereditary angioedema due to C1-inhibitor deficiency. Allergy Asthma Clin Immunol. 2010;6(1):18.

Received: 27 Dec 2024 | **Accepted:** 21 Feb 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 292-301
DOI: 10.54005/geneltip.1607698

ORIGINAL ARTICLE

Evaluation of Health Perceptions with the Use of Traditional and Complementary Medicine in Patients Receiving Radiotherapy

Radyoterapi Alan Hastalarda Geleneksel ve Tamamlayıcı Tıp Kullanımı ile Sağlık Algılarının Değerlendirilmesi

[1]Ulku saygili Duzova, [2]Burak Deli, [2]Fatma nida Karahan, [2]Hamit Basaran, [2]Mursel Duzova

[1]Department of Nursing, Faculty of Nursing, Selcuk University, Konya, Türkiye
[2]Department of Radiation Oncology, Faculty of Medical Faculty, Selcuk University, Konya, Türkiye

Correspondence

Ulku Saygili Duzova,
Department of Nursing, Faculty of Nursing, Selcuk University, Konya, Türkiye

E-Mail: ulkusaygili@selcuk.edu.tr

How to cite ?

Saygili Duzova U, Deli B, Karahan FN, Basaran H, Duzova M. Evaluation of Health Perceptions with the Use of Traditional and Complementary Medicine in Patients Receiving Radiotherapy. Genel Tıp Derg. 2025;35 (2): 292-301

ABSTRACT

Aim: This study aims to evaluate the attitudes of cancer patients receiving Radiotherapy (RT) toward Traditional and Complementary Medicine (TCM), their health perceptions, the TCM methods they employ, and the connections between these factors.
Methods: This descriptive, cross-sectional, and correlational study was conducted with 82 patients receiving treatment at the Radiation Oncology Clinic of Selçuk University Faculty of Medicine Hospital. Data were collected using a demographic information form, the Attitudes Toward Traditional and Complementary Medicine Scale (CACMAS), and the Perception of Health Scale (PHS).
Results: A total of 52.4% of participants reported using TCM methods, with the most commonly used methods being religious practices (87.8%), manipulative approaches (massage and reflexology; 46.4%), phytotherapy (31.7%), meditation (12.2%), hypnosis (4.9%), guided imagery (2.4%), and energy-based approaches (Reiki, bioenergy, and healing energy; 1.2%). Among the participants, 26.8% obtained information from family, 14.7% from TV and social media, 12.2% from healthcare professionals, and 46.3% reported not knowing TCM. The mean CACMAS score was 97.21±30.74, and the mean PHS score was 43.48±9.01. Participants who perceived their economic status as poor had significantly higher CACMAS scores ($p<0.05$). Although no direct strong correlation was found between the CACMAS and PHS scores, strong positive correlations were observed between the 'Cognitive Perspective on Complementary Medicine' subscale and moderate positive correlations with the 'Dissatisfaction with Modern Medicine' and 'Holistic Perspective on Health' subscales.
Conclusions: This study demonstrates that the sociodemographic characteristics, disease stages, and economic conditions of cancer patients undergoing RT may influence their use of TCM methods and health perceptions. Among participants, the most frequently preferred methods were religious practices, manipulative approaches, and phytotherapy, with most individuals utilizing these methods based on information obtained from social media, family, and their social circles.

Keywords: Cancer, Health Perception, Radiotherapy, Traditional and Complementary Medicine

ÖZ

Amaç: Bu çalışma, radyoterapi alan kanser hastalarının Geleneksel ve Tamamlayıcı Tıp'a yönelik tutumlarını, sağlık algılarını ve kullandıkları yöntemleri inceleyerek, bu unsurlar arasındaki ilişki değerlendirmeyi amaçlamıştır.
Gereç ve Yöntemler: Tanımlayıcı, kesitsel ve ilişkisel bir tasarıma sahip olan bu çalışma, Selçuk Üniversitesi Tıp Fakültesi Hastanesi Radyasyon Onkolojisi Kliniği'nde tedavi gören 82 hasta ile gerçekleştirilmiştir. Veriler, tanıtıcı bilgi formu, Geleneksel ve Tamamlayıcı Tıp'a Karşı Tutum (GETAT) Ölçeği ve Sağlık Algısı Ölçeği (SAÖ) kullanılarak toplanmıştır.
Bulgular: Katılımcıların %52.4'ü GETAT yöntemlerini tercih etmiş, en sık kullanılan yöntemler arasında dini uygulamalar (%87.8), manipülatif yaklaşımlar (masaj ve refleksoloji; %46.4), fitoterapi (%31.7), meditasyon (%12.2), hipnoz (%4.9), hayal kurma teknikleri (%2.4) ve enerji yaklaşımları (reiki, bioenerji ve şifa enerjisi; %1.2) yer almıştır. Katılımcıların %26.8'i bilgiyi aileden, %14.7'si TV ve sosyal medyadan, %12.2'si sağlık profesyonellerinden edindiğini, %46.3'ü ise GETAT hakkında bilgi sahibi olmadığını belirtmiştir. CACMAS puan ortalaması 97.21±30.74, PHS puan ortalaması ise 43.48±9.01 olarak bulunmuştur. Ekonomik durumu kötü algılayan bireylerin CACMAS puanlarının anlamlı derecede yüksek olduğu belirlenmiştir ($p<0.05$). GETAT ve SAÖ arasında doğrudan güçlü bir ilişki bulunmamakla birlikte, CACMAS alt boyutlarından "Tamamlayıcı Tıbba Düşünsel Bakış" ile güçlü, "Modern Tıbba Memnuniyetsizlik" ve "Sağlığa Bütüncül Bakış" ile orta düzeyde pozitif ilişkiler saptanmıştır.
Sonuçlar: Bu çalışma, radyoterapi alan kanser hastalarının sosyodemografik özelliklerinin, hastalık evrelerinin ve ekonomik durumlarının GETAT yöntemleri ve sağlık algıları üzerinde etkili olabileceğini ortaya koymuştur. Katılımcılar arasında en sık tercih edilen yöntemler dini uygulamalar, manipülatif yaklaşımlar ve fitoterapi olup, bu yöntemler çoğunlukla sosyal medya, aile ve çevreden edinilen bilgilerle kullanılmaktadır.

Anahtar Kelimeler: Geleneksel ve Tamamlayıcı Tıp, Kanser, Radyoterapi, Sağlık Algısı

Introduction

Traditional and Complementary Medicine (TCM) encompasses methods that have been practiced across various cultures for thousands of years to promote health and well-being, often complementing modern medicine. The primary goal of TCM is to restore body balance through natural and holistic approaches to support patients' health and improve their recovery. In Türkiye, practices such as acupuncture, phytotherapy, hypnosis, ozone therapy, and reflexology are officially regulated by the Regulation on

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

Traditional and Complementary Medicine Practices, published in 2014 (1). However, further research and standardizations are necessary to ensure the efficacy and safety of these practices. Attitudes toward TCM are influenced by cultural background, educational level, and personal beliefs. While some view TCM as complementary to modern medicine, others consider it an alternative to conventional treatments. Certain TCM practices, particularly those of Chinese origin, have gained increasing attention in recent years, with approximately half of the population in developed countries reportedly using these methods (2, 3). Although TCM is often described as offering holistic care that promotes self-care and well-being, concerns persist regarding health risks associated with unregulated practices. For example, improper use of herbal remedies can lead to toxic effects, while neglecting prescribed medications may pose serious risks. Additionally, relying on unreliable information sources may prevent individuals from finding effective and safe solutions to their health issues (3, 4).

Cancer patients resort to TCM for various reasons including personal beliefs, stress reduction, previous positive experiences, physical improvement, perceived safety, recommendations from family and friends, and managing side effects of conventional treatments such as fatigue, nausea, vomiting, and diarrhea (5). For cancer patients, it is crucial to opt for reliable and evidence-based treatment methods and avoid debatable practices. This is particularly important in managing symptoms like pain, which can arise at any stage of the disease. Understanding the TCM methods preferred by cancer patients and their health perceptions is a valuable area of research (6-9). The use of TCM among cancer patients undergoing RT has gained significance due to its potential to alleviate treatment-related side effects and improve quality of life. TCM methods are progressively used to manage symptoms such as fatigue, pain, and anxiety, which are common among this patient group (10). Existing literature indicates that practices like acupuncture, phytotherapy, meditation, and aromatherapy during RT could be potentially beneficial for alleviating physical and psychological symptoms. However, further scientific data are needed to validate the effectiveness and safety of these methods (11). The practice of TCM is closely linked to patients' health perceptions, treatment attitudes, knowledge levels, and cultural beliefs. Identifying the characteristics and motivations of patients who practice TCM during RT may aid in developing a holistic care model (12).

Health perception refers to an individual's thoughts, feelings, expectations, and biases regarding their health. A positive health perception, defined as 'good health perception,' is linked to a greater tendency to adopt and maintain health-promoting behaviors. Conversely, negative health perceptions, or 'poor health perception,' may hinder such behaviors. Individuals with an internal center of control over their health are more likely to prioritize their well-being, adopt healthy lifestyles, and explore alternative care approaches (13). For cancer patients, health perception is particularly complex due to the physical, psychological, and social impacts of the disease. Their health perception is shaped not only by the diagnosis and treatment process but also by their self-efficacy and overall outlook on health. A cancer diagnosis often triggers anxiety, stress, and uncertainty, which can adversely affect quality of life (14). Moreover, the methods employed during treatment and the approach of healthcare professionals play a significant role in shaping health perception. Supportive care, psychological support, and patient education are crucial for enhancing health perception, improving treatment adherence, and boosting overall quality of life (15, 16).

This study aimed to evaluate the health perceptions and TCM usage of patients undergoing RT. During RT, patients' perceptions of treatment and attitudes toward health are crucial factors influencing their adherence to treatment and overall well-being. In addition, the relationship between patients' health perceptions and their inclination toward TCM methods is examined.

What are the average CACMAS scores of patients undergoing RT?

What are the health perceptions of patients receiving RT?

What TCM methods are used by patients undergoing RT?

It is also recommended to add the following research question: Is there a relationship between CACMAS and PHS scores of patients undergoing RT?

Materials and Methods

Design

This descriptive, cross-sectional, and correlational study was conducted between October and December

2024.

Participants and Setting

The participants in this study are cancer patients undergoing treatment at the Radiation Oncology Clinic of Selçuk University Faculty of Medicine Hospital. The sample size was calculated using the G*Power 3.1.9.4 software with a 95% confidence level. Based on the mean score (103.99 ± 22.03) from the 'CACMAS' scale in a study conducted by Dursun et al. (2019), the effect size was determined to be 0.40853, and the required sample size was calculated to be 67 participants with 95% power and a 95% confidence interval (17). Considering potential data loss and participant dropout, a 20% increase was added to the sample size, resulting in a total of 82 participants. Inclusion criteria for the study included patients undergoing RT who were literate and agreed to participate. Exclusion criteria included patients under 18 years of age, illiterate individuals, those who refused to participate, patients with recurrent diseases, individuals without a histologically confirmed diagnosis, and those unable to communicate for any reason.

Data Collection

Data for the study were collected through face-to-face interviews with patients receiving treatment at the Radiation Oncology Clinic of Selçuk University Medical Faculty Hospital, using a structured questionnaire. The data were gathered during outpatient clinic visits of patients undergoing RT. All participants were informed about the study's purpose and content, and their voluntary consent was obtained before administering the questionnaire. The process adhered to ethical principles, and the survey took approximately 15 to 20 minutes to complete. A total of 82 patients participated in the study and completed the questionnaire.

Data Collection Tools

The data about demographic characteristics were collected using a form prepared by the researchers. In addition, the Complementary, Alternative, and Conventional Medicine Attitude Scale (CACMAS) and the Perception of Health Scale (PHS) were used.

Demographic Information Form

The form, developed by the researchers based on the existing literature, included questions about participants' sociodemographic characteristics, disease status, medication usage, and other relevant information (11, 12, 17).

Complementary, Alternative, and Conventional Medicine Attitude Scale (CACMAS)

The CACMAS was developed by McFadden et al. (2010) and adapted into Turkish, with its validity and reliability established by Köse et al. (2018) (18). There is no cutoff score for the scale, and higher scores reflect a more positive attitude toward traditional and complementary medicine (TCM). The scale consists of 22 positive items and 5 negative items. Negative items were reverse-scored during the analysis. The items are scored on a 7-point Likert scale, with 1 indicating 'strongly disagree' and 7 indicating 'strongly agree.' The scale comprises three subscales, which are: 'Cognitive Approach to Complementary Medicine,' 'Dissatisfaction with Modern Medicine,' and 'Holistic View of Health. In this study, the Cronbach's alpha coefficient for the scale was calculated to be 0.747 (4).

Perception of Health Scale (PHS)

The PHS, developed by Diamond et al., consists of 15 items scored on a 5-point Likert scale. The scale includes four subdimensions, which are: 'Center of Control,' 'Self-Awareness,' 'Certainty,' and 'Importance of Health.' The validity and reliability of the Turkish version were established by Kadıoğlu and Yıldız in 2012 (13). Negative items were reverse-scored during the analysis. The total score on the scale ranges from 15 to 75, with higher scores indicating a better health perception. In this study, the Cronbach's alpha coefficient for the scale was calculated to be 0.745.

Data Analysis

The data were analyzed using version 22.0 of the Statistical Package for the Social Sciences (SPSS). The Kolmogorov-Smirnov test was used to assess the normality of the data distribution. Descriptive statistics, such as frequency, percentage, mean, and standard deviation were used. For comparative analyses, one-way ANOVA and Pearson correlation were used. The absolute values of Pearson correlation coefficient (r) were interpreted as follows: 0–0.19 = very weak, 0.2–0.39 = weak, 0.4–0.59 = moderate, 0.6–0.79 = strong, and 0.8–1 = very strong correlation (19). Statistical significance was considered at $p < 0.05$.

Ethical Considerations

Patients were evaluated after the approval was obtained from the Ethics Committee (Decision No: 2024/646). The study followed the principles of the Declaration of Helsinki and adhered to ethical

guidelines throughout all stages. Participants were informed about the purpose of the study and the data collection tools and their consent was obtained in the first question of the online survey. Permission to use the scales was obtained from the authors via email.

Results

The distribution of marital status, gender, place of residence, and economic status perception is considered. Regarding marital status, 76.8% of participants were married, and 23.2% were single. In terms of gender, 45.1% of the participants were female and 54.9% were male. Regarding place of residence, 46.3% of the participants lived in urban areas, 31.7% in districts, and 22.0% in villages. Concerning the perception of economic status, 15.8% perceived their economic status as good, 42.7% as moderate, and 41.5% as poor. Regarding marital status, the mean CACMAS score for married individuals was 96.95±22.08, while the mean PHS score was 44.04±9.63. As for single individuals, the mean CACMAS score was 96.64±21.21, while the mean PHS score was 41.63±6.39. In terms of gender, females had a mean CACMAS score of 97.23±19.59 and a mean PHS score of 41.73±7.48, while males had a mean CACMAS score of 96.61±23.57 and a mean PHS score of 44.93±9.95. Based on place of residence, individuals living in urban areas had a mean CACMAS score of 95.05±23.97 and a mean PHS score of 41.03±6.32. Those living in districts had a mean CACMAS score of 99.38±23.39 and a mean PHS score of 46.65±12.55, while individuals in villages had a mean CACMAS score of 97.06±12.35 and a mean PHS score of 44.11±6.25. Concerning the perception of economic status, individuals perceiving their economic status as good had a mean CACMAS score of 90.03±17.35 and a mean PHS score of 42.67±7.18. Individuals who

Table 1. Distribution of Mean Scores of CACMAS and PHS According to Socio-Demographic Characteristics of Patients

Variables	Mean±SD	Min-Max	CACMAS Mean±SD	PHS Mean±SD
Age	62.93±12.67	28-83		
Test Value p			r: -0.198 p: 0.099	r: -0.029 p< 0.799
	n	**%**		
Marital Status				
Married	63	76.8	96.95±22.08	44.04±9.63
Single	19	23.2	96.64±21.21	41.63±6.39
Test Value p			t: 0.051 p: 0.960	t: 1.025 p: 0.309
Gender				
Female	37	45.1	97.23±19.59	41.73±7.48
Male	45	54.9	96.61±23.57	44.93±9.95
Test Value p			t: 0.124 p: 0.902	t: -1.615 p: 0.110
Place of residence				
Urban [1]	38	46.3	95.05±23.97	41.03±6.32
District [2]	26	31.7	99.38±23.39	46.65±12.55
Rural[3]	18	22.0	97.06±12.35	44.11±6.25
Test Value p			F: 0.298 P: 0.744	F: 3.234 p: 0.045
Significance*				1<2
Perceived economic status				
High[1]	13	15.8	90.03±17.35	42.67±7.18
Moderate[2]	35	42.7	99.83±28.51	41.91±11.51
Low[3]	34	41.5	102.88±21.78	45.44±6.11
Test Value p			F: 3.323 p< 0.045	F: 1.407 p: 0.251
Significance*			3>2	

t: Independent groups t-test. F: ANOVA test. r: Pearson correlation *Tukey HSD, CACMAS: Alternative and Conventional Medicine Attitude Scale, PHS: Perception of Health Scale

perceived their economic status as moderate had a mean CACMAS score of 99.83±28.51 and a mean PHS score of 41.91±11.51, while those who perceived their economic status as poor had a mean CACMAS score of 102.88±21.78 and a mean PHS score of 45.44±6.11. A statistically significant difference was found in the PHS scores based on place of residence, with individuals living in districts (46.65±12.55) scoring significantly higher than those in urban areas (41.03±6.32) ($p<0.05$). Regarding the perception of economic status, individuals who perceived their economic status as poor had significantly higher CACMAS scores (102.88±21.78) compared to those with a moderate perception of economic status (99.83±28.51) ($p<0.05$) (Table 1).

The study also assessed the distribution of histopathological stage, cancer type, treatment method, comorbidity, and smoking status. Among the participants, 43.9% were in stage 2, 31.7% in stage 3, and 13.4% in stage 4. Regarding cancer type, prostate cancer had the highest proportion at 32.9%, while skin cancer had the lowest (3.7%). Regarding treatment methods, 55.6% underwent only RT, while 44.4% underwent both RT and surgery. Comorbidities were present in 48.8% of participants, while 51.2% had no comorbidities. Additionally, 76.8% of participants

Tablo 2. Distribution of Mean CACMAS and PHS Scores According to Patients' Health Characteristics

Variables	n	%	CACMAS Mean±SD	PHS Mean±SD
Histopathological Stage				
Stage I	9	11.0	92.22±20.41	38.88±7.52
Stage II	36	43.9	96.77±21.69	42.25±6.83
Stage III	26	31.7	101.56±22.23	48.26±10.90
Stage IV	11	13.4	89.800±22.35	40.00±7.38
Test Value p			F: 0.872 p: 0.460	F: 4.517 p: 0.006
Significance*				4>3>2
Cancer Type				
Lung Cancer	7	8.5	93.85±26.79	44.28±7.45
Breast Cancer	17	20.7	97.12±22.17	43.76±7.36
Gynecological Cancer	13	15.9	101.69±17.89	39.38±7.21
Prostate Cancer	27	32.9	96.44±23.77	46.55±11.58
Head-Neck Cancer, Sarcoma	15	18.3	97.07±21.48	40.66±6.69
Skin Cancer	3	3.7	85.00±13.89	44.33±4.04
Test Value p			F: 0.321 p: 0.899	F: 1.526 p: 0.192
Treatment				
RT	65	55.6	94.56±21.25	44.67±10.36
RT+Surgery	52	44.4	99.90±25.46	41.95±7.01
RT+Surgery+CT			98.83±18.90	42.44±7.49
Test Value p			F: 0.491 p: 0.614	F: 0.794 p: 0.456
Presence of Comorbidities				
Yes	40	48.8	95.61±19.99	42.20±6.24
No	42	51.2	98.12±23.54	44.71±10.96
Test Value p			t: -0.510 p: 0.611	t: -1.268 p: 0.209
Smoking Status				
Yes	19	23.2	95.68±21.70	42.68±6.29
No	63	76.8	97.26±21.94	43.73±9.71
Test Value p			t: -0.275 p: 0.784	t: -0.441 p: 0.660

t: Independent groups t test. F: ANOVA test. r: pearson korelasyon, CACMAS: Alternative and Conventional Medicine Attitude Scale, PHS: Perception of Health Scale, RT: Radiotherapy, CT: Chemotherapy

reported being non-smokers, while 23.2% were smokers. Based on histopathological stage, the mean CACMAS and PHS scores were as follows: stage 1 (92.22±20.41, 38.88±7.52), stage 2 (96.77±21.69, 42.25±6.83), stage 3 (101.56±22.23, 48.26±10.90), and stage 4 (89.80±22.35, 40.00±7.38). A significant difference was found in PHSS scores between stages, with stage 1 having significantly lower scores than stage 2 (p=0.006). Regarding cancer type, the highest CACMAS score was observed in gynecological cancers (101.69±17.89), while the lowest was found in skin cancer (85.00±13.89). For PHS scores, the highest was observed in prostate cancer (46.55±11.58), while the lowest was found in gynecological cancers (39.38±7.21). However, these differences were not statistically significant (p > 0.05). Regarding treatment methods, participants undergoing only RT had a mean CACMAS score of 94.56±21.25 and a mean PHS score of 44.67±10.36. Those undergoing both RT and surgery had a mean CACMAS score of 99.90±25.46 and a mean PHS score of 41.95±7.01, with no significant differences (p>0.05). Participants with comorbidities had a mean CACMAS score of 95.61±19.99 and a mean PHS score of 42.20±6.24. On the other hand, those without comorbidities had a mean CACMAS score of 98.12±23.54 and a mean PHS score of 44.71±10.96. No significant differences were observed (p>0.05). Smokers had a mean CACMAS score of 95.68±21.70 and a mean PHS score of 42.68±6.29, while non-smokers had a mean CACMAS score of 97.26±21.94 and a mean PHS score of 43.73±9.71. No significant differences were found (p>0.05) (Table 2).

Among the participants, 53.7% reported knowing CACMAS, while 46.3% stated they did not. Sources of information included family (26.8%), TV/social media (14.7%), and healthcare professionals (12.2%). A total of 46.3% of participants reported not knowing CACMAS. Among the participants, 52.4% preferred using CACMAS methods, and 59.8% believed these methods were beneficial. Regarding the frequency of use, 31.7% reported using CACMAS whenever possible, 8.5% used it 1–2 times a week, and 17.1% used it 1–2 times a month. Additionally, 61% of participants reported being aware of the risks associated with using CACMAS. Reasons for use included recommendations from others (15.9%), challenges of medical treatments (4.9%), side effects (2.4%), and perceived safety of alternative treatments (9.8%). While undergoing RT, 12.2% of participants reported using CACMAS methods, with religious practices (87.8%) being the most common, followed by phytotherapy (31.7%) and manipulative approaches (46.4%). Other methods such as meditation, hypnosis, imagery, and energy therapies were used less frequently (Table 3).

Table 3. Patients' TCM Usage Status

Variables	n	%
Knowledge About TCM		
Yes	44	53.7
No	38	46.3
Source of Information on TCM		
Family Members	22	26.8
TV and Social Media	12	14.7
Healthcare Professionals	10	12.2
Unaware of the Source	38	46.3
Preference of TCM		
Yes	43	52.4
No	39	47.6
Perception of TCM as Beneficial		
Yes	49	59.8
No	33	40.2
TCM Usage Frequency		
As Frequently as Possible	26	31.7
1–2 Times per Week	7	8.5
1–2 Times per Month	14	17.1
Awareness of Risks Associated with TCM Use		
Yes	50	61.0
No	32	39.0
Reasons for TCM Use		
Social Influence and Recommendations	13	15.9
Challenges in Conventional Medical Treatment	4	4.9
Managing Side Effects of Medical Treatment	2	2.4
Perception of Alternative Treatments as Safe	8	9.8
TCM Use During RT		
Yes	10	12.2
No	72	87.8

TCM Methods	Yes	No	Yes	No
Meditation	n	n	%	%
Religious Practices	4	78	4.9	95.1
Hypnosis	72	10	87.8	12.2
Relaxation Exercise	2	80	2.4	97.6
Visioning	15	67	18.3	81.7
Manual Therapies: Massage, Physical	8	74	9.8	90.2
Exercise Energy-Based Therapies: Reiki,	38	44	46.4	53.7
Acupressure, Reflexology	7	75	8.5	91.5
Alternative Systems I: Acupuncture	7	75	8.5	91.5
Alternative Systems II: Leech Therapy	6	76	7.8	92.2
Phytotherapy	26	56	31.7	68.3

TCM: Traditional and Complementary Medicine, RT: Radiotherapy

The average CACMAS Scale score was found 97.21±30.74. Subscale scores were as follows: Cognitive Approach to Complementary Medicine (28.81±11.74), Dissatisfaction with Modern Medicine (23.13±10.45), and Holistic View of Health (45.21±9.99). The mean PHS scale score was 43.48±9.01, with subscale scores as follows: Center of Control (16.47±6.50), Self-Awareness (7.60±2.54), Certainty (13.40±3.49), and Importance of Health (6.00±2.24) (Table 4).

Table 4. Distribution of Patients' Mean Scores Across CACMAS and PHS Subscales

Scales and Subdimensions	Number of Items	Mean±SS	Min-Max	Cronbach alpha
CACMAS	**27**	**97.21±30.74**	**51-158**	**0.747**

Intellectual View of Complementary Medicine	8	28.81±11.74	8-56	
Dissatisfaction with Modern Medicine	10	23.13±10.45	10-57	
Holistic View of Health	9	45.21±9.99	9-63	
PHS	**15**	**43.48±9.01**	**27-96**	**0745**
Center of Control	5	16.47±6.50	6-61	
Self-Awareness Certainty Importance of Health	3 4 3	7.60±2.54 13.40±3.49 6.00±2.24	3-13 4-20 3-14	

CACMAS: Alternative and Conventional MedicineAttitude Scale, PHS: Perception of Health Scale

The CACMAS showed a strong positive correlation with a Cognitive Approach to Complementary Medicine (r = .839), a moderate correlation with Dissatisfaction with Modern Medicine (r = .592), and a moderate correlation with Holistic View of Health (r = .557). The PHS Scale showed a strong positive correlation with the Center of Control (r = .869), a moderate correlation with the Certainty subscale (r = .620), and a weak correlation with the Importance of Health subscale (r = .382). A weak correlation was found between the CACMAS and the PHS (r = .217), with a significant correlation observed between Certainty and the PHS Scale (r = .251). Additionally, positive correlations were found between Certainty and Center of Control (r = .468) and between the Importance of Health and Self-Awareness (r = .404) (Table 5).

Discussion

Table 5. Correlation Between CACMAS and PHS Scores

	1	2	3	4	5	6	7	8	9
CACMAS Scale	1								
Intellectual View of Complementary Medicine	.839**	2							
Dissatisfaction with Modern Medicine	.592**	.313**	3						
PHS Holistic View of Health	.557**	.297**	-0.151	4					
Control Center	0.164	0.213	0.117	-0.019	5				
PHS Perception of Health Scale	0.217	0.21	0.189	0.025	.869**	6			
PHS Importance of Health	-0.018	-0.065	0.045	0.189	0.042	.382**	7		
Self-Awareness	0.029	-0.041	0.026	0.065	-0.16	0.132	.404**	8	
Certainty	.251*	0.218	.222*	0.055	.468**	.620**	-0.03	-.350**	9

r: Pearson correlation coefficient. *p<0.05. **p<0.001, CACMAS: Alternative and Conventional MedicineAttitude Scale, PHS: Perception of Health Scale

This study examines the relationship between patients' attitudes toward complementary and alternative medicine use, their health perceptions, and demographic characteristics. The findings provide important insights into the relationships between patients' perspectives on TCM, their dissatisfaction with modern medicine, and their holistic approach to health and health perceptions.

This study explores the use of TCM among patients undergoing RT by examining its prevalence and the reasons for their preference. The findings reveal that most patients (87.8%) use religious practices as the primary TCM method. This suggests that religious practices have a significant influence on individuals' perceptions of spiritual and physical well-being. Understanding the role of religious practices in health perception within Turkish culture can provide valuable guidance in clinical settings. Healthcare professionals, particularly those in culturally and religiously rich areas like Konya, should acknowledge patients' pursuit of spiritual healing and shape treatment processes accordingly (14). Integrating religious practices with modern medicine could improve patient compliance and treatment outcomes. The existing literature supports the frequent use of religious rituals as a coping mechanism, particularly among individuals with cancer (5, 20). Manipulative approaches (e.g., massage, exercise) were the second most commonly preferred method, with a prevalence of 46.4%. This highlights the common preference for methods that promote physical relaxation and stress management. However, the usage rates of energy-based approaches (e.g., Reiki, acupressure, reflexology) and alternative systems (e.g., acupuncture, leech therapy) remained notably low (8.5% and 7.8%, respectively), suggesting limited societal awareness or potential concerns about their reliability. Accessibility and cost factors may also contribute significantly to these low usage rates (21). These findings are consistent with the existing literature (5).

The study found that the use of TSM during RT was relatively low at 12.2%. This suggests that healthcare professionals' warnings about the safety and efficacy of TCM have had a significant influence on patients.

During intensive treatment processes such as RT, patients tend to rely more on modern medicine and avoid alternative methods. According to the existing literature, the use of TSM in oncology is often limited due to a lack of communication with healthcare professionals or insufficient information about the side effects of these methods (4). The most common reason reported by patients for using TCM was recommendations from their social environment (15.9%), highlighting the clear influence of social circles on individuals' health behaviors. Additionally, reasons such as the challenges of medical treatment (4.9%) and the development of side effects (2.4%) were less commonly cited as reasons for opting for CACMAS. These findings demonstrate that while patients primarily trust modern medicine, they may evaluate complementary approaches under the influence of their social environment (5).

The study found no significant effect of age, marital status, or gender on the mean CACMAS scores. However, the place of residence variable showed a significant difference in health perception scores. Patients residing in district-level areas had higher health perception scores, suggesting that these individuals may have better access to healthcare services or a more consistent approach to health-related matters. A study conducted in Ghana on rural and urban populations revealed differences in health perceptions between rural and urban residents (22). Similarly, individuals with a 'poor' perception of their economic status had higher CACMAS scores, suggesting that economic conditions might drive individuals to seek alternative treatments. Another research conducted in Japan examined how social determinants influence the use of complementary and alternative medicine, finding that socioeconomic factors play a decisive role in TCM usage (23).

Perception of Health Scale (PHS) scores varied significantly across cancer stages. Patients in stage 3 had higher PHS scores, suggesting that these individuals may prioritize their health more or be more focused on combating their disease. These results align closely with the literature (24). However, there was no significant difference in CACMAS across cancer stages, suggesting that patients' inclination towards TCM might be independent of their disease stage. The literature indicates that as cancer progresses, patients' search for spiritual support and health-related self-awareness tends to increase, which is consistent with our findings (14). There was no significant difference in either CACMAS or PHS scores based on cancer type, suggesting that patients with different types of cancer exhibit similar attitudes toward complementary and alternative medicine. However, the finding that breast cancer patients' CACMAS scores were similar to those of other groups suggests that this group might also be open to complementary therapies alongside modern medicine. Literature supports that breast cancer patients are more active in seeking psychological support and tend to opt for alternative methods during this process (5, 14).

No significant difference was found in CACMAS based on treatment types such as RT or surgery. However, patients undergoing only RT had slightly lower CACMAS, suggesting that this group relies more on modern medicine. Patients undergoing intensive treatment processes, such as RT combined with surgery or chemotherapy, may seek complementary support to alleviate side effects during treatment. The presence of comorbidities did not have a statistically significant effect on CACMAS or PHS scores. However, the lower CACMAS scores among patients with comorbidities suggest that these individuals may rely more on modern treatments. The presence of additional diseases may increase trust in conventional treatments or reduce interest in alternative methods. The literature indicates that individuals with multiple conditions typically show greater trust in modern medicine and limited interest in alternative approaches. No significant difference was found in PHS scores based on smoking status. However, patients who smoked had slightly lower PHS scores, implying that smoking may negatively affect their health perception. The literature frequently emphasizes that smoking can reduce overall health awareness and negatively impact health perceptions. Smoking should be regarded as a limiting factor in both disease management and the inclination toward alternative methods.

No significant correlation was found between the CACMAS and the PHS. However, a strong positive relationship was found between the subscales 'Cognitive Perspective on Complementary Medicine' and 'Dissatisfaction with Modern Medicine' in the CACMAS. This suggests that individuals dissatisfied with modern medicine are more likely to adopt a positive attitude toward complementary medicine. Additionally, significant correlations were found between the "Holistic Perspective on Health" subscale and the other TCM subscales. These findings suggest that individuals' attitudes toward TCM are connected

to a holistic view of health. The findings of our study reveal the relationship between patients' attitudes toward complementary and alternative medicine, their health perceptions, and their demographic characteristics. In particular, the fact that religious practices are the most frequently preferred TCM methods highlights how the perception of spiritual and physical well-being in Turkish culture is influenced by such practices. In this context, it is recommended that healthcare professionals recognize patients' search for spiritual support and tailor their treatment processes with cultural sensitivity. However, it is crucial that the healthcare team is adequately informed about safe TCM methods and provides guidance to patients in this regard. It is stated in the literature that oncology patients generally do not communicate adequately with healthcare professionals about the use of TCM or lack sufficient information about the side effects of these methods. For patients to safely use TCM methods alongside modern medical treatments, it is essential to enhance the knowledge of healthcare professionals. It is recommended that courses on TCM applications be incorporated more extensively into medical and nursing education programs, continuous education programs for the healthcare team be organized, and guideline documents be created on this subject. Additionally, regulations should be established to ensure the safe use of TCM within healthcare systems. Establishing TCM consultancy units in healthcare institutions, where patients can access reliable information, and integrating evidence-based methods into clinical guidelines would be an important step. Thus, patients can benefit from CAM methods without disrupting their modern medical treatments. Such arrangements will enhance patient safety and enable healthcare professionals to guide patients consciously.

Conclusion

This study significantly contributes to understanding how patients perceive the balance between modern medicine and complementary medicine, and how this perception influences their health views. "Healthcare professionals should develop effective communication strategies, especially with individuals dissatisfied with modern medicine, and provide reliable information about complementary medicine. Additionally, given the impact of demographic factors such as economic status and place of residence on TCM usage, it is recommended that local health policies be adjusted to address these factors. The cultural heritage of Konya and Mevlana has profoundly influenced the Turkish community's perception of both spiritual and physical health. In this context, future research could further investigate the role of religious and spiritual practices in the use of TCM. Furthermore, understanding and incorporating spiritual practices into treatment processes could contribute positively to individuals' physical and mental well-being.

Conflict of interest

The author declares that there is no conflict of interest.

Financial support

There was no funding for this study.

Acknowledgments

The authors would like to thank all the participants.

References

1. Akalın B, İrban A, Özargun G. Türkiye'de geleneksel ve tamamlayıcı tıp uygulamalarının mevcut standartları ve iyileştirme önerileri. Sağlık Profesyonelleri Araştırma Dergisi. 2023;5(1):49-69.

2.Arevalo MVPN, Robredo JPG, Valenzuela S, et al. The role of traditional, complementary, and alternative medicine in cancer care in the Philippines. Chin Clin Oncol. 2022;11(6):49-.

3.Hoenders R, Ghelman R, Portella C, et al. A review of the WHO strategy on traditional, complementary, and integrative medicine from the perspective of academic consortia for integrative medicine and health. Front Med. 2024;11:1395698.

4.Kıskaç N, Kıskaç M, Zorlu M, Karatoprak C, Çakırca M. Erişkin bireylerin geleneksel ve tamamlayıcı tıp tutumlarının değerlendirilmesi. MAS J Appl Sci. 2024;9(1):127-134.

5.Yousefi M, Reihani H, Heydari M, Nasimi Doost Azgomi R, Hashempur MH. Complementary and alternative medicine use among cancer patients in Iran: A systematic review. Prev Med Rep. 2024;39:102644.

6.Ashrafizadeh H, Rassouli M. Traditional, complementary, and alternative medicine in cancer care: Challenges and opportunities. Asia Pac J Oncol Nurs. 2024;11(1).

7.Choi S, Karki Kunwor S, Im H, et al. Traditional and complementary medicine use among cancer patients in Asian countries: A systematic review and meta-analysis. Cancers. 2024;16(18):3130.

8.Samuels N, Ben-Arye E, eds. Integrative medicine for cancer-related pain: A narrative review. Healthcare. 2024.

9.Liu J, Mao JJ, Wang XS, Lin H. Evaluation of Traditional Chinese Medicine herbs in oncology clinical trials. Cancer J. 2019;25(5):367-371.

10.Fakhoury KR, Hu J, Kim E, et al. An integrative medicine

educational program for radiation oncology patients: Patient-reported outcomes. Adv Radiat Oncol. 2024;9(2):101350.

11.Lettner S, Kessel KA, Combs SE. Complementary and alternative medicine in radiation oncology. Strahlenther Onkol. 2017;193(5):419-426.

12.Pihlak R, Liivand R, Trelin O, et al. Complementary medicine use among cancer patients receiving radiotherapy and chemotherapy: Methods, sources of information, and the need for counseling. Eur J Cancer Care. 2014;23(2):249-254.

13.Kadıoğlu H, Yıldız A. Sağlık Algısı Ölçeği'nin Türkçe çevriminin geçerlilik ve güvenilirliği. Turkiye Klin J Med Sci. 2012;32(1):47-53.

14.Duzova US, Duzova M, Altinel B. The effect of sleep quality on attitudes toward death in breast cancer survivors. Support Care Cancer. 2024;32(10):1-12.

15.Menekli T, Doğan F, Elkıran ET. Kanserli hastalarda hastalık algısı ve yaşam kalitesi. Harran Univ Med J. 2020;17(3):467-474.

16.Danışkan İ, Bilgiç D, Okumuş H. Jinekolojik onkoloji hastalarının destekleyici bakım gereksinimleri ve etkileyen faktörler. Jinekoloji-Obstetrik Neonatoloji Med J. 2024;21(3):196-205.

17.Dursun Sİ, Vural B, Keskin B, Kaçar HK, Beyhan A, Kadıoğlu H. Yetişkinlerde geleneksel/tamamlayıcı tıp tutumu ile sağlık okuryazarlığı ve sağlık algısı arasındaki ilişki. Halk Sağlığı Hemşireliği Dergisi. 2019;1(1):1-10.

18.Elif K, Ekerbiçer HÇ, Erkorkmaz Ü. Complementary, alternative, and conventional medicine attitude scale: Turkish validity reliability study. Sakarya Tıp Dergisi. 2018;8(4):726-736.

19.Swinscow TDV, Campbell MJ. Statistics at square one. London: BMJ; 2002.

20.Mercadante S, Adile C, Ricci M, et al. The role of religiosity in symptom expression of advanced cancer patients. Am J Hosp Palliat Care. 2022;39(6):705-709.

21.Marcolin ML, Tarot A, Lombardo V, et al. The effects of foot reflexology on symptoms of discomfort in palliative care: A feasibility study. BMC Complement Med Ther. 2023;23(1):66.

22.Boateng R, Yawson AE, Adoma PO. Rural-urban and socio-demographic differentials in perceived health state among aging population in Ghana. J Health Popul Nutr. 2023;42(1):92.

23.Miwa J, Ichikawa R, Shibuya A, et al. Social determinants affecting the use of complementary and alternative medicine in Japan: An analysis using the conceptual framework of social determinants of health. PLoS One. 2018;13(7):e0200578.

24.Chung KC, Muthutantri A, Goldsmith GG, et al. Symptom impact and health-related quality of life (HRQoL) assessment by cancer stage: A narrative literature review. BMC Cancer. 2024;24(1):884.

25.Choi S, Karki Kunwor S, Im H, Choi D, Hwang J, Ahmed M, Han D. Traditional and complementary medicine use among cancer patients in Asian Countries: A Systematic Review and Meta-Analysis. Cancers (Basel). 2024 Sep 11;16(18):3130. doi: 10.3390/cancers16183130.

Received: 14 Nov 2024 | **Accepted:** 06 Mar 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 302-308
DOI: 10.54005/geneltip.1584179

ORIGINAL ARTICLE

The Relationship between The Thoughts of Hemodialysis Patients on Sleep Quality, and Depression and Anxiety Levels

Hemodiyaliz Uygulanan Hastaların Uyku Kalitesine İlişkin Görüşlerinin Depresyon ve Anksiyete Düzeyleri ile İlişkisi

[1]Selvi Ceran, [2]Arda Bağcaz, [2]Bahar Güçiz Doğan

[1]Başkent University Faculty of Medicine, Department of Psychiatry, Ankara, Türkiye
[2]Hacettepe University Faculty of Medicine, Department of Psychiatry, Ankara, Türkiye
[3]Hacettepe University Faculty of Medicine, Department of Public Health, Ankara, Türkiye

Correspondence

Selvi Ceran, MD
Başkent University Faculty of Medicine, Department of Psychiatry
064901 Bahcelievler, Ankara, Türkiye

E-Mail: selviceran@hotmail.com

How to cite ?

Ceran S, Bağcaz A, Güçiz doğan B. The Relationship between The Thoughts of Hemodialysis Patients on Sleep Quality, and Depression and Anxiety Levels. Genel Tıp Derg. 2025;35 (2): 302-308

ABSTRACT

Background/aims: This study aimed to determine the level of sleep quality among patients undergoing hemodialysis, assess their awareness of, and examine the relationship between sleep quality and levels of depression and anxiety symptoms, as well as the demographic characteristics and clinical features of the disease.
Methods: In this descriptive study, the Pittsburgh Sleep Quality Index (PSQI), Beck Anxiety Inventory (BAI), and Beck Depression Inventory (BDI) were administered to 123 hemodialysis patients. Factors associated with sleep quality were analyzed using univariate analysis, considering age, sex, education level, disease duration, hemodialysis duration, and possible depression and anxiety as related variables. A correlation analysis was conducted to examine the relationship between sleep quality and anxiety and depression scores.
Results: The percentage of poor sleep quality among the patients was 47.2%, with 12.2% showing signs of possible depression and 30.1% indicating possible anxiety disorder. Notably, among those with poor sleep quality, only 40.0% perceived their sleep quality as poor. Patients with poor sleep quality had significantly higher levels of depression ($U = 850.500$, $p < .001$) and anxiety symptoms ($U = 820.500$, $p < .001$).
Conclusion: A significant proportion of hemodialysis patients experience poor sleep quality, yet nearly half of them are unaware of it. There is a strong relationship between diminished sleep quality and elevated mental health symptoms in this population. Routine sleep quality evaluation and collaboration with psychiatric professionals appear essential for this patient group.

Keywords: Anxiety, depression, hemodialysis, sleep quality

ÖZ

Amaç: Bu çalışmanın amacı hemodiyaliz uygulanan hastalarda uyku kalitesi düzeylerini, hastaların buna ilişkin farkındalıklarını belirlemek, uyku kalitesinin depresyon belirti düzeyi, anksiyete belirti düzeyi, demografik özellikler ve hastalığın klinik özellikleri ile ilişkisini incelemektir.
Yöntem: Bu tanımlayıcı çalışmada, 123 hemodiyaliz hastasına Pittsburgh Uyku Kalitesi İndeksi (PSQI), Beck Anksiyete Envanteri (BAI) ve Beck Depresyon Envanteri (BDI) uygulanmıştır. Uyku kalitesi ile ilişkili faktörler; yaş, cinsiyet, eğitim düzeyi, hastalık süresi, hemodiyaliz süresi ve olası depresyon ve anksiyete değişkenleri göz önünde bulundurularak tek değişkenli analiz ile incelenmiştir. Uyku kalitesi ile anksiyete ve depresyon skorları arasındaki ilişkiyi değerlendirmek için korelasyon analizi yapılmıştır.
Bulgular: Kötü uyku kalitesi düzeyi %47,2, olası depresyon %12,2, olası anksiyete bozukluğu %30.1 olarak saptanmıştır. Uyku kalitesi kötü olarak belirlenen hastaların sadece %40,0'ı uyku kalitelerinin kötü olduğu görüşündedir. Bu grupta depresyon ($U=850,500$, $p<,001$) ve anksiyete belirti şiddeti ($U=820.500$, $p<,001$) daha yüksektir.
Sonuç: Hastaların önemli bölümünün uyku kalitesinin kötü olduğu, ancak bu hastaların yaklaşık yarısının uyku kalitelerinin kötü olduğunun farkında olmadığı görülmüştür. Hemodiyalize giren hastalarda uyku kalitesinin azalması ile eşlik eden ruhsal belirtiler arasında kuvvetli bir ilişki mevcuttur. Bu gruptaki hastaların uyku kalitesi açısından rutin olarak değerlendirilmesi ve psikiyatri hekimleri ile işbirliği içinde çalışılması önemlidir.

Anahtar Kelimeler: Anksiyete, depresyon, hemodiyaliz, uyku kalitesi

Introduction

Patients with end-stage renal disease (ESRD) commonly experience sleep disorders (1). In the general population, the prevalence of insomnia is reported to be between 3-29%; however, in patients with ESRD undergoing hemodialysis, this prevalence increases significantly to 50-75%. Similarly, sleep apnea, which affects 3-7% of the general population, is seen in 25-45% of hemodialysis patients. The prevalence of restless legs syndrome, typically around 3% in the general population, rises to 20-30% among those undergoing hemodialysis (2-6). Additionally, sleep quality in hemodialysis patients has been found to decline compared to the pre-hemodialysis stage (7). These patients also experience higher rates of daytime sleepiness than the general population (8).

It has been reported that healthcare personnel working with hemodialysis patients often fail to recognize the symptoms and severity of sleep disorders in this population (9). However, unrecognized and untreated sleep problems in hemodialysis patients are associated with increased mortality and morbidity, accelerated

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

aging, and a heightened risk of cardiovascular disease (10-13). Additionally, these sleep disturbances are linked to higher levels of fatigue and depression (14-15). Identifying sleep problems and their contributing factors in hemodialysis patients is crucial, as addressing these issues can significantly reduce mortality and morbidity.

Sleep problems are known to be common symptoms of depression and anxiety. Hemodialysis patients experience higher rates of anxiety disorders and stress compared to the general population (15-16). However, there are limited studies that comprehensively examine the interplay between these psychological factors—such as anxiety and depression—and the clinical characteristics related to hemodialysis, which may contribute to the etiology of insomnia in this patient group.

This study aimed to determine the level of poor sleep quality among hemodialysis patients and assess their awareness of sleep issues. Additionally, it sought to explore the relationship between sleep quality and levels of depression and anxiety symptoms, as well as demographic and clinical characteristics.

Method

The population of this descriptive study comprised 190 individuals diagnosed with ESRD who were receiving hemodialysis at two dialysis centers affiliated with Selcuk University Faculty of Medicine. It was aimed to reach all patients (n=190) treated at the aforementioned centers. However, 28 individuals (14.7%) were excluded due to dementia, other severe psychiatric conditions, mental disabilities, or significant visual and hearing impairments. Additionally, 39 patients (20.6%) declined to participate in the study. As a result, the final sample consisted of 123 participants (64.7%).

Among the participants, seven (6.3%) were illiterate. These patients only completed the questionnaire administered through face-to-face interviews and answered the questions asked by the researchers to assess subjective sleep quality. They did not complete the self-report scales (PSQI, BAI, and BDI).

Additionally, three participants (2.4%) were excluded from the comparative analyses based on the PSQI due to missing data; one of these individuals also had incomplete responses on the BAI and BDI. As a result, the comparative analyses were conducted with data from 113 participants (59.5%). There were no significant differences in age or sex distribution between the 123 included participants and the 67 excluded individuals ($p = 0.78$ and $p = 0.86$, respectively).

Ethical approval for the study (approval numbers KA18/31 and 18/46) was obtained from the Non-Interventional Clinical Research Ethics Committee of Selcuk University Faculty of Medicine.

Measurements

The sociodemographic data were collected using a questionnaire prepared by the researchers. This form gathered information on age, sex, marital status, employment status, physical and mental illnesses, family history of illness, smoking, and alcoholic beverage use, duration since the diagnosis of chronic kidney disease, etiology of the disease, frequency of hemodialysis sessions, and duration of hemodialysis treatment. To assess participants' subjective perception of sleep quality, the question, "In the last month, how would you rate your sleep quality considering issues like difficulty falling asleep, waking up frequently and having trouble falling back asleep, waking up early, and feeling unrested?" was posed, with response options ranging from "very poor" to "very good."

A numerical rating scale from "0" to "10" was used to assess complaints of pain and itching over the last month. For bodily pain, the scale ranged from "0" (no pain) to "10" (unbearable pain), and for itching, it ranged from "0" (no itching) to "10" (very severe itching). The questionnaire was pre-tested with 20 patients with ESRD who were not in the study group and who applied to the outpatient clinic and revised according to the feedback. This questionnaire was administered to all patients through face-to-face interviews.

Sleep quality

The Pittsburgh Sleep Quality Index (PSQI), which was developed by Buysse et al. (1989), consists of 24 questions in total, 19 of which are self-reported and 5 answered by a spouse or roommate (17). It includes 7 components: Subjective Sleep Quality, Sleep Latency, Sleep Disorders, Sleep Duration, Habitual Sleep Efficiency, Sleep Medication Use, and Daytime Dysfunction. Each component is evaluated on a 0-3 scale and the sum of the seven components results in a total score ranging from 0 to 21. A total score greater than 5 indicates "poor sleep quality" (18). The Turkish validity and reliability study of the scale was conducted by Ağargün et al. In the current study, only the score derived from the first 19 items, which were

answered by the participants themselves, was used (19).

Anxiety Level

Anxiety levels were measured using the Beck Anxiety Inventory (BAI). This self-report scale was developed by Beck in 1988 to assess the severity of anxiety (20). It consists of 21 questions, each scored on a scale of 0-3 points. The interpretation of the scores is as follows: 0-7 points indicate minimal anxiety symptoms, 8-15 points indicate mild anxiety symptoms, 16-25 points indicate moderate anxiety symptoms, and 26-63 points indicate severe anxiety symptoms. The Turkish validity and reliability study of the scale was conducted by Ulusoy et al (21).

Depression Level

The Beck Depression Inventory (BDI) is a self-report scale developed to assess depression symptoms (22). It consists of 21 questions, with each item scored between 0 and 3 points. The total score is the sum of the scores from all the items. A total score above 17 points is considered the cut-off for depression. The Turkish validity and reliability study of this scale was conducted by Hisli et al. (23).

Data analysis

Data analysis was performed using IBM SPSS Statistics for Windows v.26 (IBM Corp., Armonk, NY). Since the continuous variables (age, ESRD duration, hemodialysis duration, BDI, BAI, and PSQI scores) did not follow a normal distribution, pairwise comparisons were conducted using the Mann-Whitney U test. Pearson Chi-Square and Fisher's Exact tests were used to compare categorical variables. Spearman's rank correlation was used to assess the relationships between age, sleep quality, anxiety, and depression scores. A p-value of <0.05 was considered statistically significant.

Results

Of the 123 participants, 59.3% (n = 73) were male, with a mean age of 59.4 ± 14.1 years. More than half had a high school education or higher (n = 68, 55.3%). Most participants were married (n = 92, 74.8%), had children (n = 101, 82.1%), and lived in nuclear families (n = 96, 78.0%). Only a small proportion were employed (n = 19, 15.4%), with the rest being retired or unemployed.

The mean duration of living with chronic kidney disease was 10.5 ± 8.9 years, with 56.1% (n = 69) diagnosed more than six years ago. More than half (n = 67, 54.5%) had been on hemodialysis for over three years, with an average hemodialysis duration of 6.3 ± 6.9 years. Additionally, 17% (n = 21) had previous renal transplant rejection history.

A diagnosed psychiatric illness was reported by 14.6% (n = 18) of participants. Specifically, four individuals were diagnosed with depression, one with an anxiety disorder, and one with a sleep disorder. Currently, 8.9% (n = 11) were taking psychiatric medications. The most common comorbid physical conditions were hypertension (32.0%), diabetes mellitus (31.0%), and coronary artery disease (4.8%).

In the past month, 41.5% (n=51) of the participants reported experiencing bodily pain, and 37.4% (n=46) reported experiencing itching in the last month.

Possible depression, anxiety disorders, and poor sleep quality in participants

The percentage of participants with possible depression (BDI score ≥17), possible anxiety disorder (BAI score ≥8), and the distribution of sleep quality, along with subjective opinions about sleep quality based on the cut-off scores of the scales are shown in Table 1.

Table 1. Distribution of Hemodialysis Patients by Possible Depression, Possible Anxiety, and Sleep Quality (Ankara, 2018)

n	%	
Possible Depression (n=115*)		
No (BDI<17)	100	87.0
Yes (BDI≥17)	15	13.0
Possible Anxiety Disorder (n=115*)		
No (BAI<8)	78	67.8
Yes (BAI≥8)	37	32.2
Sleep Quality (n=113)**		
Poor (PSQI>5)	58	51,3
Good (PSQI≤5)	55	48,7
Subjective sleep quality (n=123)		
Very poor	5	4.1
Poor	24	19.5
Fair	43	35.0
Good	26	21.1
Very good	25	20.3

BAI: Beck Anxiety Inventory, BDI: Beck Depression Inventory, PSQI: Pittsburgh Sleep Quality Index

*Seven patients were excluded from the analyses due to illiteracy, and one patient was excluded for not completing the scales.

**Seven patients were excluded from the analyses due to illiteracy, and three patients were excluded for not completing the scales.

Table 2. Sleep Quality of Hemodialysis Patients by Sociodemographic and Clinical Characteristics (Ankara, 2018)

	Good Sleeper (PSQI<5)		Poor Sleeper (PSQI>5)		Total	p
Characteristics	n	%	n	%*	n	
Age (median [IQR] (years)	64[17]		58.5[21.5]		63[18]	0.22[a]
Sex						
Female	16	40.0	24	60.0	40	0.17[b]
Male	39	53.4	34	46.6	73	
Education Level						
Literate/Primary school	12	40.0	18	60.0	30	0.54[b]
Middle school	8	53.3	7	46.7	15	
High school	10	43.5	13	56.5	23	
University/Master's degree	25	55.6	20	44.4	45	
Employment Status						
Unemployed	13	48.1	14	51.9	27	0.98[b]
Employed:	9	47.4	10	52.6	19	
Retired	33	49.3	34	50.7	67	
Marital Status						
Single	7	46.7	8	53.3	15	0.77[b]
Married	41	47.7	45	52.3	86	
Divorced/widowed	7	58.3	5	41.7	12	
ESRD duration (median [IQR], years)	7[16]		8[9.5]		8[10]	0.54[a]
Hemodialysis duration (median [IQR], years)	4[5]		4[6.3]		4[6]	0.73[a]
Wait-listed for transplantation						
Yes	31	49.2	32	50.8	63	0.89[b]
No	24	48.0	26	52.0	50	
History of transplant rejection						
Yes	10	50.0	10	50.0	20	0.89[b]
No	45	48.4	48	51.6	93	
Psychiatric history						
No	5	31.3	11	68.8	16	0.13[b]
Yes	50	51.5	47	48.5	97	
Physical Comorbidity						
No	16	48.5	17	51.5	33	0.98[b]
Yes	39	48.8	41	51.3	80	
Pain in the last month						
No	37	53.6	32	46.4	69	0.19[b]
Yes	18	40.9	26	59.1	44	
Pruritus in the last month						
No	39	54.2	33	45.8	72	0.12[b]
Yes	16	39.0	25	61.0	41	
Smoking status						
Smoker	10	41.7	14	58.3	24	0.56[b]
Non- smoker	20	46.5	23	53.5	43	
Ex-smoker	25	54.3	21	45.7	46	
Alcoholic beverage consumption						
Occasional drinker	6	46.2	7	53.8	13	0.92[b]
Never	32	47.8	35	52.2	67	
Former drinker	17	51.5	16	48.5	33	
BDI scores (median [IQR]	4[8]		11[10]		7 11	<0.001[a]

Possible depression (BDI≥17)						
No	52	53.1	46	46.9	98	0.02[c]
Yes	3	20.0	12	80.0	15	
BAI scores (median [IQR]	2[7]		9[8]		5[6]	<0.001[a]
Possible anxiety disorder (BAI ≥8)						
No	44	56.4	34	43.6	78	0.01[b]
Yes	11	31.4	24	68.6	35	
Total	55	48.7	58	51.3	113	

*IQR: interquartile range BAI: Beck Anxiety Inventory, BDI: Beck Depression Inventory PSQI: Pittsburgh Sleep Quality Index, ESRD: End-stage renal disease * Row percentages*

Mann-Whitney U test, b: Chi-square test, c: Fisher's exact test

Univariate analysis: Comparison of groups with good and poor sleep quality

Participants were divided into two groups: those with poor sleep quality (PSQI > 5) and those with good sleep quality (PSQI ≤ 5). No significant differences were found between the two groups in terms of age, sex, education, marital status, duration of ESRD, duration of hemodialysis, pain and pruritus complaints in the last month, and history of psychiatric disease. However, both depression scores (U = 850.500, p < .001) and anxiety scores (U = 820.500, p < .001) were significantly higher in the group with poor sleep quality. The comparison of hemodialysis patients with good and poor sleep quality by sociodemographic and clinical characteristics is shown in Table 2.

Patients' subjective views on sleep quality-related factors

As shown in Table 3, the group with poor sleep quality consistently reported more negative subjective assessments of their sleep. However, only 40.0% of the patients with poor sleep quality described their sleep quality as poor(very poor and poor).

Table 3. Sleep Quality of Hemodialysis Patients Measured with the PSQI by Subjective Sleep Quality Assessments

Subjective Sleep Quality	Good Sleeper (PSQI<5)		Poor Sleeper (PSQI>5)	
	n	%	n	%
Very poor	-	-	4	6.9
Poor	1	1.8	19	32.8
Fair	14	25.5	25	43.1
Good	19	34.5	6	10.3
Very good	21	38.2	4	6.9
Total	55	100.0	58	100.0

PSQI Pittsburgh Sleep Quality Index

There was no significant difference in the proportion of "possible" depression between the groups reporting good and poor sleep quality (χ^2= 1.363, p=.243). On the other hand, the percentage of patients with "possible" anxiety disorders was higher in the group with perceived poor sleep quality (χ^2= 5.754, p=.016).

Correlation between age, depression, anxiety, and sleep quality scores

There was a moderate, positive, and statistically significant correlation between anxiety and depression scores and sleep quality scores, with no correlation to age, as presented in Table 4.

Table 4. Correlation Between Age, Depression, Anxiety, and Sleep Quality Scores (Ankara, 2018)

Variables	1	2	3	4
1. Age	1			
2. BDI	r_s =-0.135 p=0.147	1		
3. BAI	r_s =-0.179 p=0.054	r_s =0.660 **p<0.001**	1	
4. PSQI	r_s =-0.094 p=0.320	r_s =0.451 **p<0.001**	r_s =0.433 **p<0.001**	1

BAI: Beck Anxiety Inventory, BDI: Beck Depression Inventory PSQI: Pittsburgh Sleep Quality Index rs: Spearman's correlation coefficient

Discussion

The most important finding of the study was that poor sleep quality was observed in nearly half of the patients (47.0%), a result consistent with previous studies in this field (7,16). However, only 39.5% of those identified as having poor sleep quality through the PSQI rated their sleep as poor or very poor. This discrepancy suggests that a large proportion of patients may not be fully aware of their impaired sleep quality.

We found that depression and anxiety levels were higher in females, aligning with previous research findings. While poor sleep quality was more common among women compared to males, this difference was not statistically significant. Previous studies have reported conflicting findings regarding the association between sleep quality and sex in patients undergoing hemodialysis. While some studies have found that poor sleep quality is more common in females

(15,17), others have reported no significant difference (7,8,12,16). Similar to previous studies on patients undergoing hemodialysis (7,16), our sample had a higher proportion of male participants. The lack of a significant difference in sleep quality between sexes in our study may be due to the relatively low number of female participants.

Our findings regarding the relationship between the duration of hemodialysis and sleep quality contrast with previous studies, which have reported that insomnia tends to increase with longer durations of hemodialysis (3,8,16). Pain and uremia-associated pruritus are other common factors in hemodialysis patients that are frequently implicated in insomnia (25-27). However, in our study, there was no significant relationship between pain and pruritus experienced in the last month and sleep quality. These contradictory findings may be attributed to differences in the sample characteristics and the methods used to assess pruritus and pain. In our study, 80.0% of patients with depression and 68.7% of patients with anxiety were found to have poor sleep quality. This finding is consistent with previous studies indicating that depression and anxiety are related to poor sleep quality (7,16,17). Therefore, screening for depressive symptoms is crucial for improving sleep quality and managing associated morbidity and mortality.

The literature presents conflicting findings regarding the relationship between anxiety levels and sleep quality (15). Our study indicates a significant relationship between anxiety levels and sleep quality, with a stronger association observed between possible anxiety disorders and subjective reports of poor sleep quality. In contrast, possible depression was not linked to patients' subjective opinions about poor sleep quality. These findings suggest that sleep issues related to anxiety symptoms may be more readily reported, while impairments in sleep quality due to depressive symptoms may go underreported. Given the high proportion of depression in the hemodialysis population and its impact on sleep quality, these results underscore the need for routine screening of depression symptoms. Furthermore, healthcare providers should not rely solely on patients' self-assessments to detect sleep problems.

This study has several limitations. First, the results cannot be generalized to the entire hemodialysis patients, as only patients from two dialysis centers affiliated with a specific institution were included. Additionally, being a descriptive study, it identifies factors related to sleep quality but does not provide insight into the direction of these relationships. Third, the sample size may be limited to detect some significant differences. In addition, the entire target sample could not be reached. The use of self-reported inventories for assessing sleep quality, anxiety, and depression is another limitation, as it may lead to recall bias. We also did not assess other psychiatric disorders that may be associated with poor sleep quality. Another limitation is the assessment of sleep quality using self-report scales rather than objective measurement methods. Analytical studies with larger, more representative samples are necessary to establish causal relationships.

Conclusion

We found that a significant majority of patients with elevated depression and anxiety levels also exhibited poor sleep quality highlighting a heightened risk for comorbid mental health disorders in this population. Although objective methods (such as polysomnography and actigraphy) are considered the best approach for evaluating sleep problems in hemodialysis patients, the results of this study highlight the value of using self-report scales as well. This approach can help ensure that sleep issues in patients who do not actively report complaints are not overlooked by clinicians. Given that depression is commonly associated with impaired sleep, poor sleep quality in hemodialysis patients may serve as a potential indicator of underlying depression, suggesting that such screenings may contribute to the early detection of possible depression and anxiety disorders. In conclusion, this study underscores the importance of thorough assessment and inquiry, as insomnia in hemodialysis patients may go unnoticed without detailed evaluation.

References

1.Fonseca NT, Urbano JJ, Nacif SR, Silva AS, Peixoto RAO, Urbano GJ, et al. A systematic review of sleep disorders in patients with chronic kidney disease undergoing hemodialysis. J Phys Ther 2016; 28:2164e70.

2.Merlino G, Piani A, Dolso P, Adorati M, Cancelli I, Valente M, Gigli GL. Sleep disorders in patients with end-stage renal disease undergoing dialysis therapy. Nephrol Dial Transplant. 2006;21: 184–190.

3.Sabbatini M, Minale B, Crispo A, Pisani A, Ragosta A, Esposito R, et. al. Insomnia in maintenance hemodialysis patients. Nephrol Dial Transplant. 2002;17: 852–856.

4.Theofilou P. Association of insomnia symptoms with kidney disease quality of life reported by patients on maintenance dialysis. Psychol Health Med. 2013; 18:70–78.

5.Szentkiralyi A, Czira ME, Molnar MZ, Kovesdy CP, Remport A, Szeifert L, et al. High risk of obstructive sleep apnea is a risk factor of death censored graft loss in kidney transplant recipients: an observational cohort study. Sleep Med 2011;12(3):267e73.

6.Lubas MM, Ware JC, Szklo-Coxe M. Sleep apnea and kidney transplant outcomes: findings from a 20-year (1997-2017) historical cohort study. Sleep Med. 2019; 63:151-158.

7.Adejumo OA, Edeki IR, Mamven M, Oguntola OS, Okoye OC, Akinbodewa AA, et al. Sleep quality and associated factors among patients with chronic kidney disease in Nigeria: a cross-sectional study. BMJ Open. 2023;13(12): e074025.

8.Velu S, Rajagopalan A, Arunachalam J, Prasath A, Durai R. Subjective Assessment of Sleep Quality and Excessive Daytime Sleepiness in Conventional Hemodialysis Population: A Single-Center Experience. Int J Nephrol Renovasc Dis. 2022; 15:103-114.

9.Weisbord SD, Fried LF, Mor MK. Renal provider recognition of symptoms in patients on maintenance hemodialysis. Clin J Am Soc Nephrol 2007; 2:960.

10.Elder S.J., Pisoni R.L., Akizawa T., Fissell R, Andreucci VE, Fukuhara S, et al. Sleep quality predicts quality of life and mortality risk in hemodialysis patients: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrology Dialysis Transplantation 2008; 23(3), 998–1004

11.Yang XH, Zhang BL, Gu YH, Ztopla XL, Guo LL, Jin HM. Association of sleep disorders, chronic pain, and fatigue with survival in patients with chronic kidney disease: a meta-analysis of clinical trials. Sleep Med. 2018; 51:59-65.

12.Han Q, Liu B, Lin S, Li J, Liang P, Fu S, et. al. Pittsburgh Sleep Quality Index score predicts all-cause mortality in Chinese dialysis patients. Int Urol Nephrol. 2021; 53(11):2369-2376.

13.Topal M, Erkus E. Improving sleep quality is essential for enhancing soluble Klotho levels in hemodialysis patients. Int Urol Nephrol. 2023;55(12):3275-3280.

14.Kaneez M, Zaidi SMJ, Zubair AB, Rehan M, Hassan A, Sarwar Z, et. al. Sleep Quality and Compliance to Medical Therapy Among Hemodialysis Patients with Moderate-to-Severe Depression: A Cross-Sectional Study. Cureus. 2021;13(2): e13477.

15.Al Naamani Z, Gormley K, Noble H, Santin O, Al Maqbali M. Fatigue, anxiety, depression, and sleep quality in patients undergoing hemodialysis. BMC Nephrol. 2021;22(1):157.

16.Kose S, Mohamed NA. The Interplay of Anxiety, Depression, Sleep Quality, and Socioeconomic Factors in Somali Hemodialysis Patients. Brain Sci. 2024;14(2):144.

17.Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193-213.

18.Sutton EL. Psychiatric disorders and sleep issues. Medical Clinics,2014; 98(5), 1123-1143.

19.Agargün MY, Kara H, Anlar O. Pittsburgh Uyku Kalitesi İndeksinin geçerliği ve güvenirliği. Türk Psikiyatri Dergisi 1996; 7: 107-15.

20.Beck AT, Epstein N, Brown G, Ster RA. An inventory for measuring clinical anxiety: psychometric properties. J Consul Clin Psychol 1988; 56:893-897.

21.Ulusoy M, Şahin NH, Erkmen H. Turkish version of the Beck Anxiety Inventory: Psychometric properties. J Cognit Psychother 1996; 12:163-172.

22.Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961; 4:561-571.

23.Hisli N. Beck Depresyon Ölçeği'nin bir Türk örnekleminde geçerlik ve güvenirliği. Psikoloji Dergisi 1988; 6:118-122.

24.Sekercioglu N, Curtis B, Murphy S, Barrett B. Sleep quality and its correlates in patients with chronic kidney disease: a cross-sectional design. Renal Failure 2015;37(5):757–762.

25.Novak M., Shapiro C.M., Mendelssohn D., Mucsiet I. Diagnosis and management of insomnia in dialysis patients. Seminars in Dialysis 2006; 19, 25–31.

26.Harris TJ, Nazir R, Khetpal P, Peterson RA, Chava P, Patel SS, et al. Pain, sleep disturbance and survival in hemodialysis patients. Nephrol Dial Transplant 2012; 27:758e65.

27.Rehman IU, Chohan TA, Bukhsh A, Khan TM. Impact of Pruritus on Sleep Quality of Hemodialysis Patients: A Systematic Review and Meta-Analysis. Medicina (Kaunas). 2019;55(10):699

Received: 17 Oct 2024 | **Accepted:** 06 Mar 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 309-318
DOI: 10.54005/geneltip.1568895

ORIGINAL ARTICLE

Evaluation Of Nutritional Habits, Self-Respect, Body Perception, and Healthy Life Attitude in Adolescents

Adölesanlarda Beslenme Alışkanlıkları, Özsaygı, Beden Algısı ve Sağlıklı Yaşam Tutumunun Değerlendirilmesi

[1]Hilal Doğan Güney, [2]Özlem Özer Altundağ, [3]Reyhan Aydın Doğan

[1]Department of Nutrition and Dietetic, Safranbolu District Health Directorate, Karabük, Türkiye
[2]Department of Gastronomy and Culinary Arts, Faculty of Tourism, Karabuk University, Karabük, Türkiye
[3]Departments of Midwifery, Faculty of Health Sciences, Karabuk University, Karabük, Türkiye

Correspondence

Hilal Doğan Güney
Safranbolu District Health Directorate, Nutrition and Diet Polyclinic, Safranbolu, Karabuk, Türkiye

E-Mail: hilaldogan21@gmail.com

How to cite ?

Doğan Güney H, Özer Altundağ Ö, Aydın Doğan R. Evaluation Of Nutritional Habits, Self-Respect, Body Perception, and Healthy Life Attitude in Adolescents. Genel Tıp Derg. 2025;35 (2): 309-318

ABSTRACT

Aim: Adolescents' acquisition of positive eating behaviors is important for the prevention of eating disorders. This study was conducted to evaluate eating habits, self-esteem, body perception, and healthy living attitudes in adolescents.
Methods: The study was conducted with the participation of 160 adolescents (65 boys, 95 girls) between the ages of 11-14 years who were continuing their education in secondary education institutions in the Safranbolu district of Karabük province. The data were collected by using a questionnaire including sociodemographic information, anthropometric measurements, general health and nutritional habits, Body Image Scale, Attitudes Toward Healthy Eating Scale, Adolescent Healthy Lifestyle Choices Scale, and Rosenberg Self-Esteem Scales. Anthropometric data were evaluated using the WHO BMI-for-age growth curves for ages 5-19 years. The obtained data were entered into the "WHO Antro Plus" computer program and the results were obtained as z-score.
Results: 59.4% of the adolescents were girls, 40.6% were boys, mean age was 13.44±0.82 years, mean body weight was 50.54±9.28 kg, mean height was 152.20±4.51 cm, and mean BMI-for-age-Z score was 0.49±1.41. It was found that 47.5% of the adolescents considered themselves overweight, 80.63% were satisfied with their weight, 14.38% had attempted dieting in the last year, and 55% received information about nutrition from a doctor. It was found that the mean value of the VAS was good at 158.55 ± 9.27, high at 64.44 ± 2.28, moderate with 53.11 ± 3.67, and moderate with 21.74 ± 2.50 on the Rosenberg Self-Esteem Scale.
Conclusion: The results of the study emphasize the need to increase awareness of adolescents' body perception, healthy living attitudes, and nutritional behaviors. The findings provide information that can guide the development of adolescent-specific nutrition protocols and future studies.

Keywords: Adolescent, body image, body mass index, healthy eating,

ÖZ

Amaç: Adolesanların olumlu beslenme davranışları kazanması ortaya çıkabilecek yeme bozuklukları hastalıklarının önlenmesi açısından önemlidir. Bu çalışma adölesanlarda beslenme alışkanlıkları, benlik saygısı, beden algısı ve sağlıklı yaşam tutumlarının değerlendirilmesi amacıyla gerçekleştirilmiştir.
Yöntem: Araştırma 11-14 yaş arası 160 adölesanın (65 erkek, 95 kız) katılımı ile Karabük İli Safranbolu ilçesine bağlı ortaöğretim kurumlarında öğrenimlerine devam eden adolesanların katılımı ile gerçekleştirilmiştir. Katılımcıların sosyodemogafik bilgilerini, antropometrik ölçümlerini, genel sağlık ve beslenme alışkanlıklarını içeren anket soruları ile Vücut Algısı Ölçeği, Sağlıklı Beslenmeye İlişkin Tutum Ölçeği, Adolesan Sağlıklı Yaşam Biçimi Seçimleri Ölçeği, Rosenberg Benlik Saygısı Ölçeklerini içeren anket formu kullanılarak veriler toplanmıştır. Antropometrik veriler WHO 5-19 yaş için Yaşa Göre BKİ büyüme eğrileri kullanılarak değerlendirilmiştir. Elde edilen veriler "WHO Antro Plus" bilgisayar programına girilerek sonuçlar z-skor olarak elde edilmiştir.
Bulgular: Adolesanların %59,4'ü kız, %40,6'sı erkek, yaş ortalamaları 13,44±0,82 yıl, vücut ağırlığı ortalaması 50,54±9,28 kg., boy ortalaması 152,20±4,51 cm, yaşa göre BKI-Z skoru ortalaması 0,49±1,41'dır. Adolesanların %47,5'inin kendisini fazla kilolu olarak gördüğü, %80,63'ünün kilosundan memnun olduğu, %14,38'inin son bir yıl içinde diyet yapma girişiminde bulunduğu ve %55'inin beslenme ile ilgili bilgiyi doktordan aldığı saptanmıştır. Adolesanların Vücut Algısı Ölçeği ortalaması 158,55 ± 9,27 ile iyi; Sağlıklı Beslenmeye İlişkin Tutumlar Ölçeği ortalaması 64,44 ± 2,28 ile yüksek; Adolesan Sağlıklı Yaşam Biçimi Seçimleri Ölçeği ortalaması 53,11 ± 3,67 ve Rosenberg Benlik Saygısı Ölçeği ortalamasının 21,74 ± 2,50 ile orta değere sahip olduğu bulunmuştur.
Sonuç: Çalışmanın sonuçları, adolesanların beden algısı, sağlıklı yaşam tutumları ve beslenme davranışlarına yönelik farkındalığın artırılması gerektiğini vurgulamaktadır. Elde edilen bulgular, adolesanlara özgü beslenme protokollerinin geliştirilmesine ve gelecekteki çalışmalara rehberlik edebilecek bilgiler sunmaktadır.

Anahtar Kelimeler: Adolesan, Sağlıklı Beslenme, VKİ, Vücut Algısı

Introduction

The World Health Organization defines adolescence as the period between childhood and adulthood, between the ages of 10 and 19 (1). The worldwide prevalence of obesity in children and adolescents (5-19 years) increased from 4% to 18% from 1975 to 2016 (1). In addition, the prevalence of obesity among adolescents in the USA (United States of America) increased from 13.9% in 2000 to 18.5% in 2016 (2,3). Due to the numerous medical and psychosocial complications associated with childhood obesity and its impact on future healthcare costs, it is recognized as an important public health problem (4). Several longitudinal studies highlight the strong association of childhood and adolescent obesity with persistence

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

into adulthood; Excessive adiposity in childhood, increased cardiometabolic risk in adolescents and adults, and the risk of developing cardiovascular diseases and diabetes in the future are also indicators of poor quality of life (5,6).

Adequate and balanced nutrition is essential to support and maintain health and safety in early childhood. Nutrition is one of the environmental factors with its demographic, socio-economic, behavioral, and motivational aspects that affect the development of intelligence based on genetic effects (7). With a healthy nutrition program, studies have observed that adolescents' cognitive skills, such as concentration and memory, improve, and their energy levels, mental states, and academic performances improve (5,8). In contrast, higher consumption of unhealthy foods such as fast food and sugar-sweetened beverages has been associated with behavioral problems, poor concentration, obesity, and emotional development problems (5). Since nutrition is a modifiable factor, interventions to correct malnutrition habits in adolescents are important (8). Various studies report that the attitudes acquired and internalized during this period have a great impact on adulthood and that young people should take care of their physical, psychological, and social health (9). Health promotion during this period can prevent, delay, or change chronic diseases in adulthood such as low self-concept, low self-perception, or eating problems (10).

The terms self-esteem and self-concept are interrelated. Self-esteem is a person's view of his or her potential, self-efficacy, self-worth, and self-definition (10,11). Self-concept is the perception that the subject develops about herself, that is, what she can achieve, what others believe she is, and how she plans to be (12). Both concepts contribute to the formation of the identity of adolescent individuals. It is necessary to develop good self-esteem and self-concept among adolescents. Having a low self-concept is an adolescent individual; These terms are of great importance in young people, as they predispose them to develop psychiatric pathologies such as depression, anxiety, or feelings of humiliation (11,13). Since adolescence is a period of rapid emotional, social, and physical change, body dissatisfaction may occur (14). Body dissatisfaction in adolescents can cause higher body mass index (BMI), low self-esteem, poor quality of life, eating disorders, prevalence of unhealthy weight loss strategies, sadness, suicidal ideation, low physical activity, motivation, and technology addiction (14,15). The prevalence of body dissatisfaction is higher in adolescent girls than in boys, and body dissatisfaction is seen more in overweight adolescents compared to individuals with normal body weight (16). While adolescent girls' body dissatisfaction is associated with the urge to be more fit, adolescent boys' body dissatisfaction is associated with higher muscularity urges (17). Body dissatisfaction is associated with abnormal eating behaviors, and studies show that unhealthy eating behaviors are an indicator of a higher risk of eating disorders and are associated with the development of obesity in later life (18).

Adolescence is a critical period of intense physical, psychological, and social changes. Acquiring unhealthy eating habits, increasing childhood obesity and problems such as low self-esteem and body dissatisfaction can lead to long-term physical and psychological health risks. Research shows that healthy habits acquired during childhood and adolescence play an important role in the prevention of chronic diseases in adulthood. Therefore, assessing and improving the lifestyle habits, nutritional behaviors and body perceptions of adolescents is important for improving public health. In the literature, there are awareness-based or informed approaches to change adolescents' eating behaviors (2,5, 6,16). In this context, this study aimed to evaluate eating habits, self-esteem, body perception, and healthy living attitudes in adolescents.

Material and Methods

This cross-sectional study was carried out with the participation of 160 adolescents (65 boys, 95 girls) between the ages of 11-14 living in Karabuk. The research sample consisted of adolescents who continue their education in secondary education institutions in the Safranbolu district of Karabük province. Participants' socio-demographic information (year of birth, parental education level, and occupation), anthropometric measurements, general health, nutritional habits, number of main and snack meals consumed daily, skipping meals, reasons for skipping meals, dietary motivations and Body Image Scale (BIS), Related to Healthy Eating Data were collected using a questionnaire including Attitude Scale, Adolescent Healthy Lifestyle Choices Scale, and Rosenberg Self-Esteem Scales. The questionnaire was applied face to face to the participants and it took about 15 minutes to complete the questionnaire.

Ethical aspect of the study

Ethics committee approval was obtained from the Social and Human Sciences Research Ethics Committee of xxx University (Decision number 5 and date: 23.02.2022), and necessary permissions were obtained from the Provincial Directorate of National Education to conduct the study. The voluntary participation of each adolescent and his family was ensured. The study was conducted under the principles of the Declaration of Helsinki.

Anthropometric Measurements

The BMI values of the participants were calculated by dividing the body weight by the square of the height (in meters). Anthropometric data were evaluated using the World Health Organization's (WHO) 2007 BMI growth curves for ages 5-19 years. The obtained data were entered into the "WHO Antro Plus" computer program and the results were obtained as Z-scores. According to this; in overweight detection: >+1 SD (over 85th percentile) (BMI 25 kg/m2 equivalent for 19 years old), and in obesity detection: >+2 SD (over 97th percentile) (BMI 30 kg/m2 equivalent for 19 years old)), <-2 SD for weak and ≤+1 SD - ≥-2 SD for normal were used (19).

Body Image Scale (BIS)

The BIS used to obtain research data was developed by Secord and Jourard (1953). The scale was translated into Turkish by Hovardaoğlu in 1986, and the Cronbach Alpha coefficient was found to be r=0.91 (Hovardaoğlu, 1992). The scale consists of 40 items. The scale determines the person's satisfaction with 40 different body parts or functions. Scores from 1 to 5 are given for each item, and the total score to be obtained from the scale, which has response options such as "I don't like it at all," "I don't like it," "I'm undecided," "I like it" and "I like it very much," varies between 40 and 200 points (20). In our study, the Cronbach Alpha value for the Body Image Scale was determined as 0.76.

Attitudes Towards Healthy Eating Scale (ATHE)

Tekkurşun Demir and Cicioğlu developed the scale, and the same researchers performed validity and reliability analyses. It includes a total of 21 questions, consisting of Knowledge About Nutrition, Emotion About Nutrition, Positive Nutrition, and Malnutrition, which are the sub-sections of the Attitudes Towards Healthy Eating Scale. The lowest score that can be obtained from the scale is 21, and the highest score is 105. It is explained that the participants from ATHE have an attitude towards healthy eating with 21 points shallow, 23-42 points low, 43 63 points medium, 64 84 points high, and 85-105 points ideally high. The ratings for the positive items on the scale are "Strongly Disagree," "Disagree," "I am undecided," "Agree," and "Strongly Agree" (21). In our study, the total score of the Attitudes Towards Healthy Eating Scale was determined as Cronbach's alpha value of 0.77. The Cronbach's alpha values of the sub-dimensions of the scale were as follows; Knowledge About Nutrition sub-dimension 0.69; Emotion About Nutrition sub-dimension 0.68; Positive Nutritions sub-dimension 0.66; Malnutritions sub-dimension 0.65.

Adolescent Healthy Lifestyle Choices Scale (AHLCS)

The scale was developed by Bernadette Melynk in 2006. This scale measures the tendency of adolescents to make healthy lifestyle choices such as choosing healthy food, participating in physical activity, reducing stress, and avoiding sedentary activities such as watching television (22). The scale consists of 16 items in total. The scale requires a 5-point Likert-type response for each item. "Strongly disagree" was evaluated as 1, "Disagree" 2, "Neither agree nor disagree" 3, "Agree" 4, and "Strongly agree" 5 points. Accordingly, adolescents get the lowest score of 16 and the highest score of 80 on the scale. (23). In our study, the Cronbach's Alpha value of the Adolescent Healthy Lifestyle Choices Scale was determined as 0.70.

Rosenberg Self-Esteem Scale

It is a self-report scale that evaluates self-perception, developed by Rosenberg in 1965. The self-esteem scale consists of 63 items and 12 sub-categories. There is also a short form of the Rosenberg self-esteem scale consisting of 10 items. The short form was used in the research. Çuhandaroğlu carried out the Turkish validity and reliability study of the scale. It is a 4-point Likert scale. Scoring ranges from 10 to 40 (Very true= 4, Very false=1). 1.,2.,4.,6. and item 7 is correct 3.,5.,8.,9. and item 10 are reverse scored. A score of 10-20 indicates low self-esteem, a score of 20-30 medium, and a score of 30-40 indicates high self-esteem (24,25). In our study, the Cronbach Alpha value of the Rosenberg Self-Esteem Scale was determined as 0.68.

Statistical Analysis

Statistical analysis of the research was evaluated using a computer-aided analysis program. SPSS 20.0 data analysis program was used to analyze the research

data (correlation, frequency). Since the Skewness and Kurtosis values of the data remained within the +2.0/-2.0 limit range, it was observed that the data showed a normal distribution (George, 2011). The socio-demographic characteristics of the participants and the mean scores of the scales used are given as mean, standard deviation, and percentage distribution. The relationship between the scales and BMI and Z Score was analyzed with One-way ANOVA. Tamhane and Tukey's Posthoc analysis determined a significant difference. The factors affecting the Adolescent Healthy Lifestyle Choices Scale were explained by linear regression. The relationship between the scales and socio-demographic variables was analyzed by Pearson correlation. The study findings were analyzed at a 95% confidence interval and $p<0.05$ significance level.

Results

The mean age of the participants was 13.44±0.82 years; the mean body weight was 50.54±9.28 kg. The mean height was 152.20± 4.51 cm, and the mean BMI - Z score for age was 0.49±1.41 was found to be. 59.38% of the participants are girls, and 40.63% are boys. 47.50% of individuals consider themselves overweight, 80.63% are satisfied with their weight, 14.38% attempted to diet in the last year, and 55.00% receive information about nutrition from a doctor. They were detected (Table 1).

Table 1. Socio-demographic characteristics of the participants

Features		Mean±SD	Lower-Over (Median)
Age (years)		13.44± 0.82	12-16 (14)
Weight		50.54±9.28	33.90-65.60 (52.90)
Height		152.20± 4.51	142.0-160.40 (152.85)
BMI		21.85±4.12	13.40 31.00 (22.15)
BMI-Z Score Value by Age		0.49±1.41	-3.41- 2.78 (0.84)
		n	%
Gender	Women	95	59.38
	Men	65	40.63
Defining health in general	Very good	40	25.00
	Good	47	29.38
	Middle	65	40.63
	Poor	8	5.00
Evaluate current body weight	Weak	6	3.75
	Normal	63	39.38
	Overweight	76	47.50
	Obese	15	9.38
Satisfaction with body weight	I am not satisfied	31	19.38
	I am satisfied	129	80.63
Status of attempting to lose weight in the past year	Never happened	137	85.63
	I tried several times	23	14.38
Source of information about nutrition	Nutritionist	17	10.63
	Doctor	88	55.00
	Radio and TV	22	13.75
	Newspaper	11	6.88
	Other	22	13.75
Self-sufficient and balanced nutritional status	Yes	133	83.13
	No	27	16.88
Frequency of eating main meals per day	2 main meals	27	16.88
	3 main meals	133	83.13
Frequency of eating snacks per day	None	35	21.88
	1 snack	5	3.13
	2 snacks	75	46.88
	3-4 snacks	45	28.13
Meal skipping status	I Skip Meals	13	8.1
	I Don't Skip Meals	147	91.9
Which meal is usually skipped?	I Don't Skip Meals	147	91.88
	Morning	5	3.13
	Noon	6	3.75
	Evening	2	1.25
Reason for skipping meals	I Don't Skip Meals	147	91.88
	Lack of time - get up late	3	1.88
	Not wanting - without appetite	9	5.63
	Other	1	0.63
BMI-Z Score Classification by Age	Weak	10	6.3
	Normal	78	48.8
	Overweight	54	33.8
	Obese	18	11.3

When we examine the current weight evaluation status of the participants according to their BMI distribution, 50.00% of the underweight adolescents are evaluated as usual, 40.00% as overweight, and 10.00% as obese. Of the adolescents with normal BMI distribution, 6.41% evaluate their current weight as underweight, 37.18% as normal, 47.44% as overweight, and 8.97% as obese. Of the adolescents in the overweight BMI distribution, 14.29% rated their current weight as underweight, 57.13% as normal, 14.29% as overweight, and 14.29% as obese. When the BMI distributions by gender are examined, 7.36% of female adolescents are underweight, 48.42% are normal, 35.80% are

overweight, and 8.42% are obese. On the other hand, 4.62% of male adolescents are underweight, 49.23% are normal, 30.77% are overweight, and 15.38% are obese (Table 2).

The factors affecting the participants' scale of Adolescent Healthy Lifestyle Choices were analyzed by linear regression, and the regression model was found to be statistically significant (F= 225.00; p=0.00).

Table 2. Distribution of BMI-Z scores by gender and how the participants see their current weight

		BMI Z-Score Distribution by Age								
		Weak		Normal		Overweight		Obese		Total
		n	%	n	%	n	%	n	%	n
Evaluate your current weight.	Weak	-	-	5	6.41	-	-	1	14.29	6
	Normal	5	50.00	29	37.18	25	38.46	4	57.13	63
	Overweight	4	40.00	37	47.44	34	52.31	1	14.29	76
	Obese	1	10.00	7	8.97	6	9.23	1	14.29	15
	Total	10	100	78	100	65	100	7	100	160
Gender	Women	7	7.36	46	48.42	34	35.80	8	8.42	95
	Men	3	4.62	32	49.23	20	30.77	10	15.38	65

The mean Body Image Scale of the participants was 158.55±9.27; the average of the Attitudes Towards Healthy Eating Scale was 64.44±2.28; the mean score of the Knowledge About Nutrition sub-dimension was 20.59±1.83; that of the Emotion Towards Nutrition sub-dimension was 19.33±1.79; that of the Positive Nutritions sub-dimension was 13.19±1.83; the mean score of the Malnutrition sub-dimension was 12.7±1.57; the mean score of the Adolescent Healthy Lifestyle Choices Scale was 53.11±3.67, and the average of the Rosenberg Self-Esteem Scale was found to be 21.74±2.50 (Table 3).

Table 3 Evaluation of the Participants according to the Scales

Features	**Cronbach Alpha Values**	**Mean±SD**	**Median (Lower-Upper)**
BIS	0.76	158.55 ± 9.27	159.5 (135 - 177)
ATHE	0.77	64.44 ± 2.28	65 (57 - 71)
Knowledge About Nutrition(KAN)	0.69	20.59 ± 1.83	21 (15 - 25)
Emotion Towards Nutrition (ETN)	0.68	19.33 ± 1.79	19 (15 - 23)
Positive Eating habits (PEH)	0.66	13.19 ± 1.83	13 (10 - 20)
Bad Eating Habit (BEH)	0.65	12.7 ± 1.57	13 (8 - 18)
Adolescent Healthy Lifestyle Choices Scale	0.70	53.11 ± 3.67	53 (43 - 60)
Rosenberg Self-Esteem Scale	0.68	21.74 ± 2.50	22 (17 - 27)
Distribution of the participants according to the sub-dimensions of the scales			
		n	%
Rosenberg Self-Esteem Scale	Low Self-Esteem	55	34.4
	Medium Self-Esteem	105	65.6
ATHE	Medium	50	31.3
	High	110	68.8

Since the Emotion Towards Nutrition sub-dimension score did not show a significant relationship in the model, it was not included in the study. In the study, a significant correlation was found between Body Image Scale, Attitudes Towards Healthy Eating Scale, Knowledge About Nutrition, Positive Nutrition, and Malnutrition scale scores (Table 3). A 1-unit increase in the BIS score increased the Adolescent Healthy Lifestyle Choices Scale score by 0.04 times, a 1-unit increase in ATHE decreased by 0.69 times, a 1-unit increase in the KAN sub-dimension score increased 1.63 times, Positive Nutritions It was observed that a 1-unit increase in the sub-dimension score increased it 1.74 times, and a 1-unit increase in the Bad Eating Habits sub-dimension score decreased 0.59 times. Age, BMI, and Rosenberg Self-Esteem Scale scores were found to not affect (Table 4).

The relationship between the participants' Age, Weight, Height, BMI, and Z score with the scales is examined in Table 5. As a result of the analysis, a significant correlation was observed at 0.05 between the values marked with *and at the level of 0.01 with the parameters marked with **.

In the study, there was a significant relationship between the source of information about nutrition and the Rosenberg Self-Esteem Scale (F=3.32; p=0.01). It was seen that the significant difference was due to the participants who received information from the newspaper. It was observed that the Rosenberg Self-Esteem Scale score of the participants who received information from the newspaper was higher than those who received information from the other dietitian (Table 6). It was seen that the significant difference

Table 4. Examination of the factors affecting the Adolescent Healthy Lifestyle Choices using a linear regression model

Features	B0 (%95CI)	B1	SH	Test Request.	p	r1	r2
Fixed (Constant)	43.18 (34.1- 52.26)		4.59	9.40	0.00		
Age (years)	-0.15 (-0.36- 0.06)	-0.03	0.11	-1.44	0.15	-0.07	-0.12
BMI (kg/m^2)	-0.01 (-0.05- 0.04)	-0.01	0.02	-0.31	0.76	-0.09	-0.02
BIS	0.04 (0.01- 0.07)	0.11	0.01	2.95	0.00	0.56	0.23
ATHE	-0.69 (-0.82- -0.56)	-0.43	0.07	-10.44	0.00	0.33	-0.65
KAN	1.63 (1.42- 1.83)	0.81	0.10	15.67	0.00	0.56	0.79
Positive Eating habits (PEH)	1.74 (1.63- 1.85)	0.87	0.06	30.45	0.00	0.67	0.93
Bad Eating Habits (BEH)	-0.59 (-0.73- -0.45)	-0.25	0.07	-8.40	0.00	0.16	-0.56
Rosenberg Self-Esteem Scale	0.03 (-0.04- 0.1)	0.02	0.04	0.87	0.38	0.22	0.07

F= 225,00; p=0,00; R=0,96; R2: 0,92; SH:1,05

Table 5. Relationship of Age, Weight, Height, BMI, and Z score of adolescents with scales

	N=160	1	2	3	4	5	6	7	8	9	10	11	12	13
1	Age (years)	1												
2	Body weight (kg)	0.01	1											
3	Height (cm)	0.10	0.09	1										
4	BMI	-0.03	.950**	-.220**	1									
5	Z score	-0.13	.922**	-.218**	.963**	1								
6	BIS	.164*	-.175*	-0.04	-.159*	-.169*	1							
7	ATHE	0.03	-0.09	0.10	-0.12	-0.09	.302**	1						
8	Adolescent Healthy Lifestyle Choices Scale	-0.07	-0.12	-0.05	-0.09	-0.11	.562**	.334**	1					
9	Rosenberg Self-Esteem Scale	0.06	-.156*	-0.10	-0.12	-.164*	.219**	-0.09	.221**	1				
10	KAN	0.15	-.215**	-0.03	-.198*	-.198*	.740**	.636**	.560**	.157*	1			
11	Emotion Towards Nutrition (ETN)	-0.09	-0.03	-0.10	0.01	-0.02	.428**	-0.13	.795**	.245**	.198*	1		
12	Positive Eating Habits (PEH)	-.215**	0.01	0.03	0.01	0.01	-0.03	.158*	.669**	0.05	-0.07	.420**	1	
13	Bad Eating Habits (BEH)	-0.07	-0.14	0.02	-0.14	-0.15	-0.02	-.312**	.159*	0.12	0.00	0.00	.317**	1

*significant at 0.05 level, ** significant at 0.01 level

was due to the participants who received information from the newspaper. It was observed that the Rosenberg Self-Esteem Scale score of the participants who received information from the newspaper was higher than those who received information from the other dietitian.

A statistically significant relationship was found between the BMI values of the adolescents and the scores of the Attitudes Towards Healthy Eating Scale and Knowledge About Nutrition sub-dimensions (p values 0.03; 0.01, respectively). It was determined that normal and overweight students caused the significant difference between, Attitudes Towards

Table 6. The relationship between the source of information about nutrition and the Rosenberg Self-Esteem Scale

Features N=160		**Rosenberg Self-Esteem Scale**			
		Mean±Sd	**n**	**Test Request***	**p**
Source of information about nutrition	Nutritionist	20,88 ± 2,06[a]	17	3,32	0,01
	Doctor	21,92 ± 2,53[ab]	88		
	Radio and Television	21,45 ± 2,52[ab]	22		
	Newspaper	23,82 ± 2,4[b]	11		
	Other	20,95 ± 2,13[a]	22		

a-b: There is no difference between values with the same letter. *One Way ANOVA

Healthy Nutrition and BMI values, and the significant difference between Knowledge About Nutrition sub-dimension scores and BMI values was caused by underweight and overweight students and normal and overweight students (Table 7).

It was determined that the significant difference between the Z-Score values and the Positive Nutrition sub-dimension was between obese and obese children (Table 8).

Discussion

Table 7. The relationship between BMI values of adolescents and SBIT and BHB sub-dimension scores

Features n=160<		ATHE		KAN	
		Mean±Sd	n	Mean±Sd	n
BMI	Weak	64,6 ± 1,81[ab]	43	20,93 ± 1,7[a]	43
	Normal	64,83 ± 2,35[a]	76	20,82 ± 1,65[a]	76
	Overweight	63,54 ± 2,47[b]	39	19,77 ± 2,15[b]	39
	Obese	64,00 ± 1,41[ab]	2	21,00 ± 0,0[ab]	2
	Total	64,44 ± 2,28	160	20,59 ± 1,83	160
Test Request*		2,96		3,69	
p		0,03		0,01	

a-b: There is no difference between values with the same letter. *One Way ANOVA

A relationship was found between the Z-Score values of the adolescents and the Adolescent Healthy Lifestyle Choices Scale, Knowledge About Nutrition, and Positive Nutritionsub-dimension scores (p values 0.04; 0.03; 0.02, respectively). It was determined that the significant difference between the Z-Score values and the Adolescent Healthy Lifestyle Choices Scale and Knowledge About Nutrition sub-dimensions was between underweight and normal-weight children.

Adolescence is a period of maturation in biological, psychological, mental, and social aspects. During this period, body perception is influenced by various factors, including gender, age, body characteristics, self-esteem, media influence, and community views. Studies demonstrate the efficacy of awareness-based and information-oriented approaches in improving adolescents' eating behaviors. A comparison of the mean anthropometric characteristics of the study participants (mean age: 13.44 years; BMI: 21.85)

Table 8. The relationship between the Z-Score values of the adolescents and the AHLCS, KAN, and Positive Eating Habits (PEH) sub-dimension scores

Features N=160		**AHLCS**		**KAN**		**Positive Eating Habits (PEH)**	
		Mean±Sd	**n**	**Mean±Sd**	**n**	**Mean±Sd**	**n**
Z Score	Weak	55,10 ± 2,64[a]	10	21,20 ± 1,99[a]	10	13,7 ± 1,89[ab]	10
	Normal	53,26 ± 3,59[b]	78	20,99 ± 1,53[b]	78	13,1 ± 1,88[ab]	78
	Overweight	52,19 ± 3,9[ab]	54	20,19 ± 1,92[ab]	54	12,87 ± 1,53[a]	54
	Obese	54,17 ± 3,22[ab]	18	19,78 ± 2,24[ab]	18	14,28 ± 2,14[b]	18
	Total	53,11 ± 3,67	160	20,59 ± 1,83	160	13,19 ± 1,83	160
Test Request*		2,74		3,28		3,09	
p		**0,04**		**0,03**		**0,02**	

a-b: There is no difference between values with the same letter. *One Way ANOVA

with the data obtained from the Turkey Nutrition and Health Survey highlights the significant health implications of overweight and obesity rates. These findings underscore the necessity to promote healthy life attitudes during adolescence (19,26).

It was observed that the adolescents participating in the study had a normal BMI. The proportion of female participants was 59.38%, 40.63% described their general health status as moderate, 47.50% considered themselves overweight and 80.63% monitored their weight. It is noteworthy that only 14.38% of the participants reported being satisfied with their diet in the past year, and a mere 55.00% received nutrition information from a doctor. These findings underscore the critical need for targeted nutrition education and interventions during adolescence. Our results align with a previous study, which demonstrated that most adolescents have an intermediate BMI (15). However, globally, high BMI persists as one of the most pressing public health challenges. The relatively normal BMI levels observed in this study may be attributed to several factors, including concerns about appearance and efforts to maintain weight control for personal fulfillment. This finding highlights the role of societal and individual factors, such as body image awareness, in influencing adolescents' health behaviors. Beyond comparisons with previous studies, our findings have broader implications. Adolescents' moderate perception of their health status despite having a normal BMI suggests potential gaps in health literacy or a possible underestimation of their well-being. From a social perspective, this underscores the necessity for health education programs that are designed to provide information and, in addition, to cultivate confidence in understanding and managing personal health.

In terms of the health of individuals in the adolescent period, It is recommended not to skip meals, to consume regular meals, and to have an adequate and balanced diet (27,28). Our study determined that 83.1% of individuals consumed three main meals a day, and the rate of skipping meals was 8.1%. In our study, the rate of individuals who did not skip meals was high (91.9%). It was determined that the most skipped meal was lunch. When we look at the studies, it is seen that adolescents skip meals, unlike our study. 6-8 in Düzce. In a study conducted with 350 students in the third grade, 24% of boys and 21.4% of girls skipped meals, and it was reported that the most skipped meal was lunch (29). Our study also determined that adolescents who skip meals have higher BMI values than those who do not or sometimes skip meals.

Attitude toward healthy eating is one of the determinants of healthy eating behavior (27). Gönen et al., in their study with 296 sports science students, revealed a positive relationship between attitudes toward healthy eating and self-esteem (30). This study found a significant relationship between Body Image Scale, Attitudes Towards Healthy Eating Scale, Knowledge About Nutrition, Positive Nutrition, and Bad Eating Habits scale scores. Age, BMI, and Rosenberg Self-Esteem Scale values were found not to affect the Adolescent Healthy Lifestyle Choices Scale. In this context, it can be said that the attitude towards healthy eating will be effective in gaining healthy eating behavior, and healthy nutrition will increase the person's self-esteem. Again, it can be said that individuals with high self-esteem will pay attention to a healthy diet, which will contribute to their general health.

The mean Body Image Scale of the participants was 158.55±9.27; The mean of the Attitudes Towards Healthy Eating scale was 64.44±2.28; the Knowledge About Nutrition sub-dimension mean was 20.59±1.83; the Emotion Towards Nutrition sub-dimension mean 19.33±1.79; Positive Nutritions sub-dimension mean 13.19±1.83; Bad Eating Habit sub-dimension mean 12.7±1.57; The mean of Adolescent Healthy Lifestyle Choices Scale was 53.11±3.67, and the mean of the Rosenberg Self-Esteem Scale was found to be 21.74±2.50 (Table 3). When this scale is considered separately according to gender, it is seen that there is no significant difference between male and female students ($p>0.05$). In the study conducted by Özmet on healthy lifestyle behaviors in overweight and obese adolescents in 2018, the mean Adolescent Healthy Lifestyle Choices Scale was reported as 52,764 ± 9,459 (27). This result is similar to the result of our study. In our study, the mean Attitudes Towards Healthy Eating Scale of adolescents was 64.67 ± 2.17 for girls and 64.10 ± 2.41 for boys. A study conducted on university students in 2022 stated that the mean of Attitudes Towards Healthy Eating Scale was 68.35 ± 10.98 for female students and 69.06 ± 11.05 for male students (31). These values are like our study.

A statistically significant correlation was found between the BMI values of adolescents and the Attitudes Towards Healthy Eating Scale and Knowledge About Nutrition sub-dimension scores. It was determined that normal and overweight students caused a significant

difference between Attitudes Towards Healthy Nutrition scales and BMI values. The significant difference between Knowledge About Nutrition sub-dimension scores and BMI values was caused by underweight and overweight students and normal and overweight students (Table 7). Adolescents with normal BMI values were found to have higher mean Attitudes Towards Healthy Nutrition Scale scores than overweight adolescents. This shows that normal body weight adolescents are more sensitive to healthy nutrition than overweight adolescents. In the study conducted by Bıdıl in 2020, the average score of healthy eating according to the gender of the individuals was examined, and no significant difference was found between the scores of the sub-dimensions Knowledge About Nutrition, Emotion for Nutrition, Positive Nutrition, and Bad Nutrition (32). In this study, no significant difference was observed according to gender.

In the study carried out by Erdoğan et al. in 2023, it was determined that there was a significant difference between the body weight variable of the participants and the Bad Nutrition sub-dimension mean score of the Attitudes Towards Healthy Eating Scale and, while there was no statistically significant difference between the mean scores of all sub-dimensions of Attitudes Towards Healthy Eating Scale and according to gender (31). In our study, while there was no significant difference between the mean scores of the sub-dimensions of the Attitudes Towards Healthy Eating Scale and according to gender, a significant relationship was also found between the Z-Score values and the scores of the Adolescent Healthy Lifestyle Choices Scale, Knowledge About Nutrition, and Positive Nutritions sub-dimensions. It was determined that the significant difference between the Z-Score values and the Adolescent Healthy Lifestyle Choices Scale and Knowledge About Nutrition sub-dimensions was between underweight and normal-weight children. The mean scores of the Healthy Lifestyle Choices Scale in normal-weight adolescents are higher than those of lean adolescents. In addition, when the mean Knowledge About Nutrition sub-dimension values of adolescents are compared, the value of thin adolescents is considerably higher than that of obese adolescents (Table 8). This shows that thin adolescents try to have more information about nutritional information than obese ones.

Conclusion

Nutrition is at the forefront of the criteria that have essential effects on protecting and improving health in adolescence, as in every age period. When the results are evaluated, it can be said that adolescents are sufficient in creating or applying a healthy eating model but insufficient in body perception. In this case, it can trigger psychological eating disorders with the misconception of body perception and the accompanying psychological change, which is more common in adolescence. Obesity, common in today's adolescents, can pave the way for eating disorders such as anorexia nervosa, bulimia nervosa, and binge eating. In this regard, it is essential to carry out studies to increase the awareness of adolescents' body perceptions in schools or public service ads to raise healthy generations. This study will shed light and guide future studies in this context.

Conflict of interest

This research does not contain any conflict of interest with any institution or organization.

Financial support

This research did not receive any financial support from any institution or institution.

Acknowledgment

We thank all participants.

References

1.World Health Organization (2021) Obesity and Overweight. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight (accessed on 1 April 2022).

2.Fryar CD, Carroll MD, Ogden CL (2018) Prevalence of overweight, obesity, and severe obesity among children and adolescents aged 2–19 years: the United States, 1963–1965 through 2015–2016. NCHS Health E-Stats https://stacks.cdc.gov/view/cdc/58669 (accessed on 1 April 2022).

3.Skinner AC, Perrin EM, Skelton JA (2016) Prevalence of obesity and severe obesity in US children, 1999–2014. Obesity 24: 1116–1123.

4.Daniels SR, Hassink SG (2015) The Role of the Pediatrician in Primary Prevention of Obesity. Pediatrics 136: 275–292.

5.Chung ST, Onuzuruike AU, Magge SN (2018) Cardiometabolic risk in obese children. Ann N Y Acad Sci 1411: 166–183.

6.Verwied-Jorky S, Schiess S, Luque V, Grote V, Scaglioni S, Vecchi F, Martin F, Stolarczyk A, Koletzko B (2011) European Childhood Obesity Project Methodology for longitudinal assessment of nutrient intake and dietary habits in early childhood in a transnational multicenter study. J Pediatr Gastroenterol Nutr 52: 96–102.

7.Moreno LA, Bel-Serrat S, Santaliestra-Pasías AM, Rodríguez G (2013) Obesity prevention in children. World Rev Nutr Diet 106: 119–126.

8.Valerio G, Maffeis C, Saggese G, Ambruzzi MA, Balsamo A, Bellone S, Bergamini M, Bernasconi S, Bona G, Calcaterra V (2018) Diagnosis, treatment and prevention of pediatric obesity: A consensus position statement of the Italian Society for Pediatric Endocrinology and Diabetology and the Italian Society of Pediatrics. Ital J Pediatr 44: 1-21.

9.Carrillo HA, Ramírez-Vélez R (2019) Adherence to the Mediterranean diet in a sample of Colombian schoolchildren: An evaluation of the psychometric properties of the KIDMED questionnaire. Nutr Hosp 37: 73–79.

10.Fhon JRS, Caire MA, Júnior JAVM, Rodrigues RA (2017) Estilo de vida asociado a autoestima y variables demográficas en estudiantes de enfermería. Rev Científica Cienc Salud 9: 72–78.

11.Ospino GAC, Barbosa CP, Suescún J, Oviedo HC, Herazo E, Arias AC (2017) Validez y dimensionalidad de la escala de autoestima de Rosenberg en estudiantes universitarios. Pensam Psicológico 15: 29–39

12.Casas AG, García PLR, Guillamón AR, García-Cantó E, Pérez-Soto JJ, Marcos LT, López PT (2015) Relación entre el estatus de peso corporal y el autoconcepto en escolares. Nutr Hosp 31: 730–736.

13.Daniela CA, Fernanda MM (2016) Más allá de la cultura: Validación de un modelo multidimensional de autoconcepto en adolescentes argentinos. Escr. De Psicol. -Psychol Writ 9: 33–41.

14.Anez E, Fornieles-Deu A, Fauquet-Ars J, López-Guimerà G, Puntí-Vidal J, Sánchez-Carracedo D (2018) Body Image Dissatisfaction, physical activity and screen- time in Spanish adolescents. J Health Psychol 23: 36–47.

15.Duchesne A, Dion J, Lalande D, Bégin C, Émond C, Lalande G, McDuff P (2017) Body dissatisfaction and psychological distress in adolescents: Is self-esteem a mediator? J Health Psychol 22: 1563–1569.

16.Voelker DK, Reel JJ, Greenleaf C (2015) Weight status and body image perceptions in adolescents: Current perspectives. Adolesc Health Med Ther 6: 149–158.

17.Texeira MD, Pereira AT, Marques MV, Saraiva JM, de Macedo AF (2016) Eating behaviors, body image, perfectionism, and self-esteem in a sample of Portuguese girls. Rev Bras Psiquiatr 38: 135–140.

18.Lampard AM, Maclehose RF, Eisenberg ME, Larson NI, Davison KK, Neumark-Sztainer D (2015) Adolescents who engage exclusively in healthy weight control behaviors: Who are they? Int J Behav Nutr Phys Act 13: 1–10

19.World Health Organization. Adolescent Health (2021) https://www.who.int/health-topics/adolescent-health#tab=tab_1 (accessed on 1 April 2022).

20.Kundakçı AH (2005) Üniversite öğrencilerinin yeme tutumları, benlik algısı, vücut algısı ve stres belirtileri açısından karşılaştırılması. Yayımlanmamış Yüksek Lisans Tezi, Ankara Üniversitesi Sosyal Bilimler Enstitüsü, Ankara.

21.Kaya Ö, Cicicoğlu Hİ, Demir GT (2018) The attitudes of university students towards sports: attitude and metaphorical perception. European Journal of Physical Education and Sport Science 5(1): 115-133. http://dx.doi.org/10.5281/zenodo.1593401

22.Melynk BM, Jacobson D, Kelly S, O'Haver J, Small L, Mays MZ (2009) Improving Mental Health, Healthy Lifestyle Choices, and Physical Health of Hispanic Adolescents: A Randomized Controlled Pilot Study. Journal of School Health 79(12): 575-584.

23.Sümen A, Öncel S (2017) Türkiye'de lise öğrencilerinin sağlıklı yaşam biçimi davranışlarını etkileyen faktörler: Sistematik derleme. Eur J Ther 23(2): 49-94.

24.Çuhadaroğlu F (1986) Adolesanlarda Benlik Saygısı. Yayımlanmamış Yüksek Lisans Tezi. Hacettepe Üniversitesi Sosyal Bilimler Enstitüsü, Ankara.

25.Rosenberg M (1965) Society and the Adolescent Self-Image. Princeton University Press.

26.Ibili E, Billinghurst M (2019) The relationship between self-esteem and Social Network Loneliness: A study of trainee school counselors. Malaysian Online Journal of Educational Technology 7(3):39-56.

27.Özmet TD (2018) Determination of Healthy Lifestyle Behaviors in Overweight and Obese Adolescents and Factors Affecting Healthy Lifestyle Choices for the Future. Master's Thesis. Istanbul University, Institute of Health Sciences, Department of Public Health, Istanbul.

28.Yılmaz G, Şengür E, Turasan İ (2022) Investigation of healthy eating attitude scores of university students during Covid 19 period. National Journal of Sport Sciences 6(1): 1-10.

29.Serter Yiğit Y. (2006) A research on nutritional knowledge levels, habits, and obesity status of students attending 6th, 7th, and 8th grades of İsmet Paşa Primary School in Düzce Province. Master's Thesis. Gazi University, Faculty of Educational Sciences, Ankara.

30.Gönen M, Ceyhan MA (2022) The Relationship Between Attitudes Toward Healthy Nutrition and Self-Esteem of Students of the Faculty of Sports Sciences. Sciences (Ijoess) 13(48): 625-637.

31.Erdoğan R, Mikail TEL, Yıldırak A, Nazlıcan N, Çelik O, Nazlı V, Nazlı M (2023) Comparison of Healthy Eating Habits of High School and Secondary School Students. Journal of Sports, Health and Education Research 2(1): 9-21.

32.Bıdıl S (2020) Investigation of Badminton Athletes' Attitude Levels Regarding Healthy Nutrition. Unpublished Master's Thesis, Gazi University, Institute of Health Sciences, Department of Physical Education and Sports, Ankara.

Received: 12 Aug 2024 | **Accepted:** 24 Mar 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 319-324
DOI: 10.54005/geneltip.1530554

ORIGINAL ARTICLE

Comparison of Caudal Epidural Block Using Out-Of-Plane and In-Plane Techniques with Ultrasound in Pediatric Hypospadias Surgery: A Prospective Randomized Clinical Study

Pediatrik Hipospadias Cerrahisinde Ultrason İle Out Of-Plane Ve In-Plane Teknikler Kullanılarak Kaudal Epıdural Blok Karşılaştırması: Prospektif Randomize Klinik Bir Çalışma

[1]Mehmet Aki Kacar, [2]Faruk Cicekci, [2]Mehmet Selcuk Uluer, [2]Mehmet Sargin, [3]Metin Gunduz
[2]Emine Aslanlar, [2]Inci Kara, [2]Jale Bengi Celik

[1]Department of Anesthesiology, Aksehir State Hospital, Konya, Türkiye
[2]Department of Anesthesiology and Reanimation, Selcuk University, Medical Faculty, Konya, Türkiye
[3]Department of Pediatric Surgery, Selcuk University, Medical Faculty, Konya, Türkiye

Correspondence

Faruk Cicekci, Professor
Department of Anaesthesiology, Selcuk University, Medical Faculty
Konya, Türkiye

E-Mail: farukcicekci@yahoo.com

How to cite ?

Kacar MA, Cicekci F, Uluer MS, Sargin M, Gunduz M, Aslanlar E, Kara I, Celik JB. Comparison of Caudal Epidural Block Using Out-Of-Plane and In-Plane Techniques with Ultrasound in Pediatric Hypospadias Surgery: A Prospective Randomized Clinical Study. Genel Tıp Derg. 2025;35 (2): 319-324

ABSTRACT

Aim: To compare the success rates and postoperative pain levels of caudal epidural block (CB) applications using ultrasound-guided out-of-plane technique and in-plane techniques in pediatric hypospadias surgery.
Methods: One hundred sixty-two patients who underwent pediatric hypospadias surgery were randomized to either the in-plane or out-of-plane ultrasound-guided CB. The primary outcome was the success rate of CB. Secondary outcomes included postoperative pain levels (FLACC score), the first analgesia requirement time, the total amount of paracetamol consumption, and complications. Procedural data were collected by blinded observers.
Results: There were differences in the primary outcome of the number of needle attempts 87.8% vs. 56.3%, p<.001), the success rate at the first entry (93.9% vs. 62.5%, p<.001), the visualization rate (90.2% vs. 31.3%, p<.001), a local anesthetic (LA) spread rate (87.8% vs. 46.3%, p<.001), and the duration of block application (41.44 ± 25.87 sec vs. 78.11 ± 43.13 sec, p<.001), respectively, between the in-plane and out-of-plane groups. There were also differences between out-of-plane and in-plane FLACC scores at the 12th and 24th hours (p=.024 and p=.012, respectively), the first analgesia requirement time (p=.009), and the total amount of paracetamol consumption (p=.018) in 24-hour pain ratings. There were no differences in complications.
Conclusion: Ultrasound-guided in-plane technique is an alternative technique that is superior to the out-of-plane technique for its success rate and postoperative analgesia.

Keywords: Caudal block, hypospadias surgery, pediatric, ultrasound

ÖZ

Amaç: Pediatrik hipospadias cerrahisinde ultrason kılavuzluğunda out of-plane ve ın-plane teknikler kullanılarak yapılan kaudal epidural blok (CB) uygulamalarının başarı oranlarını ve postoperatif ağrı düzeylerini karşılaştırmak.
Yöntemler: Pediatrik hipospadias cerrahisi geçiren 162 hasta in-plane veya out of-plane ultrason kılavuzluğunda CB'ye randomize edildi. Birincil sonuç CB'nin başarı oranıydı. İkincil sonuçlar postoperatif ağrı düzeylerini (FLACC skoru), ilk analjezi gereksinim süresini, toplam parasetamol tüketim miktarını ve komplikasyonları içeriyordu. İşlem verileri kör gözlemciler tarafından toplandı.
Bulgular: Birincil sonuçlarda, iğne denemelerinin sayısı (%87,8'e karşı %56,3, p<.001), ilk girişteki başarı oranı (%93,9'a karşı %62,5, p<.001), görüntüleme oranı (%90,2'ye karşı %31,3, p<.001), lokal anestezik (LA) yayılma oranı (%87,8'e karşı %46,3, p<.001) ve blok uygulama süresi (41,44 ± 25,87 sn'ye karşı 78,11 ± 43,13 sn, p<.001) açısından sırasıyla düzlem içi ve düzlem dışı gruplar arasında farklar vardı. Ayrıca, 12. ve 24. saatlerdeki düzlem dışı ve düzlem içi FLACC skorları (sırasıyla p=.024 ve p=.012), ilk analjezi gereksinim zamanı (p=.009) ve 24 saatlik ağrı derecelendirmelerinde toplam parasetamol tüketimi miktarı (p=.018) arasında da farklar vardı. Komplikasyonlarda fark yoktu.
Sonuç: Ultrason rehberliğinde in-plane teknik, başarı oranı ve postoperatif analjezi açısından out of-plane tekniğe göre üstün olan alternatif bir tekniktir.

Anahtar sözcükler: Kaudal blok, pediatrik, ultrason, hipospadias cerrahisi

Introduction

Caudal block (CB) is an easy and effective type of central neuraxial block that is widely used in the pediatric population to provide intraoperative and postoperative analgesia in sub-umbilical surgeries. Ultrasound (US)-guided CB was first used in 2003 by Klocke et al. (1). The sacrum, sacral cornua, sacrococcygeal ligament, and sacral hiatus can be easily distinguished with ultrasound. Within the caudal epidural space, the sacral roots can be seen as hypoechoic ellipses. With the sacrococcygeal membrane in the middle of the image, the probe is rotated 90° out-of-plane and the exact position of the cornua is defined, which is especially useful in the presence of a fat pad (2). In addition, anatomic variations of the sacral hiatus and the process area can be observed clearly (3). In addition, with US, it is shown that the injection is performed correctly, the needle is advanced in the desired direction under ultrasound guidance, the sacral canal is enlarged with a local anesthetic (LA) injection, and turbulence

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

is observed in the sacral canal with color Doppler during the injection (4,5). In cases where the block is difficult, the in-plane technique may be preferred in the midline plane. The advantage of the in-plane technique is better needlepoint precision through real-time observation of the needle bar and tip. The advantage of the out-of-plane approach is that it involves a more consistent needle orientation with the long axis of the nerve and adjacent muscle/ fascia (6). Success rates in ultrasound-guided CB applications vary between 92.8% and 97%. (3,6). However, there is no study in the literature comparing the two approaches in pediatric patients for the superiority of each technique.

This study aimed to compare the success rates and postoperative pain levels of CB applications with ultrasound-guided out-of-plane and in-plane techniques in pediatric hypospadias surgery.

Materials and Methods

This study with a prospective randomized design as a clinical trial was approved by the Institutional Review Board of Selcuk University (Decision No: 2019/241), and written informed consent was obtained from all subjects participating in the trial. The trial was registered before patient enrollment at clinicaltrials.gov (NCT04671992). The study was conducted under the principles of the Declaration of Helsinki and adheres to Consolidated Standards of Reporting Trials (CONSORT) guidelines. After obtaining written parental informed consent, 170 patients defined by the American Society of Anesthesiologists-physical status (ASA-PS) I-II aged 1-10 years and undergoing hypospadias surgery between January 1st, 2021, and December 31st, 2021, were included in the study. Children with a previous neurologic or spinal disorder, coagulation anomaly, known allergy to local anesthetics, local infection in the CB region, and a history of preterm birth were excluded from the study. The ethical rules specified in the Declaration of Helsinki were adhered to throughout the study. Basal levels were recorded through routine monitoring of electrocardiogram (ECG), peripheral oxygen saturation (SpO2), and noninvasive blood pressure measurements of the patients admitted to the operating room. All patients received 0.5 mg.kg-1 midazolam peroral for premedication. Anesthesia was induced using a face mask with 7-8% sevoflurane, and 50% medical air/50% oxygen until the patient lost consciousness. After the loss of consciousness, vascular access was achieved; propofol 2-3 mg. kg-1 and fentanyl 0.5 µg.kg-1 IV were used for general anesthesia induction. After the eyelash reflex disappeared without any neuromuscular blocker drug administration, an appropriate laryngeal mask airway, supraglottic, was placed and the patient was connected to the anesthesia device for ventilation. For the maintenance of anesthesia, 2% sevoflurane and nitrous oxide were reduced, and a 50% oxygen + air mixture was used. The patients were randomized into the CP group with the out-of-plane technique (group OP) and the CP group with the US-guided in-plane technique (group IP) using a computer-generated random number table and were divided into the two groups using the closed opaque envelope method. After placing the patients in the lateral position for CB and providing asepsis of the perianal region, a sterile 7.5-10 MHz linear US probe (SONOHEALTH® Double Probes Handheld Ultrasound Scanners Highest Cost-effective D2CL-Linear) was applied transversely to the midline to obtain a transverse view of the sacral hiatus (out-of-plane technique) for group OP (Figure 1).

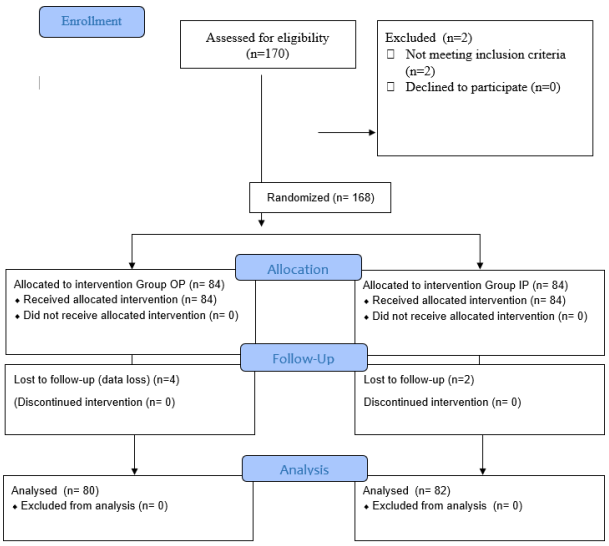


Figure 1. This randomization flow diagram displays the progress of all subjects throughout the study

The two sacral cornua were visualized as two hyperechoic structures, the sacrococcygeal ligament (SCL) as two band-like hyperechoic structures between the sacral cornua, the dorsal surface of the sacral bone as the deep structure and the sacral hiatus as the hypoechoic region between the 2 band-like hyperechoic structures

on US. The in-plane technique for group IP was obtained by rotating the US probe 90° from the transverse view of the sacral hiatus (Figure 2).

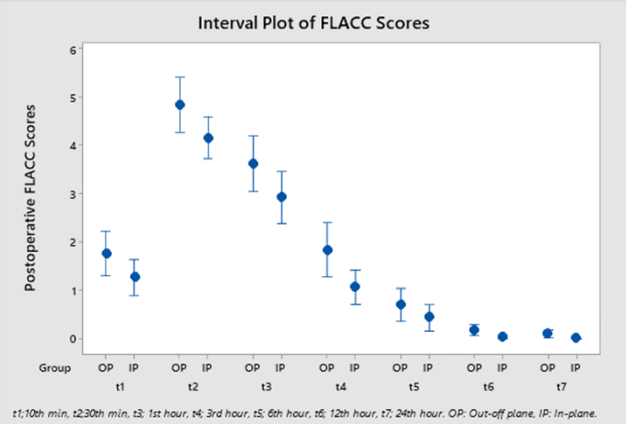


Figure 2. Comparison of Postoperative FLACC Scores in Both Groups

*p<0.001, compared to Group OP.

To obtain CP with both techniques, a 22-gauge caudal needle was inserted at the level of the sacral cornua. After observing that there was no blood or cerebrospinal fluid in aspiration, an LA injection was performed under hemodynamic and ECG monitoring, with a dose of 0.25% bupivacaine and a volume of 0.5 mL/kg. The block success rate was defined as the absence of significant motor movements after surgical induction or heart and respiratory rates exceeding 20% of baseline levels. In addition, the block application time, number of needle attempts, success at first entry, ease of visualization, and LA spread were recorded. The block application time was defined as the time between needle entry and termination of the LA application. The success rate at the first entry was defined as reaching the sacral canal or sacral hiatus with a single needle insertion at the first entry from the skin. Ease of visualization and the spread of LA visually in US were interpreted by evaluating US images.

In both groups, surgery started 10 minutes after CB administration. No intraoperative opioids or sedative drugs were used. Mean arterial pressures, heart rates, oxygen saturation, and end-tidal CO2 values of the patients were recorded every 5 minutes.

The patients were extubated and followed up in the postoperative recovery unit face, legs, activity, crying, and consolability (FLACC) at the end of the surgery. Time to first analgesia requirement, total analgesic type, amount of paracetamol consumption, and postoperative complications were recorded. In the evaluations made of the patients in both groups, if the FLACC scale was ≥4, 15 mg.kg-1 paracetamol was administered IV, and ibuprofen 10 mg.kg-1 IV for rescue analgesia was administered and recorded.

Statistical analysis

All statistical analyses were performed using the R version 3.6.0 statistics package (The R Foundation for Statistical Computing, Vienna, Austria; https://www.r-project.org). The normality of the data was checked using the Shapiro-Wilk test of normality and Q-Q plots, and the homogeneity of group variances was checked using Levene's test. Descriptive statistics for numerical variables are presented as mean ± standard deviation (minimum-maximum) and median, and descriptive statistics for categorical variables are presented as frequency (n) and percentage (%). The independent sample t-test, Welch's t-test, Fisher's exact test, and Mann-Whitney U test were used to compare the study groups (OP and IP) according to sociodemographic characteristics. The Mann-Whitney U test and Yates's continuity were used to compare CB details corrected Chi-square test. Fisher's exact test and Pearson's Chi-square test were used to assess CP complications. The Mann-Whitney U test was also used for postoperative pain clinical findings and postoperative FLACC scores. FLACC ratings are reported as medians with interquartile ranges. A p-value of <.05 was considered statistically significant.

Power analysis

The prior sample size was calculated with the "pwr" package in R version 4.0.1 software to test the success rate of CB using the two-proportion Z-test with an effect size of 0.45, and an alpha of 0.05. The results revealed that the required sample size in each group was 78 to achieve a power of 0.80. Considering the 10% dropout rate, we included 85 participants for each group.

Results

A total of 162 of 170 patients assigned for the study were included in this study. Eight patients from both groups (due to not meeting inclusion criteria, and data loss) were excluded. The remaining eligible patients were presented in the Consolidated

Reporting Standards (CONSORT) flowchart (Fig 1). There was no difference between the two groups in terms of patient and surgical characteristics (Table 1).

Table 1. Patient's demographics and clinical characteristics

	OP (*n*=80)	IP (*n*=82)	*p*-value
Age (years)	3.84±2.33 (1-10)	3.67 ± 2.54 (1-10)	.653[1]
BMI (kg/m2)	16.03±2.32 (11.41-22.91)	16.71±3.41 (12-27.78)	.135[2]
ASA I/II	76/4	80/2	.440[3]
Anesthesia time (min)	75.86±20.24 (50-130)	74.49±22.86 (40-135)	.811[4]
Operation time (min)	61.74±18.73 (39-115)	60.73±22.46 (30-120)	.618[4]

Data are presented as mean±standard deviation (minimum-maximum).

1Independent sample t-test

2Welch's t-test

3Fisher Exact test

4Mann-Whitney U test

When the CB application details were compared according to the groups, the number of needle attempts (87.8% vs. 56.3%, respectively; p<.001), the success rate at the first entry (93.9% vs. 62.5%, respectively; p<.001), the visualization rate (90.2% vs. 31.3%, respectively; p<.001), and the LA spread rate (87.8% vs. 46.3%, respectively; p<.001) were significantly higher in group IP, compared with group OP. In addition, the duration of block application was significantly longer in the OP group than in the IP group (p<.001). (Table 2)

Table 2. Details of caudal epidural block application

	OP (n=80)	IP (n=82)	*p*-value
The time of block application (sec)	78.11±43.13 (29 – 195)	41.44±25.87 (15-135)	<.001[1]
The number of needle attempts			<.001[2]
One time	45 (56.3)	72 (87.8)	
Multiple	35 (43.8)	10 (12.2)	
The success rate at first insertion	50 (62.5)	77 (93.9)	<.001[2]
The CB success rate	73 (91.3)	80 (97.6)	.097[3]
The ease of visualization			<.001[4]
Easy	25 (31.3)[a]	74 (90.2)[b]	
Middle	27 (33.8)[a]	5 (6.1)[b]	
Hard	28 (35)[a]	3 (3.7)[b]	
The spread of LA visually on US			<.001[4]
Good	37 (46.3)[a]	72 (87.8)[b]	
Middle	25 (31.3)[a]	7 (8.5)[b]	
Weak	18 (22.5)[a]	3 (3.7)[b]	

OP=Out-of-plane, IP=In-plane, CB=Caudal epidural block, LA=Local anesthetic; Data are presented as mean±standard deviation (minimum-maximum) or frequency (n) and percentile (%).

1Mann-Whitney U test

2Yates continuity corrected chi-square test

3Fisher's exact test

4Pearson's chi-square test

For FLACC ratings at 12th and 24th hours, the in-plane technique was not superior to the out-of-plane technique, respectively (median FLACC 0; IQR, [0-0] vs. 0; IQR, [0-0], p=.024; Figure 1). There was no difference in median FLACC ratings at 10th (2.0; IQR, [0-3.0] vs. 0; IQR, [0-2.0]; p=.106), 30th min (5.0; IQR, [3.0-6.0] vs. 4.0; IQR, [3.0-5.0]; p=.062), 1st (3.0; IQR, [2.0-5.75] vs. 3.0; IQR, [0-4.25]; p=.123), 3td (0; IQR, [0-3.75] vs. 0; IQR, [0-2.0]; p=.068) and 6th hours (0; IQR, [0-0] vs. 0; IQR, [0-0]; p=.253) respectively (Fig 1).

When comparing the postoperative pain of both groups according to clinical characteristics, the first analgesia requirement time was longer (p=.009) and the total amount of paracetamol consumption was higher in group IP compared with group OP (p=.018). The amount of rescue analgesia was similar between the groups (p=.191). (Table 3). Caudal epidural block complications were similar between the groups (Table 4).

Table 3. Characteristics of postoperative clinical pain

	OP (n=80) Median (min-max)	IP (n=82) Median (min-max)	*p*-value
The first analgesia requirement time (min)	30 (30-180)	60 (30-180)	.009[1]
The total amount of paracetamol consumption (mg)	300 (150-1000)	150 (100-900)	.018[1]
The amount of rescue analgesia (mg)	300 (200-400)	225 (100-300)	.191[1]

Data are presented as median (minimum-maximum).

[1]Mann-Whitney U test

Table 4. Complications of caudal block.

	OP (n=80)	IP (n=82)	*p*-value
Vascular puncture	1	0	.494[1]
Subcutaneous bulging	1	3	.620[1]
Dural puncture	1	0	.494[1]
Local anesthetics toxicity	0	0	>.999[1]
Respiratory depression	0	0	>.999[1]

Values are presented as numbers.

[1]Fisher's exact test

Discussion

Ultrasound-guided OP versus IP techniques in pediatric hypospadias surgery resulted in a decrease in FLACC scores, total paracetamol consumption amounts, and prolongation of the first analgesia requirement in the first 12 hours postoperatively. In addition, CB shortened the application time, decreased the number of needle attempts, increased the success rates at the first entry, provided easy visualization, and provided

good LA dissemination.

Caudal anesthesia is often preferred for pain control during and after surgery in pediatric surgery. The introduction of ultrasonography into anesthesia practice affects block success and its use may reduce complications associated with blind blocks. Ultrasonographic guidance ensures the precise delivery of LA drugs around targeted peripheral nerves (7). Visualization of anatomic landmarks and nerves increases the success of the block while also preventing possible complications related to critical structures. US guidance is even more important in regional anesthesia procedures because critical structures are located closer to target tissues in children than in adults (8). Although there is no study comparing IP and OP techniques for CP, these techniques have been compared in various anesthesia procedures such as peripheral nerve block and central vascular access (9-11). In this study, OP and IP techniques were examined in terms of the determination of anatomic points using US, visualization of BP, and visualization of LA distribution, which Abukawa et al. (12) also noted. It has been revealed that the IP technique can be advantageous in terms of visualization of the anatomic structure and monitoring of LA distribution. In this study, it was thought that when the IP technique could follow along the caudal longitudinal axis and the needle's progression to the desired anatomic region was simultaneously observed, the desired place of injection could be visualized optimally, and the LA injection would be followed more clearly from beginning to end. Considering the difficulty in visualization and the disadvantage in following the LA spread in OP applications performed with the OP technique, local anesthetic has been shown to spread in a wider region in the epidural area, since it is difficult to determine the proximity of the needle to the target area. Thus, we believe that the amount of LA penetrating the nerve in this OP technique is less than in the IP technique. Although there is no statistical difference between the two techniques in terms of block success rates, it is thought that this may explain the lower success of the OP technique in terms of the shortening of the first analgesia requirement time, the increase in the total amount of paracetamol consumption, and the increase in the postoperative FLACC scores at the 12th hour and later in postoperative follow-ups.

In the study conducted by Ahiskalioglu et al. on 140 patients (ASA I-II) aged 5-12 years in which they compared US-guided CP applications and the conventional method, the use of US was recommended because it reduced complications in caudal injections and increased the success rate of the first punctures (7). In our study, considering the advantages of US use in CP, when OP and IP techniques used in US-guided CP applications were compared in terms of postoperative complications, it was determined that the two techniques were not superior to each other in terms of complications. In a study by Karaca et al.(13), in which the authors compared US-guided and conventional caudal block in children (ASA-I) and 266 children aged 6 months to 6 years, it was found that as the patient's age decreased, the anatomic signs could not be well defined; therefore, it might be more difficult to perform the block in younger children. It has been shown that there is always a risk of dural puncture or other complications such as vascular puncture, soft tissue swelling, intraosseous injections, and systemic toxicity as the needle passes through the sacral canal (13). As a result of the study, although the success rate between the groups was not different, it was observed that the use of US during pediatric CP procedures was effective in reducing complications and increasing the success rate of the first puncture, and it was recommended to use US guidance, especially in children aged <6 years or those weighing <16 kg. In addition to this study, although there were no significant differences in complications in our study, it was concluded that the IP technique was more appropriate in increasing the success rates of the first punctures.

There were several limitations in the study. CB is used at various dermatome levels of pediatric surgery. However, only BP comparisons were made for hypospadias surgery in this study. Another limitation was that the duration of the motor block in the postoperative period was not taken into account.

Conclusion

It was concluded that the ultrasound-guided OP versus IP technique in pediatric hypospadias surgery was better in terms of FLACC scores, total paracetamol consumption, and time to the first analgesia in the first 12 hours postoperatively. In addition, in the IP technique, the CB application time was shortened, the number of needle attempts decreased, first entry success rates

increased, visualization was easier, and it provided good LA dissemination. Therefore, the ultrasound-guided IP technique should be considered an effective alternative technique for CB, which is more commonly used for the CB success rate and postoperative analgesia.

Financial support

The authors received Scientific Research Project of Selcuk University (BAP) financial support for the research and/or authorship of this article.

Conflict of interest

No author has a conflict of interest that relates to the content discussed in this article.

References

1.Klocke RT, Jenkinson T, Glew D. Sonographically guided caudal epidural steroid injections. Journal of ultrasound in medicine. 2003;22(11):1229-1232.

2.Roberts S, Ultrasonographic guidance in pediatric regional anesthesia. Part 2: techniques. Pediatric Anesthesia, 2006;16(11):1112-1124.

3.Kao SC, Lin SC. Caudal epidural block: an updated review of anatomy and techniques. BioMed research international, 2017;2017:1-5.

4.Eksert, S. and S. Ender, Kaudal Blok Uygulanan Pediatrik Hastalarda Ultrason ile Konvansiyonel Kör Tekniğin Karşılaştırılması. Celal Bayar Üniversitesi Sağlık Bilimleri Enstitüsü Dergisi, 2019;6(2):111-114. (Turkish)

5.Roberts, SA, Guruswamy V, Galvez I. Caudal injectate can be reliably imaged using portable ultrasound–a preliminary study. Pediatric Anesthesia, 2005;15(11):948-952.

6.Wang LZ, Hu XX, Zhang YF, Chang XY. A randomized comparison of the caudal block by sacral hiatus injection under ultrasound guidance with traditional sacral canal injection in children. Pediatric Anesthesia, 2013;23(5):395-400.

7.Ahiskalioglu A, Yayik AM, Ahiskalioglu EO, et al. Ultrasound-guided versus conventional injection for caudal block in children: a prospective randomized clinical study. Journal of Clinical Anesthesia, 2018;44:91-96.

8.Ecoffey C. Pediatric regional anesthesia–update. Current Opinion in Anesthesiology, 2007;20(3):232-235.

9.Fredrickson M, Danesh□Clough T. Ultrasound□guided femoral catheter placement: a randomized comparison of the in□plane and out□of□plane techniques. Anaesthesia, 2013;68(4):382-390.

10.Schwenk ES, Gandhi K, Baratta, JL, et al. Ultrasound-Guided Out-of-Plane vs. In-Plane Interscalene Catheters: A Randomized, Prospective Study. Anesth Pain Med, 2015;5(6):e31111.

11.Takeshita J, Tachibana K, Nakajima Y, et al. Long-axis in-plane approach versus short-axis out-of-plane approach for ultrasound-guided central venous catheterization in pediatric patients: A randomized controlled trial. Pediatric Critical Care Medicine, 2020;21(11):996-1001.

12.Abukawa Y, Hiroki K, Morioka N, et al. Ultrasound versus anatomical landmarks for caudal epidural anesthesia in pediatric patients. BMC Anesthesiology, 2015;15(1):1-4.

13.Karaca O, Pinar HU, Gokmen Z, Dogan R, Ultrasound-guided versus conventional caudal block in children: A prospective randomized study. European journal of pediatric surgery, 2019;29(06):533-538.

Received: 14 Dec 2024 | **Accepted:** 24 May 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 325-333
DOI: 10.54005/geneltip.1522589

ORIGINAL ARTICLE

The Current Prevalence of Alzheimer's Disease and Related Factors in Individuals Aged 65 and over in Konya City Center of Türkiye

Türkiye'nin Konya İl Merkezinde 65 yaş ve Üzeri Bireylerde Alzheimer Hastalığının Güncel Prevalansı ve İlişkili Faktörler

[1]Dilara Cari Gungor, [2]Figen Guney, [3]Mehmet Uyar, [3]Hasan Kucukkendirci, [3]Tahir Kemal Sahin

[1]Neurologist and Intensive Care Unit Research Fellow, Department of Neurology and Intensive Care Unit, Faculty of Medicine, Selcuk University, Konya, Türkiye
[2]Deparment of Neurology, Faculty of Medicine, Necmettin Erbakan University, Konya, Türkiye
[3]Deparment of Public Health, Faculty of Medicine, Necmettin Erbakan University, Konya, Türkiye

Correspondence

Dilara CARI GUNGOR, MD.
Neurologist and Intensive Care Unit Research Fellow, Department of Neurology and Intensive Care Unit, Faculty of Medicine, Selcuk University, Konya, Türkiye

E-Mail: dcarigungor@hotmail.com

How to cite ?

Cari Gungor D, Guney F, Uyar M, Kucukkendirci H, Sahin TK. The Current Prevalence of Alzheimer's Disease and Related Factors in Individuals Aged 65 and over in Konya City Center of Türkiye. Genel Tıp Derg. 2025;35 (2): 325-333

ABSTRACT

Aim: The prevalence of Alzheimer's Disease (AD) is unknown in many regions of our country. This study aimed to determine the prevalence of AD and its associated factors in the Konya city center located in the Central Anatolia region (Türkiye).
Methods: A study population of 240 subjects aged 65 and older was randomly selected from 14 family health centres. A face-to-face procedural interview, and neurological and psychiatric tests, including the mini-mental state examination, clock drawing score, basic and instrumental daily life activities, mental status examination, and geriatric depression scale, were performed. Co-morbidities, used drugs, risks, and protective factors were questioned.
Results: The average age was 71.5±5.8; 52.5% of them were male, and 47.5% were women. The prevalence of AD was 7.5%; 2.5% of them had mild, and 5% had advanced AD. While AD rates were higher in illiterate people and primary school graduates, it was lower in people with regular physical and mental activity. More abnormalities were found in general information, reasoning, abstraction, and executive functions in people with AD. As the daily and instrumental life activities deteriorated, the frequency of AD increased. Geriatric depression was higher in the AD group.
Conclusions: Türkiye is both a European and an Asian country and the locations of this study are urban areas of the Central Anatolian Region. Our prevalence was slightly higher than current data of European countries. The presence of AD was found to be associated with mental state abnormalities, deteriorated daily and instrumental life activities, and increased geriatric depression.

Keywords: Alzheimer's disease; prevalence; related factors; activities of daily living; geriatric depression

ÖZ

Amaç: Ülkemizin birçok bölgesinde Alzheimer Hastalığı (AH) prevalansı bilinmemektedir. Bu çalışmada İç Anadolu Bölgesi'nde (Türkiye) yer alan Konya il merkezinde AH prevalansının ve ilişkili faktörlerin belirlenmesi amaçlanmıştır.
Gereç ve Yöntemler: Çalışmaya 14 aile sağlığı merkezinden rastgele seçilen 65 yaş ve üzeri 240 kişi seçilmiştir. Yüz yüze görüşme proseduru ile, mini-mental test, saat çizme skoru, temel ve enstrümantal günlük yaşam aktiviteleri, mental durum muayenesi ve geriatrik depresyon ölçeği dahil olmak üzere nörolojik ve psikiyatrik testler yapıldı. Komorbiditeler, kullanılan ilaçlar, riskler ve koruyucu faktörler sorgulanmıştır.
Bulgular: Bireylerin ortalama yaşı 71.5 ± 5.8 idi; %52.5'i erkek, %47.5'i kadındı. AD prevalansı %7,5 bulundu; %2,5'inde hafif, %5'inde ileri AD vardı. Okuma yazma bilmeyenlerde ve ilkokul mezunlarında AD oranları daha yüksek, düzenli fiziksel ve zihinsel aktivite yapanlarda daha düşüktü. AD'li kişilerde genel bilgi, muhakeme, soyutlama ve yürütücü işlevlerde daha fazla anormallikler bulundu. Günlük ve enstrümantal yaşam aktiviteleri kötüleştikçe AD sıklığı artmakta idi. Geriatrik depresyon AD grubunda daha yüksekti.
Sonuçlar: Türkiye hem bir Avrupa hem de bir Asya ülkesidir ve bu çalışmanın lokasyonu İç Anadolu Bölgesi'nin kentsel alanlarıdır. Prevalansımız Avrupa ülkelerinin güncel verilerinden biraz daha yüksektir. AH varlığı mental durum anormallikleri, günlük ve enstrümantal yaşam aktivitelerinde bozulma ve artmış geriatrik depresyon ile ilişkili bulunmuştur.

Anahtar Kelimeler: Alzheimer hastalığı; prevalans; ilişkili faktörler; günlük yaşam aktiviteleri; geriatrik depresyon

Introduction

Alzheimer's Disease (AD) is a progressive neurodegenerative disease characterized by impairment of memory and cognitive functions, and inability in daily life activities (1). AD affects a significant segment of the population because it can lead to some psychosocial problems not only in the affected individuals but also in their caregivers and relatives. It is the most common form of dementia and makes up the vast majority of all dementia cases.

Although many risk and protective factors are discussed for disease, the most important risk factor is advancing age. The prevalence of AD is increasing exponentially every 5 years after age 65. The highest prevalence is in the eighth decade and above.

The prevalence of AD may differ by country and region. The estimated prevalence of dementia in 60-year-olds and over is 4.7% in Central Europe and up to 8.7% in North Africa and the Middle East. There has been an increase in Asia and Africa in the last few years. Population-based prevalence studies are inadequate, but the known prevalence of AD is 4.4%

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

in individuals aged 65 and older; the prevalence of all causes of dementia is 6.4% in Europe (2,3).

In our country, the prevalence of AD was reported at 10% in individuals aged 70 and older who live in Istanbul in the Marmara Region (4). However, the prevalence of AD or dementia is unknown in many regions of our country.

This study aimed to determine the prevalence of AD and its associated factors in the Konya city center in the Central Anatolia region.

Materials And Methods

Study Population

The study protocol was approved by the Local Ethical Committee (Decision No: 2016-599), and all patients or first-degree relatives signed written informed consent forms before enrolling in the study. The study was conducted under the principles of the Declaration of Helsinki.

The study was conducted in the Meram, Karatay, and Selçuklu, which are the towns of the Konya city center. The study population was determined by the Public Health and Medical Statistics Department of Necmettin Erbakan University according to scientific sampling methods. The sample size was found to be 240 with 80% power and 5% deviation, assuming the prevalence in 65-year-olds and older as an average of 10% (5). Two hundred forty subjects aged 65 and older were randomly selected from records of different 14 family health centers (FHC) in these three regions. All individuals in our country are registered to this FHC system. According to current data, the population of the Meram region is 344,500; the Karatay region is 339,000; the Selçuklu region is 662,000 persons, and the rate of the population ages 65 and over is 6,5% in these central districts. Therefore, 60 persons from the Meram and Karatay regions, respectively, and 120 persons from the Selçuklu region were included in the study. The Selçuklu region is known as the region with higher population density and higher education-income levels compared to the other two regions. In this way, the participants were from different socio-cultural and economic segments. The study was completed in one month.

Examination Tests

A face-to-face procedure interview, neurologic and psychiatric tests including Mini-Mental State Examination (MMSE), Clock Drawing Test (CDT) score, Basic and Instrümental Activities of Daily Living (BADL and IADL, respectively), mental status examination, geriatric depression scale were performed. Additionally, demographic characteristics, co-morbidities, drugs used, risks, and protective factors for AD were questioned and recorded. These interrogations and tests took an average of 20 min for each individual.

The validated Turkish version (6) of the standardized MMSE (sMMSE) (7) and modified version of the sMMSE (sMMSE-il) for illiterate subjects (8) were used. The MMSE, the main evaluation test of this study, consisted of components including time and space orientation, memory recording, attention and calculation, recall, language, and drawing shapes; a total of 30 points were evaluated. A score of 24 points and above was determined to be normal, 18–23 was considered mild AD, and 17 and below was designated advanced AD.

In the CDT evaluation, a ready circle was given, correctly placed "12" was 3 points; if the numbers were correctly placed plus 1 point; if the hour and minute hands were correctly placed plus 1 point; and if the time was correctly marked plus 1 point.

Additionally, mental state examinations were performed, including general information, reasoning, abstraction, and executive functions, for example, from which direction does the sun rise? What do you do if you see a lost child? Name 10 objects that begin with the letter 'K' in 1 min?...

The following criteria of BADL, including eating, drinking, dressing-undressing, combing hair, shaving, walking, going to bed, getting up from bed, using the toilet, bathing, performing housework, going outside, shopping, and the presence of incontinence, and those of IADL (including: using the phone, traveling by vehicles, cooking, counting money, using medications), were questioned. There was one question for each activity, including eight questions about basic life activities and seven questions regarding instrumental life activities. These activities were evaluated as normal (0 points), incomplete (1 point), or complete (2 points) deterioration, and a score was calculated (9-13).

A Geriatrics Depression Scale with 30 questions was performed on the participants; 1 point was scored for each answer, and a total score of 0–10 is accepted as normal; 11–13 corresponds with mild depression;

14 and above means severe depression (14, 15).

Exclusion Criteria

The neuropsychiatric drug use and presence of neuropsychiatric disorders such as schizophrenia, psychosis, bipolar disorder, cerebrovascular events, and advanced Parkinson's were determined as exclusion criteria because these situations could affect the reliability of the tests. Also, advanced co-morbidities that disrupted living standards and quality, such as advanced cancer, cirrhosis, kidney, pulmonary and heart failure, blindness, and deafness, were excluded.

Statistical Analysis

All data were analyzed using SPSS statistics version 18 (SPSS Inc., Chicago, IL, USA). Non-categoric values were given as a mean ± SD. The student's t-test was used for the analysis of the normally distributed variables. Kruskal Wallis and Mann-Whitney tests were used for non-normally distributed variables. The Chi-square test was used for the comparison of categorical variables. A $p<0.05$ was considered statistically significant.

Results

Demographic Characteristics

Two hundred and fifty-nine people were interviewed to reach the target of 240 persons. Of these, 14 of them did not agree to participate in the study. Five participants were excluded due to exclusion criteria.

The average age of all participants was 71.5 ± 5.8 years (minimum: 65 years; maximum: 98 years). There were 126 males (52.5%) with a mean age of 72.2 ± 5.5 and 114 females (47.5%) with a mean age of 70.7 ± 6.1. There was no statistical difference in terms of gender and age ($p>0.05$, independent t-test). Of the participants, 185 were married (77%), and 55 (23%) were divorced or lost his/her partner. While 184 persons (76.7%) were in the middle-to-lower education levels, 56 persons (23.3%) were in the higher education levels. Sixty-seven persons (27.9%) had low-to-middle incomes, and 173 persons (72.1%) had high-income levels.

Co-morbidities

The most common co-morbidities were hypertension (57%), diabetes mellitus (30%), osteoarthritis (30%), hyperlipidemia (23.3%), osteoporosis (20.4%), coronary artery disease (18.8%), chronic obstructive pulmonary disease or asthma (16.7%), constipation (11.7%). Respectively, obesity, psychiatric and neurologic problems, cataracts, glaucoma, cancer history, and kidney-heart-liver diseases were less frequent. Benign prostatic hyperplasia was 26% in the males. The rates of co-morbidity were, generally, similar in both males and females. However, obesity, osteoporosis, and osteoarthritis were more common in females than the males (13.2 vs 6.3%, 40 vs 3.2%, and 41.2 vs 19.8%, respectively). Although smoking was more common in the males, obstructive pulmonary disease and asthma rates were similar in both sexes.

Drugs Use

Of the participants, 197 (92.1%) were receiving single or multidrug treatment due to chronic illnesses, and 43 (17.9%) did not have any medication used regularly. The most commonly used drugs were antihypertensive and cardiac medicine (58.8%), antiplatelet agents (acetylsalicylate and clopidogrel) (26.3%), oral antidiabetics (24.6%), non-steroidal anti-inflammatory drugs (15%), inhaler drugs (12.9%), antilipidemic (12.5%), stomach-protective medicines (proton pump inhibitors, antacids, alginate) (7.1%) and less frequently insulin, vitamin support preparations, neurological drugs, antidepressants, anticoagulants.

Mini-Mental State Examination

While the MMSE score was under 24 points in 18 persons out of 240 participants (7.5%), this score was 24 and above in 222 persons (92.5%). The MMSE score was 16.50 ± 0.83 in the advanced AD group, 20.91 ± 2.10 in the mild AD group, and 28.48 ± 1.59 in the normal group without AD.

While the mean age of individuals with AD was 80.2 ± 7.7, the mean age of non-AD individuals was 70.8 ± 5.1. The mean age of the persons with AD was higher ($p<0.001$, independent t-test).

The total AD rates were similar in the males and the females (6.3/8.8%, respectively); there was no statistical difference in gender ($p=0.477$, Chi-square test). Of the 12 persons with mild AD, 4 were female (33.3%), and 8 were male (66.6%). All the 6 advanced AD cases (100%) were female. The rates of AD according to the MMSE and distribution of AD according to age ranges are shown in Figures 1 and 2.

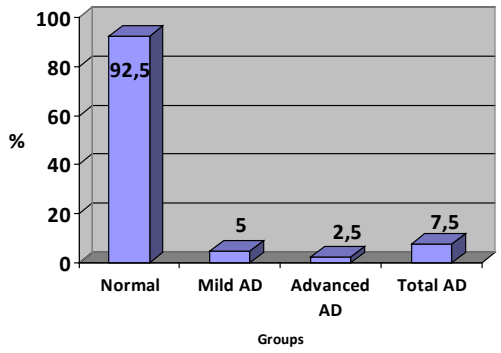


Figure 1. The rates of AD according to MMSE

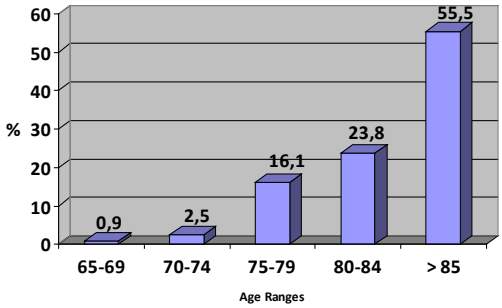


Figure 2. The distribution of AD according to age ranges

Additionally, the examination tests and related factors between AD and non-AD are displayed in Table 1.

Mental State Examinations

In our study, more abnormalities were found in mental state examinations, including general information, reasoning, abstraction, and executive functions in people with AD (p<0.001, Chi-square test, for each).

The people with advanced AD had more general information abnormalities than people with mild AD (p=0.007, Chi-square test). However, there was no statistically significant difference between persons with mild and advanced AD in point of reasoning, abstraction, and executive functional abnormalities.

Clock Drawing Scores

This score was a section where it was difficult to evaluate the functions because 30% of the study participants were illiterate, and 40% were primary school graduates. In particular, illiterate people said that they were unable to draw the clock (even if they could draw the shape in the MMSE). Some of them said that they could understand the time zone when they looked at the clock, but they could not draw it. Since this test is a clock-drawing test, time zone information is not asked; only drawing a clock was requested. Therefore, the CDT score was not used to define the presence of AD. Considering this situation, 60.8% of the participants had 6 points, and 25% had 0 points. The mean CDT score was 1.0 ± 1.6 in persons with AD and 4.5 ± 2.4 in persons without AD. This score was statistically significantly lower in persons with AD compared to those without AD (p<0.001, Chi-square test).

Basic and Instrumental Activities of Daily Living

Generally speaking, in both groups with and without AD, it was found that IADL deteriorated more compared to BADL. Both BADL and IADL were more deteriorated in people with AD compared with those without AD (p<0.001, for each independent t-test). BADL mean scores in people with AD and without AD were 1.17 and 0.14, respectively. The IADL mean scores in people with AD and without AD were 6.83 and 0.35, respectively. In our results, as the BADL and IADL deteriorated (i.e. as the scores increased), the frequency of AD increased (p<0.001, for each, Chi-square test). There was no statistical difference between mild and advanced AD in terms of IADL and BADL scores (p=0.123; 0.055, respectively).

Geriatric Depression

According to the Geriatric Depression Scale, which includes 30 questions; 23 participants (9.6%) had definite depression (14 points and above), 23 participants (9.6%) had possible depression (11–13 points), and in 194 subjects (80.8%), depression was not detected (0–10 points).

Definite or possible depression was detected in 8 of 18 (44.4%) people with AD and 382 of 222 (20.6%) people without AD. Seven of these 8 depressions in patients with AD were definite depression. People with AD had significantly higher geriatric depression compared with people without AD (p<0.001, Chi-square test).

Additionally, depression was higher in the females than in the males (27.2% and 11.9%, respectively; p=0.003, Chi-square test). According to our study results, the depression rate was higher in illiterate and primary school graduates (48.6% vs 25.3%). As the level of economic income decreased, the rate of possible and definite depression increased (54% in low-income vs 27.6% in middle-high income).

AD and Socio-economic Levels

In those people with AD (n = 18), 10 persons (55.5%) were illiterate, 6 persons (33.3%) were primary school graduates, 1 person (5.5%) was a junior-high-school graduate, and 1 person (5.5%) was a university graduate. Of the people with AD, 88.8% were illiterate and primary school graduates, 11.2% were middle and high school graduates. Alternatively, of the people without AD, 67.1% were illiterate and primary school graduates and 32.9% were middle and high school graduates.

Out of the people with AD (n=18), 3 persons (16.6%) had very low income, 6 persons (33.3%) had low income, and 9 persons (50%) had middle income. None of the high-income people had AD.

The proportion of AD was 33.3% among individuals with very low economic income. This rate was 10.3% for low-income individuals, 6.1% for middle-income individuals, and 0% for high-income individuals. Namely, as the economic income level increased, the rate of dementia decreased. Statistically, individuals from very low-income families had higher AD rates (p=0.008, Chi-square test).

AD and Habits

In terms of regular physical and mental activity, while the AD rate was 1,6% in people who had regular activities, this rate was 13.7% in people without an activity. The rate of AD was lower in people with regular physical and mental activity (p<0.001, Chi-square test)

In our study, there was no statistical relationship between the frequency of AD and smoking-alcohol use, head trauma, and toxin exposure history.

The individuals were questioned about diet types including balanced, vegetable weighted, meat weighted, pastry weighted, oily, and carbohydrate-rich. There was no statistical relationship between dietary types and AD frequency. Nine persons with AD were eating twice daily, seven persons were three times, and two persons were more than three times. A total of 76,5% of persons without AD were eating three times or more per day. The number of daily meals in persons with AD was statistically lower than that in persons without AD (p<0.001, Chi-square test). The persons with AD had more sleep disorders compared with persons without AD (50% vs 34.6%, p=0.03, Chi-square test). Of the18 AD cases, decreased sleeping was noted in 6 persons, and increased sleeping was present in 3 persons.

AD and Co-morbidities and/or Drugs

The osteoporosis rate was 38.8% in persons with AD, while this rate was 18.9% in persons without AD. This difference was statistically significant (p=0.043, Chi-square test), and the situation can be explained by the fact that patients with AD were older. There was no statistically significant relationship between AD frequency and other co-morbidities except osteoporosis. The rate of osteoarthritis was 50% in persons with AD and 28.3% in persons without AD, but it was not statistically significant (p=0.052, Chi-square test).

Similarly, there was no statistical correlation between AD and drugs such as antihypertensives, cardiac, antiplatelets, oral antidiabetics, non-steroidal anti-inflammatory drugs, inhalers, antilipidemic, gastroprotective agents, insulin, vitamins, anticoagulants, and cancer chemotherapeutics.

Tablo 1. The examination tests and related factors between AD and non-AD

Parameters	AD (n=18)	Non-AD (n= 222)	p
Age (years)	80.2 ± 7.7	70.8 ± 5.1	**<0.001**
Gender (E/F)	8 / 10	118/ 104	**0.477**
Mean MMSE score	19.4	28.4	**<0.001**
Mean CDT Score	1.0 ± 1.6	4.5 ± 2.4	**<0.001**
General Information Abnormalities (%)	16.6	1.35	**<0.001**
Reasoning Abnormalities (%)	16.6	0.45	**<0.001**
Abstraction Ability Abnormalities (%)	38.8	9.9	**<0.001**
Executive Function Abnormalities (%)	77.7	13.0	**<0.001**
Mean BADL Score	1.17 ± 1.50	0.14 ± 0.35	**<0.001**
Mean IADL Score	6.83 ± 4.70	0.35 ± 1.18	**<0.001**
Depression Rate (%)	44.4	20.6	**<0.001**
Low Education Level (%)	88.9	67.1	0.055
High Educational Level (%)	11.1	32.9	
Low Economic Income (%)	50	26.1	**0.03**
Middle-High Economic Income (%)	50	73.9	
Smoke Use / Active or History (%)	22.2	39.1	0.154
Alcohol Use / Active or History (%)	-	2.2	0.520
AD Family History (%)	11.1	10.3	0.920
Head Trauma History (%)	11.1	8.1	0.658
Chronic Toxin Exposure (%)	-	1.3	0.620
Regular Physical Activity (%)	11.1	54.5	**<0.001**
Regular Lifestyle (%)	22.2	64.4	**<0.001**
Osteoporosis Rate (%)	38.8	18.9	**0.043**
Osteoarthritis Rate (%)	50	28.3	0.054
Sleep Disorders (%)	50	34.6	**0.03**

MMSE: Mini-Mental State Examination, CDT: Clock Drawing Test, BADL and

IADL: Basic and Instrumental Activities of Daily Living, AD: Alzheimer's Disease

Discussion

There are limited studies on the prevalence of AD in Türkiye, and this study is important because it is the first study to investigate the prevalence of AD in our region. In addition, this study has the power to reflect the prevalence in the region because the Konya Province is one of the largest provinces in the Central Anatolia Region.

According to our study results using the MMSE for standardized and illiterate persons (6, 8), the prevalence of AD in the Konya city center was 7.5%, where 5% of them had mild AD, and 2.5% had severe AD.

As expected, as the age increased, the rate of AD was also increasing. When we evaluated it according to age ranges, there was a significant increase in AD rates, especially in individuals over 75 years of age.

In meta-analyses of prevalence studies, the prevalence of AD has been reported as 4–5% in 65–70-year-olds and up to 40% in the 75 to 85 age range. The highest prevalence is in the eighth decade. Our results are close to the results of this meta-analysis. The incidence of AD in men and women was similar and did not show gender differences.

The AD rate of our study (7,5%) was lower than that of the study by Gurvit H et al., which was performed in Istanbul's Kadikoy region in Türkiye. They reported the rate of AD as 11% and the rate of dementia as 20% (4). Their study results were also above European data, but their study included a population of 70-year-olds and over. Furthermore, another feature of the study was that it consisted of two phases. The first phase was similar to our study on dementia screening with MMSE. The second phase was to determine the subtypes of dementia by performing diagnostic studies for those with dementia.

In a former Italian study with a similar methodology, which was designed in 2 phases, the prevalence of dementia for individuals over 59 years of age was reported as 6.2%; 2.6% of dementia was AD, 2.2% was multi-infarct, 0.8% was mixed dementia, 0.4% was secondary dementia, 0.3% of unspecific dementia. In this study, the prevalence of dementia was 8.4% in individuals over the age of 64. The Hodkinson mental test, used to validate the Italian study as a screening test, was utilized in this study (16).

In the Korean study, conducted using the Korean version of the MMSE test, the prevalence of dementia was 9.5% in rural areas for people over 65 years old. The authors commented that this ratio was similar to Western countries. In this study, mild AD prevalence was reported as 3.4%, moderate AD prevalence was 0.7%, and advanced AD prevalence was 0.5% (17). In urban areas of Korea, dementia prevalence was reported as 6.3%, AD prevalence was 4.8%, vascular dementia prevalence was 1%, and Lewy body dementia was found to be 0.4% in the KLoSHA study that included 1118 randomly selected individuals (18). Considering the results of these 2 Korean studies, while the prevalence of dementia in Korea's rural areas was 9.5%, it was 6.3% in urban areas, and thus the prevalence of dementia in rural areas was higher than in urban areas. This may be related to their educational and income levels.

In a Chinese study that investigated dementia and its subtypes, the Chinese version of MMSE was used, and the rates of dementia have been reported to be lower than those in European countries. The prevalence of phase 1 dementia has been reported as 2,6% for individuals over 60 years old and 3.4% for individuals over 65 years old. According to the results of Phase 2, the prevalence of AD was 1.85% in patients over 65; the prevalence of vascular dementia was 1.3%; others were reported as 0.2% (19).

A recent European meta-analysis (20) reported that the prevalence of AD was 6.88% in southern European countries (Spain, Italy, and Greece) and 4.31% in northern European countries (France, Netherlands). The mean prevalence of AD in Europe was 5.05%. Prevalence was 3.31% in men and 7.13% in women and it was increasing with age in this report.

Türkiye is both a European and an Asian country and the locations of this study are urban areas of the Central Anatolian Region. Our prevalence was slightly higher than current data of European countries.

Although AD is the most common form of dementia, our study's limitation was that other subtypes of dementia were not separated. Another limitation of our study is that MMSE was considered a screening tool for AD and not a completely reliable test for

AD diagnosis, thus inducing misclassification of the outcomes. Another more reliable diagnostic tool than the MMSE could be utilized, for example, the Cambridge Cognitive Examination. However, we preferred the MMSE because it is a practical test that is widely used for screening in similar studies.

Our study was managed in terms of demographic features and related factors; although the mean age was similar in all three towns, the rate of AD was higher in the Meram region. A total of 88.8% of persons with AD were illiterate and primary school graduates. Illiteracy has been reported independently associated with a higher risk of prevalent and incident dementia, but not with a more rapid rate of cognitive decline (21). It has been reported that low educational levels are associated with dementia (22) and high educational levels protective from AD (23) in different studies. Additionally, the AD rate was higher in those with very low incomes. Some studies reported that the AD rate is also related to occupations (22). There was no statistically significant difference between dietary types and AD frequency, but the number of daily meals was lower in persons with AD. Persons with AD had more sleep disorders, especially insomnia. Osteoporosis was statistically higher in the AD group. Although not statistically significant, the rate of osteoarthritis was higher in persons with AD. Other comorbidities were similar in both groups. While there was a positive relationship between the frequency of AD and low activity, there was no correlation with other risk factors such as family history, smoking and alcohol use, depression, head trauma, and toxin exposure. The frequency of AD was less in the subjects who reported regular physical and mental activities and regular life history.

The most important method to distinguish vascular dementia in older patients is imaging methods. In addition to imaging, some co-morbidities and medication use are parameters that may indicate vascular dementia in terms of predisposition to atherosclerosis (24). In our study, there was no statistical relationship between the frequency of dementia and the presence of hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, or use of antihypertensive, antilipidemic, antiplatelet, anticoagulant, insulin, oral antidiabetic, cardiac drugs. The fact that AD and non-AD groups are similar in this respect may support the fact that vascular dementia is not prominent in the AD group.

In our study, individuals with AD had more deterioration in BADL and IADL. In other words, cognitive dysfunction was associated with impairments in daily activities. Similarly, clock drawing scores were lower in people with AD. Mental examinations, including general knowledge, reasoning, abstraction, and executive functions, were worse in individuals with AD. There was a positive relationship between definite depression and AD frequency in our study. However, it is difficult to distinguish whether this depression is related to AD or older age depression because, while dementia cases did not differ in men and women, depression was more common in women. The relationship between dementia and depression was not an unexpected finding since neuropsychiatric symptoms are common in AD. This may manifest itself in the form of behavioral and psychiatric symptoms. Sometimes depressive symptoms may be the first sign of AD, but this situation is difficult to distinguish from older age depression. In such cases, not responding to standard depression treatments may be stimulating in AD.

Conclusion

As a result, this study has revealed the current prevalence of AD and its related factors in the Central Anatolia region of Türkiye. Estimating the prevalence of the disease will make important contributions to the development of health policies. Considering the relative decrease in the young population and the increase in the geriatric population all over the world, it can be predicted that the prevalence of dementia and AD may increase in the coming years.

Conflict of Interest

All authors declared that no conflict of interest between them and all authors had access to the data and played a role in writing this manuscript.

References

1.Emre M. Alzheimer's Disease. In: Emre M. (ed) Basic Neurology Book, 1st edition, Gunes Publishing, Turkey, 2013: pp 955-962.

2.Lobo A, Launer LJ, Fratiglioni L, Andersen K, Di Carlo A, Breteler MM, et al. Prevalence of dementia and major subtypes in Europe: A collaborative study of population-based cohorts. Neurologic Diseases in the Elderly Research Group. Neurology 2000;54(11 Suppl 5):4-9.

3.Sosa-Ortiz AL, Acosta-Castillo I, Prince MJ. Epidemiology of dementias and Alzheimer's disease. Arch Med Res 2012;43(8):600-608.

4.Gurvit H, Emre M, Tinaz S, Bilgic B, Hanagasi H, Sahin H, et al. The prevalence of dementia in an urban Turkish population. Am J Alzheimers Dis Other Demen 2008;23(1):67-76.

5.World Health Organization. Sample size determination in health studies: a practical manual [e-book] WHO Library Cataloguing in Publication Data (NLM Classification: WA 950); 1991. [Internet]. Available from: https://apps.who.int/iris/handle/10665/40062. Accessed: 21.03.2021.

6.Güngen C, Ertan T, Eker E, Yaşar R, Engin F. Reliability and Validity of The Standardized Mini-Mental State Examination in The Diagnosis of Mild Dementia in Turkish Population. Turk J Psychiatr 2002;13: 273-281.

7.Folstein M, Folstein S, McHugh PR. Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12: 189-198.

8.Babacan-Yıldız G, Ur-Özçelik E, Kolukısa M, Işık AT, Gürsoy E, Kocaman G, et al. Validity and Reliability Studies of Modified Mini-Mental State Examination (MMSE-E) For Turkish Illiterate Patients With Diagnosis of Alzheimer Disease. Turk Psikiyatri Derg 2016;27(1):41-46.

9.Tekin S, Fairbanks LA, O'Connor S, Rosenberg S, Cummings JL. Activities of daily living in Alzheimer's disease: neuropsychiatric, cognitive, and medical illness influences. Am J Geriatr Psychiatry 2001;9 (1): 81-86.

10.Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of Illness in the Aged. The index of ADL: A Standardized measure of Biological and Psychosocial Function. JAMA 1963; 185: 914-919.

11.Arik G, Varan HD, Yavuz BB, Karabulut E, Kara O, Kilic MK, et al. Validation of Katz index of independence in activities of daily living in Turkish older adults. Arch Gerontol Geriatr 2015;61(3):344-350.

12.Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9(3): 179-186.

13.Isik EI, Yilmaz S, Uysal I, Basar S. Adaptation of the Lawton Instrumental Activities of Daily Living Scale to Turkish: Validity and Reliability Study. Ann Geriatr Med Res 2020;24(1):35-40.

14.Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, et al. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1983;17(1):37-49.

15.Durmaz B, Soysal P, Ellidokuz H, Isik AT. Validity and reliability of geriatric depression scale-15 (short form) in Turkish older adults. North Clin Istanb 2018;5(3):216-220.

16.Rocca WA, Bonaiuto S, Lippi A, Luciani P, Turtù F, Cavarzeran F, et al. Prevalence of clinically diagnosed Alzheimer's disease and other dementing disorders: a door-to-door survey in Appignano, Macerata Province, Italy. Neurology 1990;40(4):626-631.

17.Woo JI, Lee JH, Yoo KY, Kim CY, Kim YI, Shin YS. Prevalence estimation of dementia in a rural area of Korea. J Am Geriatr Soc 1998;46(8):983-987.

18.Jhoo JH, Kim KW, Huh Y, Lee SB, Park JH, Lee JJ, et al. Prevalence of dementia and its subtypes in an elderly urban Korean population: results from the Korean Longitudinal Study on Health And Aging (KLoSHA). Dement Geriatr Cogn Disord 2008;26(3):270-276.

19.Wang W, Wu S, Cheng X, Dai H, Ross K, Du X, et al. Prevalence of Alzheimer's disease and other dementing disorders in an urban community of Beijing, China. Neuroepidemiology 2000;19(4):194-200.

20.Niu H, Álvarez-Álvarez I, Guillén-Grima F, Aguinaga-Ontoso I. Prevalence and incidence of Alzheimer's disease in Europe: A meta-analysis. Neurologia 2017;32(8):523-532.

21.Arce Rentería M, Vonk JMJ, Felix G, Avila JF, Zahodne LB, Dalchand E, et al. Illiteracy, dementia risk, and cognitive trajectories among older adults with low education. Neurology 2019;10;93(24):2247-2256.

22.Bonaiuto S, Rocca WA, Lippi A, Giannandrea E, Mele M, Cavarzeran F, et al. Education and occupation as risk factors for dementia: a population-based case-control study. Neuroepidemiology 1995;14(3):101-109.

23.Harmanci H, Emre M, Gurvit H, Bilgic B, Hanagasi H, Gurol E, et al. Risk factors for Alzheimer disease: a population-based case-control study in Istanbul, Turkey. Alzheimer Dis Assoc Disord 2003;17(3):139-145.

24.Lee WJ, Liao YC, Wang YF, Lin YS, Wang SJ, Fuh JL. Summative Effects of Vascular Risk Factors on the Progression of Alzheimer's Disease. J Am Geriatr Soc. 2020 Jan;68(1):129-136.

Received: 20 Feb 2024 | **Accepted:** 24 Mar 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 334-339
DOI: 10.54005/geneltip.1439038

ORIGINAL ARTICLE

Evaluation of C-Reactive Protein to Albumin Ratio and Systemic Inflammation in Postmenopausal Osteoporosis

Postmenopozal Osteoporozda C-Reaktif Protein/Albümin Oranı ve Sistemik İnflamasyonun Değerlendirilmesi

[1]Esra Şahingöz Bakırcı, [2]Mustafa Bakırcı

[1]Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Yozgat Bozok University, Yozgat, Türkiye
[2]Department of Gynecology and Obstetrics, Faculty of Medicine, Yozgat Bozok University, Yozgat, Türkiye

Correspondence

Esra Şahingöz Bakırcı,
Çapanoğlu Mah. Cemil Çiçek Cad Bozok Üniversitesi Bilal Şahin Kampüsü Atatürk Yolu 7. KM Merkez/Yozgat - Türkiye

E-Mail: dresrasahingoz@gmail.com

How to cite ?

Şahingöz Bakırcı E, Bakırcı M. Evaluation of C-Reactive Protein to Albumin Ratio and Systemic Inflammation in Postmenopausal Osteoporosis. Genel Tıp Derg. 2025;35 (2): 334-339

ABSTRACT

Aim: We aimed to evaluate systemic inflammation in patients with postmenopausal osteoporosis using C-reactive protein (CRP)/albumin ratio, blood neutrophil/lymphocyte ratio (NLR), and prognostic nutritional index (PNI) and to determine its relationship with bone mineral density (BMD).
Methods: Our study has a retrospective design. A total of 363 postmenopausal female patients admitted to physical medicine and rehabilitation outpatient clinics were evaluated. Patients were divided into three groups: osteoporosis, osteopenia, and normal BMD. Demographic data, femoral neck, and lumbar total T scores, BMD values, complete blood count parameters, CRP, and albumin results were recorded. CRP/albumin ratio, NLR, and PNI were calculated.
Results: Osteoporosis was found in 102, osteopenia in 167, and normal BMD in 94 patients. In the osteoporosis group, albumin, CRP and CRP/albumin ratio were lower than the normal BMD group ($p = 0.017$; $p < 0.001$; $p = 0.032$, respectively). In the osteoporosis group, PNI was lower than the other groups ($p < 0.001$). NLR was higher in the osteoporosis group than the other groups, but not statistically significant ($p = 0.723$). We found a positive correlation between BMD with albumin and PNI.
Conclusions: The effect of inflammatory response in postmenopausal osteoporosis is not prominent. CRP/albumin ratio does not seem to be an appropriate index for osteoporosis. In light of our data, nutritional factors seem to be more effective on osteoporosis.

Keywords: Albumin, CAR, inflammation, osteoporosis, PNI

ÖZ

Amaç: Postmenopozal osteoporoz tanılı hastalarda sistemik inflamasyonu; C-reaktif protein (CRP)/albümin oranı, kan nötrofil/lenfosit oranı (NLO) ve prognostik nütrisyonel indeks (PNİ) ile değerlendirmek ve kemik mineral yoğunluğu (KMY) ile ilişkisini saptamak amaçlandı.
Gereç ve Yöntemler: Çalışmamız retrospektif bir tasarıma sahiptir. Fiziksel tıp ve rehabilitasyon polikliniklerine başvuran 363 postmenopozal kadın hasta değerlendirilmeye alındı. Hastalar osteoporoz, osteopeni ve normal KMY olarak üç gruba ayrıldı. Hastaların demografik verileri, femur boyun ve lomber total T skorları ile KMY değerleri, tam kan sayımı ölçümü parametreleri, CRP ve albümin sonuçları kaydedildi. CRP/albümin oranı, NLO ve PNİ hesaplandı.
Bulgular: Hastaların 102'sinde osteoporoz, 167'sinde osteopeni ve 94'ünde normal KMY saptandı. Osteoporoz grubunda; albümin, CRP ve CRP/albümin oranı, normal KMY grubundan düşüktü (sırasıyla $p = 0,017$; $p < 0,001$; $p = 0,032$). Osteoporoz grubunda; PNİ diğer gruplardan daha düşüktü ($p < 0,001$). NLO ise osteoporoz grubunda diğer gruplardan yüksek olmakla beraber istatistiksel olarak anlamlı değildi ($p = 0,723$). KMY ile albümin ve PNİ arasında pozitif korelasyon saptadık.
Sonuçlar: Postmenopozal osteoporozda inflamatuar yanıtın etkisi ön plana çıkmamaktadır. CRP/albümin oranı, osteoporoz için uygun bir indeks olarak görünmemektedir. Verilerimiz ışığında daha çok nütrisyonel faktörler osteoporoz üzerinde etkili görünmektedir.

Anahtar Kelimeler: Albümin, CAR, inflamasyon, osteoporoz, PNİ

Introduction

Osteoporosis is a progressive systemic disease characterized by a decrease in bone mass, deterioration of bone microstructure, increased bone fragility, and susceptibility to fractures (1). With the aging of the global population, osteoporosis and the fractures it causes have become a significant cause of mortality and morbidity. Due to the social and economic burdens this imposes, the causes, prevention, treatment, and follow-up of osteoporosis are of great importance (2).

In postmenopausal osteoporosis (PMOP), estrogen withdrawal indirectly leads to bone resorption; additionally, it is thought that low-level chronic inflammation is also effective in this resorption (3). It is stated that estrogen loss increases permanent inflammation and is effective in the development of osteoporosis (4). With the term osteoimmunology, which has come to the agenda in recent years; the effects of the immune system, inflammatory cytokines, and chronic inflammatory response on bone turnover are being tried to be explained (5). The increase in various inflammatory cytokines;

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

by inducing osteoclast differentiation, activates bone turnover toward destruction and leads to a decrease in bone mineral density (BMD). In addition, these inflammatory cytokines stimulate C-reactive protein (CRP) synthesis in hepatocytes (6). Although studies have shown that increased CRP causes a decrease in BMD, the literature remains contradictory on this issue (2, 7). Albumin is a negative acute-phase protein produced in hepatocytes, and its low levels indicate an inflammatory state (8). The CRP/albumin ratio (CAR) is a recent inflammatory marker that indicates nutritional status in addition to inflammatory status. CAR is considered a more reliable marker for assessing low-level chronic inflammation than CRP or albumin alone (9). The prognostic nutritional index (PNI) has been used to predict perioperative complications in patients undergoing cancer surgery, but recently, its association with the activity levels of various rheumatic diseases has been shown (10). It also provides information about the immune and nutritional status of patients (10, 11).

The older age group, where postmenopausal osteoporosis is more common, appears to be a risky population in terms of low-level chronic inflammation and inadequate nutrition. There are differences in the results of studies evaluating inflammation and nutritional status in PMOP patients with various parameters (2, 12, 13). We did not find any study in the literature examining CAR and PNI, which could provide insight into both inflammation and nutritional status in PMOP patients.

We aimed to evaluate the systemic inflammatory response and nutritional status in PMOP patients using CAR, PNI, and the blood neutrophil/ lymphocyte ratio (NLR) and to determine their relationship with BMD.

Materials and Methods

Our study has a retrospective design. Postmenopausal patients who presented to the physical medicine and rehabilitation department between 01/03/2021 and 01/01/2023 were screened. Postmenopausal women between the ages of 45 and 80, whose demographic information, BMD measurement, routine biochemical values, and complete blood count data were available, were included in the study.

Patients with active infection, previous hip and spine surgery, inflammatory rheumatic disease, autoimmune disease, hematological disease, malignancy, steroid use, or chronic kidney and liver failure were excluded from the study.

The patients' ages, femoral neck and lumbar total (L1-4) BMD values, and T scores were recorded. BMD was measured using dual-energy X-ray absorptiometry (Lunar Prodigy Primo). According to the criteria of the World Health Organization, a T score below −2.5 standard deviations (SD) is defined as osteoporosis; a T score between −2.5 and −1 SD is defined as osteopenia; and a T score of −1 SD and above is defined as normal BMD (14). In light of this definition, patients were evaluated in three groups: osteoporosis, osteopenia, and normal BMD according to their T scores.

Venous blood samples taken in the morning were used for CRP, albumin, and complete blood count measurements. Albumin levels were measured photometrically using the bromocresol method on the Beckman Coulter AU 5800 biochemical autoanalyzer. A complete blood count was performed on the Beckman Coulter DxH 800 autoanalyzer. Cellular analysis was based on flow cytometry principles. Platelet count was determined using the impedance (aperture impedance, DC) method, and hemoglobin measurement was carried out using a photometric method. Lymphocyte and neutrophil subgroups were evaluated using VCSn (volume, conductivity, scatter, and neutrophil lobularity) technology. CRP levels had been measured using the nephelometric method on the Beckman Coulter Image 800 system. PNI value; Calculated according to the formula 10 x serum albumin value (g/dL) + 0.005 × peripheral lymphocyte count (/mm3) (15). Low PNI values indicate the risk of malnutrition (11). CAR was calculated. High CAR values indicate increased inflammation and poor nutritional status (9). Blood NLR was calculated. NLR is calculated from complete blood count parameters and its increase indicates the systemic inflammatory response (16).

Patients were evaluated after approval was obtained by the Local Yozgat Bozok University Ethics Committee of Yozgat Bozok University (Decision No: 2017-KAEK-189, Date: 28/.04/.2023). The study was conducted under the principles of the Declaration of Helsinki.

Statistical Analysis

The data obtained were evaluated statistically

using the Statistical Package for the Social Sciences, version 20 package program (SPSS Inc., Armonk, NY, USA). The normality of numerical data distribution was examined using the Kolmogrov-Smirnov test. As descriptive statistics, variables with normal distribution were expressed as mean±standard deviation, and variables without normal distribution were expressed as median and interquartile range (25%-75%). The Mann-Whitney U test was utilized for data without normal distribution in comparison between groups; the independent test was applied to parametric data. In the correlation analysis, the appropriate Spearman or Pearson correlation tests were used. It was considered statistically meaningful when $p<0.05$.

Results

Three hundred sixty-three postmenopausal female patients were included in the study. According to T scores, 102 patients had osteoporosis, 167 had osteopenia, and 94 patients had normal BMD. Table 1 summarizes the age, BMD, and T scores of the groups.

Table 1. Age and bone mineral density analysis of the patients

	Normal BMD	Osteopenia	*Osteoporosis*	p-value
Age, years	55.83±8.59	61.23±8.41*	67.83±10.03 *†	< 0.001
Lumbar total T score (SD)	0.05 (-0.6 / 1)	-1.6 (-2.10 / -1.0) *	-3.0 (-3.3 / -2.7) *†	< 0.001
Femoral neck T score (SD)	0.10 (-0.33 / 0.8)	-1.3 (-1.70 / -0.9) *	-2.1 (-2.7 / -1.5) *†	< 0.001
Lumbar total BMD (gr/ cm^2)	1.17 (1.09 / 1.27)	0.99 (0.92 / 1.06) *	0.81 (0.77 / 0.85) *†	< 0.001
Femoral neck BMD (gr/ cm^2)	1.00 (0.95 / 1.09)	0.82 (0.77 / 0.89) *	0.73 (0.66 / 0.78) *†	< 0.001

BMD: Bone mineral density, SD: Standard deviation *Osteopenia-Normal BMD, †Osteopenia-Osteoporosis

Lumbar total and femoral neck BMD and T scores were lower in the osteoporosis group than in the osteopenia and normal BMD groups ($p < 0.001$). The average age was found to be higher in the osteoporosis group than in the other two groups ($p < 0.001$).

Biochemical data of the patients included in the study are summarized in Table 2. CRP, albumin, and CAR values were lower in the osteoporosis group than in the normal BMD group (respectively, $p = 0.017$; $p < 0.001$; $p = 0.032$). PNI was lower in the osteoporosis group than in the other two groups ($p < 0.001$). NLR was higher in the osteoporosis group but not statistically significant ($p = 0.723$). Hemoglobin values were also lower in the osteoporosis group than in the other groups ($p < 0.002$).

Table 2: Analysis of biochemical data of the patients

	Normal BMD	Osteopenia	*Osteoporosis*	p-value
Albumin (g/ dL)	4.24±0.24	4.18±0.25	4.12±0.22*	0.001
C-reactive protein (mg/ dL)	0.43 (0.3-0.7)	0.45 (0.27-0.74)	0.36 (0.21-0.54)†	0.017
CAR	0.10 (0.07-0.17)	0.11 (0.07-0.19)	0.09 (0.05-0.14) †	0.032
PNI	52.65 (50.5-56.35)	52.7 (50.05-55.2)	50.85 (48.5-53.95) *†	0.001
NLR	1.81 (1.42-2.47)	1.76 (1.5-2.38)	1.98 (1.45-2.44)	0.723
Neutrophil ($\times10^3$/µl)	3.9 (2.98-4.83)	3.8 (3.05-4.7)	3.6 (2.9-4.58)	0.369
Lymphocyte ($\times10^3$/µl)	2.1 (1.78-2.6)	2 (1.75-2.55)	1.8 (1.43-2.48)	0.029
Platelet ($\times10^3$/µl)	252.5 (224-286.25)	252 (217-296)	246 (211-281.25)	0.405
Hemoglobin (g/dL)	13.6 (12.88-14.4)	13.5 (12.85-14.2)	13.2 (12.3-13.8) *†	0.002

CAR: C-reactive protein/albumin, PNI: Prognostic nutritional index, NLR: Neutrophil/lymphocyte ratio

*Osteoporosis-normal BMD

†Osteopenia-Osteoporosis

Correlation analyses between systemic inflammatory parameters and BMD are summarized in Table 3. We found a positive correlation between albumin, PNI, and hemoglobin values with BMD. There was a negative correlation between age and BMD. We found a positive correlation between femoral neck BMD with CRP and CAR.

Discussion

Postmenopausal osteoporosis is mostly seen in advanced age and causes serious morbidities. In recent years, studies investigating systemic inflammation in the etiology of osteoporosis have increased (17, 18). In our study, we evaluated the systemic inflammatory response and nutritional status in PMOP patients with CAR, PNI, and NLR parameters. Albumin, CRP, CAR, and PNI were significantly lower in the PMOP group. Although the low levels of albumin and PNI in the PMOP group support a nutritional deficiency, the low levels of CRP and CAR in the PMOP group do not support an increase in systemic inflammation. NLR, another inflammatory parameter, was higher in the PMOP group, but not statistically significant. Contradictory results on inflammatory markers make it difficult to conclude the effect of systemic inflammation in PMOP.

A study evaluating NLR, platelet/lymphocyte ratio

Table 3: Correlation analysis between bone mineral density and inflammatory parameters

		Lumbar Total T Score	Femoral Neck T Score	Lumbar Total BMD	Femoral Neck BMD
Albumin (g/dL)	rho	0.141	0.183	0.136	0.179
	p-value	0.007	0.001	0.009	0.001
C-reactive protein (mg/dL)	rho	0.1	0.136	0.097	0.129
	p-value	0.056	0.011	0.066	0.015
CAR	rho	0.088	0.119	0.085	0.113
	p-value	0.095	0.026	0.108	0.033
PNI	rho	0.160	0.151	0.153	0.152
	p-value	0.002	0.005	0.004	0.005
Lymphocyte (×10³/µl)	rho	0.131	0.110	0.128	0.120
	p-value	0.013	0.041	0.016	0.025
Age (years)	rho	-0.370	-0.462	-0.357	-0.456
	p-value	0	0	0	0
Hemoglobin (g/dL)	rho	0.167	0.177	0.164	0.164
	p-value	0.002	0.001	0.002	0.002
NLR	rho	-0.026	-0.025	-0.03	-0.033
	p-value	0.621	0.646	0.567	0.541

CAR: C-reactive protein/albumin, PNI: Prognostic nutritional index, NLR: Neutrophil/lymphocyte ratio, BMD: Bone mineral density

(PLR), and systemic immune inflammation index (SII) in patients with osteoporosis and normal BMD found no difference between the groups or correlation with T-scores (18). In another study evaluating NLR and SII in PMOP patients, NLR was found to be significantly higher in the PMOP group. Additionally, SII has been stated as a marker that can distinguish both PMOP diagnosis and osteoporotic fracture risk. In the same study, albumin was found to be significantly lower in the PMOP group (17). Moreover, in another study evaluating SII in patients with osteoporosis, SII was found to be higher in osteoporosis patients compared to the non-osteoporotic group (19). Furthermore, in a study evaluating the inflammatory content of the diet, an increase in the dietary inflammation index was found to be associated with a higher risk of osteoporosis in women (20). Although we found NLR to be high in the osteoporosis group, it was not statistically significant. Moreover, we did not detect any correlation between NLR and BMD values. In a study evaluating the relationship between the geriatric nutritional risk index (GNRI) and osteoporosis in type 2 diabetes; GNRI was found to be lower in osteoporosis patients, and it was stated that the osteoporosis group was at nutritional risk (21). Similarly, in a study investigating the relationship between albumin and BMD, albumin levels were found to be significantly lower in the osteoporosis group compared to the normal BMD group. Albumin has been considered a protective parameter against osteoporosis and osteoporotic fractures (22). Similar to these studies; we found albumin and PNI to be lower in the PMOP group. In addition, we detected a positive correlation between albumin and PNI with BMD; this supports a nutritional deficiency in PMOP patients. However, it is difficult to support the presence of systemic inflammation with our current data. Recent studies provide evidence supporting the role of inflammation in the development of osteoporosis; however, there are also studies in the opposite direction. Therefore, no consensus has yet been reached on this matter (17-19).

In a cohort study, CRP was negatively correlated with femoral neck BMD, and tumor necrosis factor-alpha was negatively correlated with lumbar vertebral BMD in premenopausal women. In postmenopausal women, a positive correlation was found between femoral neck BMD and CRP in the group receiving hormone therapy, while no correlation was found in the group not receiving hormone therapy. These contradictory results suggest that there is no definitive link between inflammation and BMD (12). In another study evaluating the relationship between serum inflammatory markers and BMD, CRP concentration was significantly higher in the low BMD group than in the normal BMD group. In the low BMD group, a negative correlation was found between BMD and CRP. In the same study, albumin values were similar between the two groups (6). The population of this study was younger compared to our study, and the groups were homogeneously distributed in terms of age. In our study, the age of the PMOP group was

significantly higher than that of the other groups. In our study, CRP, albumin, and CAR were lower in the PMOP group; we found a positive correlation between femoral neck BMD and CRP and CAR. These results do not support increased systemic inflammation and its association with BMD.

We detected no inflammatory changes in PMOP patients. CRP, in addition to reflecting the inflammatory state, can also be affected by the patient's nutritional status and liver function since it is synthesized in the liver. Whereas NLR was higher in the PMOP group, CAR, albumin, hemoglobin, and PNI values were lower. While NLR is a marker of bone marrow-derived marker; the fact that CRP, albumin, and CAR are liver-derived markers may explain this difference. These data suggest that nutritional deficiencies, rather than a chronic inflammatory condition, may play a primary role in PMOP. A more accurate evaluation of inflammation and nutritional status can be achieved through studies conducted in age-matched groups.

Limitations of our study include the heterogeneity between groups in terms of age, which prevented the exclusion of age-related effects on biochemical parameters. In addition, the lack of body mass index data can be considered a limitation given the impact of obesity on osteoporosis and inflammation. The strengths of our study include the large sample size and the first-time evaluation of CAR and PNI in PMOP, which had not been assessed before.

Conclusion

The effect of the inflammatory response does not appear to be prominent in PMOP. CAR does not currently seem to be a suitable index for PMOP. Our data suggest that nutritional factors have a greater impact on PMOP. Since the literature remains contradictory on this matter, prospective studies evaluating the asymptomatic inflammatory response and nutritional status in PMOP patients, alongside an age- and demographically matched control group are needed.

Conflict of interest

No conflicts of interest were reported between the authors.

Financial support

None.

Acknowledgment

None.

References

1.de Villiers TJ. Bone health and menopause: Osteoporosis prevention and treatment. Best Pract Res Clin Endocrinol Metab. 2024;38(1):101782.

2.Mun H, Liu B, Pham THA, Wu Q. C-reactive protein, and fracture risk: an updated systematic review and meta-analysis of cohort studies through the use of both frequentist and Bayesian approaches. Osteoporos Int. 2021;32(3):425-435.

3.Lisco G, Triggiani D, Giagulli VA, De Pergola G, Guastamacchia E, Piazzolla G, et al. Endocrine, Metabolic, and Immune Pathogenesis of Postmenopausal Osteoporosis. Is there a Therapeutic Role in Natural Products? Endocr Metab Immune Disord Drug Targets. 2023;23(10):1278-1290.

4.Wu D, Cline-Smith A, Shashkova E, Perla A, Katyal A, Aurora R. T-Cell Mediated Inflammation in Postmenopausal Osteoporosis. Front Immunol. 2021;12:687551.

5.Guder C, Gravius S, Burger C, Wirtz DC, Schildberg FA. Osteoimmunology: A Current Update of the Interplay Between Bone and the Immune System. Front Immunol. 2020;11:58.

6.Lim HS, Park YH, Kim SK. Relationship between Serum Inflammatory Marker and Bone Mineral Density in Healthy Adults. J Bone Metab. 2016;23(1):27-33.

7.Harmer D, Falank C, Reagan MR. Interleukin-6 Interweaves the Bone Marrow Microenvironment, Bone Loss, and Multiple Myeloma. Front Endocrinol (Lausanne). 2018;9:788.

8.Gremese E, Bruno D, Varriano V, Perniola S, Petricca L, Ferraccioli G. Serum Albumin Levels: A Biomarker to Be Repurposed in Different Disease Settings in Clinical Practice. J Clin Med. 2023;12(18):6017.

9.Sunar I, Ataman S. Serum C-Reactive Protein/Albumin Ratio in Rheumatoid Arthritis and its Relationship With Disease Activity, Physical Function, and Quality of Life. Arch Rheumatol. 2020;35(2):247-253.

10.Öz N, Gezer H, Duruöz M. AB0232 The Usefulness of the Prognostic Nutritional Index (PNI) for the Disease Activity in Patients with Rheumatoid Arthritis. 2022.

11.Sun G, Li Y, Peng Y, Lu D, Zhang F, Cui X, et al. Impact of the preoperative prognostic nutritional index on postoperative and survival outcomes in colorectal cancer patients who underwent primary tumor resection: a systematic review and meta-analysis. Int J Colorectal Dis. 2019;34(4):681-689.

12.Sponholtz TR, Zhang X, Fontes JD, Meigs JB, Cupples LA, Kiel DP, et al. Association between inflammatory biomarkers and bone mineral density in a community-based cohort of men and women. Arthritis Care Res

(Hoboken). 2014;66(8):1233-1240.

13.Güzel Y. Postmenopozal Kadınlarda Kemik Mineral Dansitometri Değerleri ile Hematolojik Parametrelerin Karşılaştırılması. Dicle Tıp Dergisi. 2021;48(2):267-273.

14.Younesi Asl L, Kashanian M, Najmi Z, Mahdavi A, SafarpourLima Z. Risk factors of osteoporosis and osteopenia in postmenopausal women based on the L2-L4 BMD T score of the lumbar spine: a study in Iran. Gynecol Endocrinol. 2023;39(1):2205959.

15.Ellez HI, Keskinkilic M, Semiz HS, Arayici ME, Kisa E, Oztop I. The Prognostic Nutritional Index (PNI): A New Biomarker for Determining Prognosis in Metastatic Castration-Sensitive Prostate Carcinoma. J Clin Med. 2023;12(17):5434.

16.Albayrak H. Neutrophil-to-Lymphocyte Ratio, Neutrophil-to-Monocyte Ratio, Platelet-to-Lymphocyte Ratio, and Systemic Immune-Inflammation Index in Psoriasis Patients: Response to Treatment with Biological Drugs. J Clin Med. 2023;12(17):5452.

17.Fang H, Zhang H, Wang Z, Zhou Z, Li Y, Lu L. Systemic immune-inflammation index acts as a novel diagnostic biomarker for postmenopausal osteoporosis and could predict the risk of osteoporotic fracture. J Clin Lab Anal. 2020;34(1):e23016.

18.Pay RE, Şahin B, Ertürk Çelik G, Ustun Y. Postmenopozal osteoporozlu kadınlarda inflamatuar biyobelirteçlerin ve kemik mineral yoğunluğu ile ilişkisinin incelenmesi. Türk Kadın Sağlığı ve Neonatoloji Dergisi. 2022;4(4):165-170.

19.Zhang S, Ni W. High systemic immune-inflammation index is relevant to osteoporosis among middle-aged and older people: A cross-sectional study. Immun Inflamm Dis. 2023;11(8):e992.

20.Zhao S, Gao W, Li J, Sun M, Fang J, Tong L, et al. Dietary inflammatory index and osteoporosis: the National Health and Nutrition Examination Survey, 2017-2018. Endocrine. 2022;78(3):587-596.

21.Ji Y, Geng N, Niu Y, Zhao H, Fei W, Chen S, et al. Relationship between geriatric nutritional risk index and osteoporosis in type 2 diabetes in Northern China. BMC Endocr Disord. 2022;22(1):308.

22.Li Q, Zhu M, Liu X, Tian C, Li D, Wang H, et al. Abnormally low serum albumin levels are associated with abnormal bone mineral density and osteoporotic fractures: a retrospective studies. BMC Musculoskelet Disord. 2024;25(1):888.

Received: 03 Dec 2024 | **Accepted:** 30 Jan 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 340-345
DOI: 10.54005/geneltip.1595644

ORIGINAL ARTICLE

Assessment of the Effectiveness of Basic Life Support Training for Dental Faculty Residents

Diş Hekimliği Fakültesi Asistanlarına Verilen Temel Yaşam Desteği Eğitimi Etkinliğinin Değerlendirilmesi

[1]Funda Arun

[1]Department of Pedodontics, Division of Anesthesia, Faculty of Dentistry, Selcuk University, Konya, Türkiye

Correspondence

Funda ARUN, Assist. Prof.
Selcuk University Faculty of Dentistry, Department of Pedodontics Division of Anesthesia, Alaaddin Keykubat Campus, 42130, Selcuklu, Konya, Türkiye

E-Mail: funda.arun@selcuk.edu.tr

How to cite ?

Arun F. Assessment of the Effectiveness of Basic Life Support Training for Dental Faculty Residents. Genel Tıp Derg. 2025;35 (2): 340-345

ABSTRACT

Aim: Cardiac arrest (CA) is a leading cause of mortality worldwide, with survival outcomes heavily dependent on prompt recognition and intervention. Basic Life Support (BLS) training is critical for equipping healthcare professionals with the skills necessary to manage such emergencies effectively. Tailored BLS training is essential in dentistry, where emergencies like CA, though rare, can have severe consequences. This study evaluated the effectiveness of a structured BLS training program for dental residents at Selçuk University Faculty of Dentistry, incorporating theoretical, practical, and video-based instruction components.
Methods: A total of 151 volunteer dental residents participated in a structured BLS training program conducted between May 14-17, 2024. Training included theoretical lectures, hands-on practice on mannequins, and a preparatory video covering BLS interventions for adults, children, and infants. Knowledge acquisition was measured using pre-tests, post-tests, and a retention test one month after training. Participants' demographic data and prior BLS experience were also evaluated.
Results: Participants demonstrated significant improvement in knowledge immediately after training, with retention remaining above pre-test levels one month later. In analyzing the number of participants answering the questions correctly in the post-training tests, $p<0.001$ was found for 10 out of 12 questions. Those watching the preparatory video scored significantly higher in post-training and retention tests than those who did not, highlighting the supportive role of the videos. Most participants (91.8%) reported never performing BLS in real-life scenarios, underscoring the need for recurring hands-on training to address gaps in practical readiness.
Conclusion: This study shows that structured BLS training effectively improves knowledge acquisition and retention in dental residents. Preparatory videos aid learning. To sustain knowledge and readiness, periodic refreshers, advanced simulation technologies, and standardized BLS curricula are recommended. Incorporating BLS training into dental education helps professionals respond confidently in emergencies, enhancing patient's safety outcomes.

Keywords: Basic life support, dental education, knowledge retention

ÖZ

Amaç: Kardiyak arrest (KA), hayatta kalma sonuçlarının büyük ölçüde hızlı tanıma ve müdahaleye bağlı olduğu dünya çapında önde gelen bir ölüm nedenidir. Temel Yaşam Desteği (TYD) eğitimi, sağlık çalışanlarını bu tür acil durumları etkili bir şekilde yönetmek için gerekli becerilerle donatmak için kritik öneme sahiptir. Bireysel TYD eğitimi, KA gibi acil durumların nadir de olsa ciddi sonuçlara yol açabildiği diş hekimliğinde esastır. Bu çalışmada, Selçuk Üniversitesi Diş Hekimliği Fakültesi'ndeki diş hekimliği asistanları için teorik, pratik ve video tabanlı eğitim bileşenlerini içeren yapılandırılmış bir TYD eğitim programının etkinliği değerlendirildi.
Gereç ve Yöntemler: 14-17 Mayıs 2024 tarihleri arasında yürütülen yapılandırılmış bir TYD eğitim programına toplam 151 gönüllü diş hekimliği asistanı katıldı. Eğitim, teorik dersler, mankenler üzerinde uygulamalı pratik ve yetişkinler, çocuklar ve bebekler için TYD müdahalelerini kapsayan bir hazırlık videosu içeriyordu. Bilgi edinimi, ön testler, son testler ve eğitimden bir ay sonra yapılan bir tutma testi kullanılarak ölçüldü. Katılımcıların demografik verileri ve önceki BLS deneyimleri de değerlendirildi.
Bulgular: Katılımcılar, eğitimden hemen sonra bilgilerinde önemli bir gelişme gösterdiler ve tutma bir ay sonra test öncesi seviyelerin üzerinde kaldı. Eğitim sonrası testlerde soruları doğru cevaplayan katılımcı sayısı analizinde, 12 sorudan 10'u için $p<0,001$ bulundu. Hazırlık videosunu izleyenler, eğitim sonrası ve kalıcılık testlerinde izlemeyenlere göre önemli ölçüde daha yüksek puan aldılar ve bu da videonun destekleyici rolünü vurguladı. Katılımcıların çoğu (%91,8), gerçek yaşam senaryolarında asla TYD yapmadıklarını bildirdi ve bu da pratik hazırlıktaki boşlukları gidermek için tekrarlayan uygulamalı eğitime ihtiyaç olduğunu vurguladı.
Sonuçlar: Bu çalışma, yapılandırılmış TYD eğitiminin diş hekimliği asistanlarının bilgi edinimi ve bu bilginin kalıcılığını etkili bir şekilde artırdığını göstermiştir. Hazırlık videolarının öğrenme sürecine katkıda bulunduğu sonucu ile bilgi ve hazırlığın sürdürülebilirliği için periyodik yenilemeler, gelişmiş simülasyon teknolojilerinin kullanımı ve standartlaştırılmış TYD müfredatlarının uygulanması önermekteyiz. Diş hekimliği asistan eğitimine TYD eğitiminin dahil edilmesinin, profesyonellerin acil durumlara güvenle yanıt vermesine olanak sağlayarak hasta güvenliği ve sonuçlarının iyileştirilmesine katkıda bulunacağına inanıyoruz.

Anahtar Kelimeler: Bilgi tutma, diş hekimliği eğitimi, temel yaşam desteği,

Introduction

Cardiac arrest (CA) is the cessation of the heart's ability to pump blood effectively. It is one of the leading causes of death worldwide (1). CA reduces blood flow, increasing the risk of brain damage within four minutes, so immediate medical attention is critical (2). The first 10 minutes after CA are crucial, often called the "Golden 10." Quick action during this time significantly increases survival chances (3). Only 10% of

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

people experiencing CA outside a hospital survive, and 20% suffer neurological or moderate damage (4). Survival outcomes hinge on prompt diagnosis and intervention, involving essential actions. Basic Life Support (BLS) is the primary practice providing sufficient blood to the tissues by pumping blood from the heart after the heart(5). Cardiopulmonary resuscitation (CPR), the use of the savior respiratory and automatic external defibrillator (AED), combines skills such as chest compression and artificial respiration to maintain blood circulation to the patient's vital organs (6).

Individuals faced with situations requiring BLS must possess adequate knowledge and be prepared to implement quick and accurate first aid. BLS is an essential skill for all healthcare professionals, as it does not require specialized equipment or medication and should be understood by everyone in the field (7). BLS is a vital skill for healthcare professionals, enabling them to respond effectively in emergencies and potentially save lives.

Maintaining BLS competency and retention among dental residents is especially crucial, as they often work in unique clinical environments where emergencies can occur. The most critical medical emergency for a dentist is CA. Although unusual, deaths are reported to CA during dental treatment in dentistry (8, 9). For this reason, as a health professional, dentists should be able to recognize CA and apply BLS. Using the automatic external defibrillator (OED) and the BLS training containing cardiopulmonary resuscitation (CPR) is one of the basic skills necessary for managing emergencies in dentistry. Prior research has demonstrated the importance of structured, theory-and-practice-based BLS training programs to improve participants' knowledge, skills, and long-term retention.

This study aims to evaluate the effectiveness of a structured BLS training program provided to Selçuk University Faculty of Dentistry residents. The program utilizes theoretical and practical components, complemented by a pre-training video, to measure immediate knowledge acquisition and retention one month after training.

Materials and Methods

This study excitedly evaluated the responses of 160 dedicated volunteer dental residents participating in BLS training from May 14-17, 2024. They completed pre-tests, post-tests, and a retention test a month later. The study was approved by the Ethics Committee of the Selcuk University Faculty of Dentistry (25/04/2024-13). The BLS training was conducted by an anesthesiology and reanimation consultant over four sessions blending theoretical lectures with practical demonstrations. A week before the training, we provided the participants with a video detailing the BLS intervention steps for adults, children, and infants. The structured BLS training program was designed under the latest European Resuscitation Council (ERC) 2021 guidelines and American Heart Association (AHA) 2020 guidelines (10, 11). The videos provided to participants were also aligned with these guidelines to ensure consistency with current best practices. Although viewing the video was optional, it acted as preparatory material. Participants attended a 2-hour theoretical lecture during the training sessions, followed by supervised individual practice of chest compressions on a mannequin.

Data Collection Instruments were a Participant Information Form for collecting demographic and baseline characteristics and a BLS Knowledge Form, given as a pre-test, right after training (post-test), and again one month later (retention test). Figures 1 and 2. Before the training, participants completed a pre-test to assess baseline knowledge. Post-training knowledge was measured immediately after the session and again one month later to evaluate retention.

Age:	
Sex (Male or female):	
Did you receive Basic Life Support Training during your undergraduate education at the Faculty of Dentistry? (Yes or No)	
Have you ever experienced an incident that required Basic Life Support or First Aid? (Yes or No)	
Have you ever administered Basic Life Support /First Aid to someone? (Yes or No)	
Did your residency training include a rotation in the Department of Emergency Medicine at a medical school? (Yes or No)	
Have you watched the BLS video shared with you? (Yes or No)	

Figure 1. Participant Information Form

1.	Basic life support is a rescue attempt that trained individuals can perform without the support of medication and equipment.	YES	NO
2.	When you see someone collapse, the first thing you should do is go to them and say, "Are you okay?"	YES	NO
3.	In the ABC of first aid, B stands for respiratory examination.	YES	NO
4.	The most important cause of airway obstruction in an unconscious patient is the teeth blocking the airway.	YES	NO
5.	If the patient is unconscious but ABC is normal during the first examination, the patient is placed in the recovery position.	YES	NO
6.	The respiratory examination of a patient who has collapsed should last < 10 seconds.	YES	NO
7.	In effective breast compression, the depth of the pressure should be 5-6 cm.	YES	NO
8.	Effective chest compressions should be performed at a rate of 60-90 compressions per minute.	YES	NO
9.	Cardiopulmonary resuscitation 30 chest compression/ 2 -curtain is breathing in adults.	YES	NO
10.	Basic Life Support Algorithm includes Ambu and Oxygen support.	YES	NO
11.	Chest compression in children is made at a depth of up to 1/3 of the chest front-back diameter.	YES	NO
12.	Basic life support practices in the case of witnessing cardiopulmonary arrests in < 8-year-old children are the same as adults.	YES	NO

*Please respond by marking the checkboxes for 'Yes' or 'No' to indicate the accuracy of the following information.

Figure 2. BLS (Basic Life Support) Knowledge Form

Statistical Analysis

The data obtained from the research was analyzed using the Statistical Package for Social Sciences for Windows (SPSS), version 21.0. Descriptive statistics were used to evaluate the sociodemographic data. The repeated measurement scores of the BLS Information Form were assessed using the Friedman test, and post hoc pairwise comparisons were conducted with the McNemar test, where the variables were distributed binomially. A $p< 0.05$ value was accepted as the statistical significance.

Results

Following data collection, the values underwent statistical analysis and were tabulated.

The responses provided by the participants in the Participant Information Form are presented in Table 1. The mean age of the sample was 27.56 (SD: 2.11), and 71.3 % of the participants were female. Most residents reported having not experienced a situation requiring BLS at 88.1%. 68.7% of participants (n=110) received BLS or First Aid training during their dental undergraduate education, while 31.3% (n=50) did not. However, only 8.2% (n=13) had administered BLS or First Aid, whereas 91.8% (n=147) had never done so. When asked about watching the provided BLS video, only 35% (n=56) of the participants confirmed viewing it, while the remaining 65% (n=104) had not. A very small proportion of participants (5.7%, n=9) reported that they had previously received BLS training during their emergency department rotation at the Faculty of Medicine, and they were excluded from the study. Ultimately, 151 volunteers participated in the study after completing all pre-and post-tests.

Table 1. Responses in Participant Information Form (n, %)

			n	%
Age	20-25		**25**	**15.6**
	26-30		**123**	**76.8**
	31-35		**11**	**7.0**
	>35		**1**	0.6
Sex	Female		**114**	**71.3**
	Male		**46**	**28.7**
Responses to the questions	Did you receive Basic Life Support Training during your undergraduate education at the Faculty of Dentistry?	Yes	110	68.7
		No	50	31.3
	Have you ever experienced an incident that required Basic Life Support or First Aid?	**Yes**	19	11.9
		No	141	88.1
	Have you ever administered Basic Life Support /First Aid to someone?	Yes	13	8.2
		No	147	91.8
	Did your residency training include a rotation in the Department of Emergency Medicine at a medical school?	Yes	9	5.7
		No	151	94.3
	Have you watched the BLS video shared with you?	Yes	56	35
		No	104	65

The correct response rates for the tests administered before and after the training and for control purposes increased statistically significantly. These results indicate that the training has been advantageous (Table 2). The accuracy rates of participants watching the video are presented in Table 3.

Table 2. The correct responses of all participants.

Note: The percentage values written in bold in the table represent those that cause significant differences

All Participants n=151	Pretest Knowledge (%)	Posttest Knowledge (%)	Retentiontest Knowledge (%)	Knowledge Level Differences p-value
Question 1	94.0	94.7	**98.0**	0.006
Question 2	**88.7**	99.3	97.4	<0.001
Question 3	**77.5**	97.4	96.0	<0.001
Question 4	**92.1**	97.4	98.7	<0.001
Question 5	**43.0**	**68.2**	**88.7**	<0.001
Question 6	**79.5**	94.7	98.2	<0.001
Question 7	**86.8**	98.7	96.0	<0.001

Question 8	69.5	**23.8**	66.2	<0.001
Question 9	**84.8**	**100.0**	**92.7**	<0.001
Question 10	**53.0**	**41.1**	**31.8**	<0.001
Question 11	**89.4**	98.0	95.4	<0.001
Question 12	**45.7**	87.4	84.8	<0.001

Table 3. The correct responses for all videos watched by participants.

Note: The percentage values written in bold in the table represent those that cause significant differences

Video Watched Participants n=56	Pretest Knowledge (%)	Posttest Knowledge (%)	Retentiontest Knowledge (%)	Knowledge Level Differences p-value
Question 1	100.0	100.0	100.0	-
Question 2	96.4	100.0	100.0	0.256
Question 3	**89.3**	100.0	100.0	0.032
Question 4	98.2	100.0	96.4	0.179
Question 5	**87.5**	96.4	94.6	0.014
Question 6	**89.3**	100.0	100.0	<0.001
Question 7	100.0	100.0	100.0	-
Question 8	91.1	94.6	**87.5**	0.005
Question 9	98.2	100.0	100.0	0.371
Question 10	**83.9**	94.6	94.6	0.010
Question 11	100.0	100.0	98.2	0.391
Question 12	**92.9**	100.0	100.0	<0.001

The study participants were divided into two main groups: those viewing the preparatory video and those who did not. The group watching the video comprised 56 participants, while 104 participants did not watch the video. These groups were analyzed separately to determine the video's impact on knowledge acquisition and retention. The statistical differences between the two groups were significant. The group watching the video showed higher knowledge retention and better performance in the post-test and retention test phases ($p<0.05$). These findings indicate that preparatory video materials play a critical role in enhancing learning outcomes and knowledge retention.

Discussion

This study evaluated the effectiveness of a structured BLS training program for dental assistants, which combined theoretical lectures, practical exercises, and preparatory video materials. The results showed significant improvement in participants' knowledge immediately after the training and retention one month later, demonstrating the program's effectiveness. These findings highlight the critical role of structured BLS training in equipping dental professionals with basic emergency response skills. The advancements noted in participants' understanding emphasize the significance of integrating BLS training within dental education. Previous studies have highlighted the importance of this training for healthcare professionals, linking theoretical ideas with practical applications (12).

The research revealed that 91.8% of participants had never applied BLS in real-life scenarios, highlighting a significant deficiency in practical emergency readiness. This observation corresponds with earlier studies showing that healthcare providers, such as dentists, frequently perceive themselves as unprepared to handle emergencies stemming from a lack of hands-on experience. Abdulrahman et al. found that dentists' self-competency in performing CPR was rated poorly, with only 34.5% indicating they were proficient (13). Al-Hamad et al. found that only 45% were efficient (14). Structured and recurring BLS training can address this gap, ensuring that dental practitioners can effectively handle rare but critical emergencies like CA. They must also understand the revision cycle of BLS guidelines, which needs to be highlighted in BLS training.

The video recommended for watching before the training significantly improved the participants' performance on post-training and retention tests. This finding is consistent with existing literature suggesting that video-based learning is a powerful tool for introducing and reinforcing complex skills (15). Using video materials as complementary tools to enhance practical training highlights the value of blended learning approaches. Despite the benefits of video-based learning, it is more effective when used with additional reinforcement methods such as interactive simulations or digital assessment tools. Training incorporating cutting-edge e-learning technologies, including virtual and augmented reality, aims to replicate real-world emergencies and enhance participant engagement has gained popularity in recent times years (16, 17).

Knowledge retention dipped one month post-training but stayed significantly higher than pre-training levels in the study. This aligns with studies indicating that BLS knowledge and skills diminish without ongoing refreshers (18). The study conducted by Anderson and colleagues highlights the effectiveness of short-duration, distributed CPR training on a manikin equipped with real-time visual feedback. Their findings emphasize that such training significantly enhances CPR performance, and they further demonstrate that monthly training sessions yield superior results

compared to training intervals of months 3, 6, or 12 (19). This suggests that frequent and consistent training reinforces CPR skills and ensures better retention and application of proper techniques. Consistent retraining bolsters skill retention and confidence, making it a vital component of a thorough BLS training strategy. Including follow-up evaluations and refreshers in dental assistant training programs can ensure ongoing competence and readiness to manage emergencies.

Additionally, participants' previous BLS training, individual motivation, and familiarity with emergency protocols may affect both short-term and long-term retention of training (20). Although this study did not investigate more personalized variables, nine residents who had rotated in the emergency department and had recently received BLS training were excluded from the analysis.

Integrating BLS training within dental education is more than just an academic requirement; it's a vital necessity. Although possessing the ability to provide BLS is included as a competency within undergraduate dental education under the DUÇEP (The National Core Education Program for Undergraduate Dental Education) framework, it is essential to ensure that BLS training is revisited and updated during postgraduate education considering the latest guidelines and developments in Dentistry Faculties of Türkiye (21). This study underscores the urgent demand for emergency training programs customized for the dental field, including AED usage and CPR in the curriculum, which guarantees that dental professionals are equipped to handle emergencies that could occur during patient care. This study also adds to the growing body of evidence advocating standardized, mandatory BLS training for dental faculty residents (22). By promoting preparation, such training can significantly improve patient outcomes and reduce morbidity and mortality associated with in-office emergencies.

Conclusion

This study emphasizes how a structured BLS education program for dental residents can substantially improve knowledge acquisition and retention. The findings demonstrate the beneficial impact of video-based materials and the importance of hands-on practice for thorough learning. To tackle knowledge retention challenges and ensure dental professionals are adequately prepared for possible emergencies in the office, regular refresher courses, advanced simulation tools, and standardized training protocols should be implemented.

Conflict of interest

The author reported no potential conflict of interest or any financial or non-financial interest.

Financial support

This research received no specific grant from public, commercial, or not-for-profit funding agencies.

References

1.May, S., et al.., Improvement in non-traumatic, out-of-hospital cardiac arrest survival in Detroit from 2014 to 2016. J Am Heart Assoc, 2018. 7(16): p. e009831.

2.Lancet, T., Out-of-hospital cardiac arrest: a unique medical emergency. 2018. p. 911.

3.Mani, G., et al., A cross-sectional study to assess knowledge and attitudes related to Basic Life Support among undergraduate medical students in Tamil Nadu, India. Progress in Health Sciences, 2014. 4(1): p. 47-52.

4.Coute, R.A., et al., Annual and lifetime economic productivity loss due to adult out-of-hospital cardiac arrest in the United States: A study for the CARES Surveillance Group. Resuscitation, 2021. 167: p. 111-117.

5.Panchal, A.R., et al., Part 3: Adult Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation, 2020. 142(16_suppl_2): p. S366-S468.

6.Mac Giolla Phadraig, C., et al., Neither Basic Life Support knowledge nor self-efficacy is predictive of skills among dental students.Eur J Dent Educ, 2017. 21(3): p. 187-192.

7.Perman, S.M., et al., 2023 American Heart Association Focused Update on Adult Advanced Cardiovascular Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation, 2024. 149(5): p. e254-e273.

8.Hunter, P., Cardiac arrest in the dental surgery. BDJ Open, 1991. 170(8): p. 284-284.

9.Gonzaga, H.F.d.S., et al., Evaluation of knowledge and experience of dentists of São Paulo State, Brazil about cardiopulmonary resuscitation.Braz Dent J, 2003. 14: p. 220-222.

10.Panchal, A.R., et al., Part 3: adult basic and advanced life support: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation, 2020. 142(16_Suppl_2): p. S366-S468.

11.Olasveengen, T.M., et al., European Resuscitation Council Guidelines 2021: basic life support. Resuscitation, 2021. 161: p. 98-114.

12.Merchant, R.M., et al., Part 1: Executive Summary: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation, 2020. 142(16_suppl_2): p. S337-S357.

13.Abdulrahman, B.I., et al., Are dental professionals ready to deal with medical emergencies in their clinical office? A survey of university hospitals. Journal of Medicine and Life, 2022. 15(8): p. 979.

14.Alhamad, M., et al., Medical emergencies encountered in dental clinics: A study from the Eastern Province of Saudi Arabia. J Family Community Med., 2015. 22(3): p. 175-179.

15.Cheng, A., et al., Resuscitation education science: educational strategies to improve outcomes from cardiac arrest: a scientific statement from the American Heart Association. Circulation, 2018. 138(6): p. e82-e122.

16.Castillo, J., et al., Efficacy of virtual reality simulation in teaching basic life support and its retention at 6 months. Int J Environ Res Public Health. 2023. 20(5): p. 4095.

17.Wiltvank, I.L., et al., Redesign of a virtual reality basic life support module for medical training – a feasibility study. BMC Emergency Medicine, 2024. 24(1): p. 176.

18.Mcevoy, N., et al., What is the effect of frequent basic life support refresher sessions on health care professionals' retention of cardiopulmonary resuscitation skills. A Systematic Review, 2018. 9(29): p. 13-5.

19.Anderson, R., et al.., Optimal training frequency for acquisition and retention of high-quality CPR skills: a randomized trial. Resuscitation, 2019. 135: p. 153-161.

20.Govender, K., et al., Retention of knowledge of and skills in cardiopulmonary resuscitation among healthcare providers after training. S Afr Fam Pract, 2010. 52(5).

21.https://www.yok.gov.tr/Documents/Kurumsal/egitim_ogretim_dairesi/Ulusal-cekirdek-egitimi-programlari/dis-hekimligi.pdf).

22.Dana, E., et al.., Comparison of community-based clinical education implementation among US dental and dental hygiene education programs. J Dent Educ

Received: 14 Dec 2024 | **Accepted:** 17 Feb 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 346-351
DOI: 10.54005/geneltip.1601191

ORIGINAL ARTICLE

A Retrospective Comparative Analysis of Epidural Analgesia and Its Impact on Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios During Vaginal Delivery

Epidural Analjezi ve Vajinal Doğum Sırasında Nötrofil-Lenfosit ve Trombosit-Lenfosit Oranları Üzerindeki Etkisi: Karşılaştırmalı Bir Analiz

[1]Can Turkler, [2]Mehmet Bahadır Savas, [3]Emine Aslanalar, [4]Mehmet Kulhan

[1]Tınaztepe University Medical Faculty, Department of Gynaecology and Obstetrics, Izmir, Türkiye
[2]Tınaztepe University Medical Faculty, Department of Anesthesiology and Reanimation, Izmir, Türkiye
[3]Selcuk University Medical Faculty, Department of Anesthesiology and Reanimation, Konya, Türkiye
[4]Selcuk University Medical Faculty, Department of Gynaecology and Obstetrics, Konya, Türkiye

Correspondence

Can Turkler
Tınaztepe University Medical Faculty, Department of Gynaecology and Obstetrics, Izmir, Türkiye

E-Mail: dr_canturkler@yahoo.com

How to cite ?

Turkler C, Savas MB, Aslanlar E, Kulhan M. A Retrospective Comparative Analysis of Epidural Analgesia and Its Impact on Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios During Vaginal Delivery. Genel Tıp Derg. 2025;35 (2): 346-351

ABSTRACT

Introduction: Epidural analgesia is a widely used method for managing labor pain. While effective in pain relief, its potential effects on maternal systemic inflammation during labor remain unclear. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are established biomarkers for systemic inflammation and may provide insights into the inflammatory dynamics associated with epidural analgesia. This study aims to investigate the impact of epidural analgesia on NLR and PLR values in women undergoing normal vaginal delivery.
Methods: A retrospective case-control study was conducted involving 100 women with singleton pregnancies, evenly divided into two groups based on whether they received epidural analgesia. Hematological parameters, including NLR and PLR, were measured and analyzed. Labor duration and white blood cell (WBC) counts were also compared between groups.
Results: No significant differences in NLR ($p = 0.79$) or PLR ($p = 0.59$) values were observed between the epidural and non-epidural groups. However, WBC counts were significantly higher in the epidural group ($p = 0.007$), and labor duration was prolonged ($p < 0.001$) compared to the non-epidural group.
Conclusion: Epidural analgesia does not significantly influence NLR and PLR values, suggesting minimal systemic inflammatory effects. However, the observed increase in WBC counts and prolonged labor duration highlight the need for individualized monitoring and care. These findings provide further evidence supporting the safe use of epidural analgesia in normal vaginal delivery while identifying areas for future research.

Keywords: epidural analgesia, inflammation, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, vaginal delivery

ÖZ

Giriş: Epidural analjezi, doğum ağrısını yönetmek için yaygın olarak kullanılan bir yöntemdir. Ağrıyı gidermede etkili olsa da, doğum sırasında maternal sistemik inflamasyon üzerindeki potansiyel etkileri belirsizliğini korumaktadır. Nötrofil-lenfosit oranı (NLR) ve trombosit-lenfosit oranı (PLR), sistemik inflamasyon için belirlenmiş biyobelirteçlerdir ve epidural analjezi ile ilişkili inflamasyon dinamiklerine dair içgörüler sağlayabilir. Bu çalışma, normal vajinal doğum yapan kadınlarda epidural analjezinin NLR ve PLR değerleri üzerindeki etkisini araştırmayı amaçlamaktadır.
Yöntemler: Tekil gebelikleri olan 100 kadını içeren retrospektif bir vaka kontrol çalışması yürütüldü ve epidural analjezi alıp almamalarına göre eşit olarak iki gruba ayrıldı. NLR ve PLR dahil hematolojik parametreler ölçüldü ve analiz edildi. Doğum süresi ve beyaz kan hücresi (WBC) sayıları da gruplar arasında karşılaştırıldı.
Bulgular: Epidural ve epidural olmayan gruplar arasında NLR ($p = 0,79$) veya PLR ($p = 0,59$) değerlerinde anlamlı bir fark gözlenmedi. Ancak, epidural grupta WBC sayıları anlamlı şekilde daha yüksekti ($p = 0,007$) ve doğum süresi epidural olmayan gruba kıyasla daha uzundu ($p < 0,001$).
Sonuç: Epidural analjezi, NLR ve PLR değerlerini anlamlı şekilde etkilemez ve bu da minimal sistemik inflamatuar etkiler olduğunu düşündürmektedir. Ancak, WBC sayılarında gözlemlenen artış ve uzamış doğum süresi, bireyselleştirilmiş izleme ve bakıma olan ihtiyacı vurgulamaktadır. Bu bulgular, normal vajinal doğumda epidural analjezinin güvenli kullanımını destekleyen daha fazla kanıt sağlarken gelecekteki araştırma alanlarını belirlemektedir.

Anahtar Kelimeler: epidural analjezi, inflamasyon, nötrofil-lenfosit oranı, trombosit-lenfosit oranı, vajinal doğum

Introduction

Lumbar epidural analgesia is one of the most effective methods for pain management during vaginal delivery. Globally, 30-60% of women in labor prefer this method. Epidural analgesia increases maternal comfort by reducing labor pain, contributing to muscle relaxation and decreasing physiological stress during labor. However, this method is also associated with complications such as severe headaches, permanent nerve damage, significant drops in blood pressure, meningitis, epidural abscess, and hematoma (1).

In recent years, the role of inflammatory responses during labor has attracted attention. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are indicators of inflammation and are potentially significant biomarkers for assessing maternal inflammatory status during labor (2). In the literature, NLR and PLR have been reported to be associated with obstetric conditions such as preterm labor, gestational

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

diabetes, and preeclampsia (3, 4). However, there is insufficient research evaluating the effects of epidural analgesia on these markers.

The mechanisms through which epidural analgesia might influence inflammatory responses have been discussed in the literature. The immunomodulatory effects of local anesthetics on inflammation and the suppression of stress hormones could explain changes in inflammatory markers (5, 6). This study aimed to evaluate the effects of epidural analgesia on hematological inflammatory markers and contribute to scientific knowledge regarding the role of this method in labor.

Material and methods

Study Design and Patient Population

This retrospective case-control study was conducted at two centers in the Obstetrics and Gynecology Departments. The research was carried out in accordance with the principles of the Helsinki Declaration and received ethical committee approval (approval number: 2024/504, approval date: 08.10.2024). Data were collected from hospital databases between October 2021 and September 2024.

A total of 100 pregnant women with singleton pregnancies between 37 and 41 weeks of gestation who presented with regular uterine contractions were included in the study. Half of the cases were selected from women who received epidural analgesia, while the other half were selected from those who did not. The exclusion criteria were as follows:

• Multiple pregnancies,

• Significant structural anomalies in the fetus,

• Chromosomal aneuploidy,

•Risky pregnancy findings during follow-up (gestational diabetes mellitus, preeclampsia or eclampsia, intrauterine growth restriction, premature rupture of membranes, preterm birth, macrosomia, polyhydramnios, or oligohydramnios),

• Smoking or alcohol use,

• Chronic systemic disease in the mother,

• History of instrumental delivery (vacuum, forceps).

In the epidural analgesia group, a combination of lidocaine–epinephrine (2%) and fentanyl (100 mcg) was used. Epidural fentanyl 100 mcg after lidocaine–epinephrine test dose has been shown to provide adequate analgesia in early labor in previous studies (7). Analgesia was initiated when cervical dilation reached 4 cm during active labor. The epidural catheter was placed in the L3-L4 interspace, and all procedures were performed by an experienced anesthesia team. The same analgesia protocol was applied in both centers.

All hemogram parameter measurements were performed using a blood count analyzer within half an hour of blood collection. Laboratory parameters, including platelet count, neutrophil count, lymphocyte count, NLR, and PLR, were recorded for both groups.

Statistical analyses

The statistics software package SPSS 25 (IBM, Armonk, NY: IBM Corp.) was used for the statistical evaluations in the present study. In this study, statistical analyses were conducted to compare the Neutrophil-Lymphocyte Ratio (NLR) and Platelet-Lymphocyte Ratio (PLR) between two groups: those who underwent epidural anesthesia and those who did not. The first step involved calculating the measures of central tendency (mean) and dispersion (standard deviation) for each group to understand the distribution of NLR and PLR values. To determine if there were significant differences between the two groups, independent sample t-tests were performed for both NLR and PLR. The t-test is used to compare the means of two independent groups to see if they differ significantly. A p-value of less than 0.05 was considered statistically significant, indicating that the difference between the groups is not due to random chance.For each parameter (NLR and PLR), we computed the mean, standard deviation, and the number of participants for both groups. The results are presented in tables that summarize these statistics and the outcomes of the t-tests, including the t-statistics and p-values, along with an indication of whether the differences were statistically significant.

Results

NLR and PLR Analyses

According to Table 1, there were no statistically significant differences in NLR and PLR values between the epidural and non-epidural groups ($p = 0.79$ and $p = 0.59$, respectively). This indicates that epidural analgesia does not significantly impact inflammatory responses.

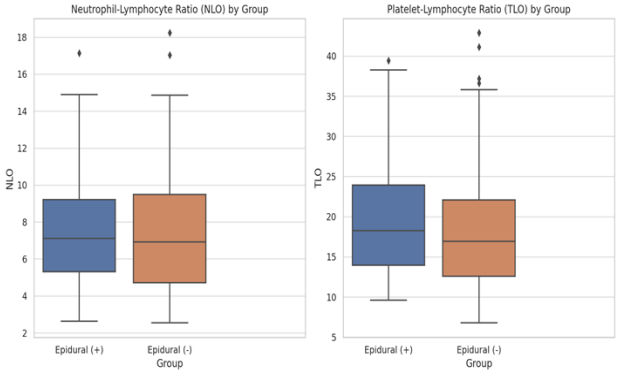
Table 1. NLR and PLR Statistics for Epidural and Non-Epidural Groups

Groups	Parame-ters	Mean	Standard Deviation	Patient Count	P value
Epidural (+)	NLR	7.70	3.10	50	p = 0.79
Epidural (-)	NLR	7.52	3.61	50	
Epidural (+)	PLR	19.76	7.39	50	p = 0.59
Epidural (-)	PLR	18.87	8.79	50	

NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio

The boxplots in Figure 1 show the distributions of NLR and PLR for both groups. The median values and distributions visually confirm the lack of significant differences between the groups.

Figure 1. The following boxplots display the distribution of Neutrophil-Lymphocyte Ratio (NLO) and Platelet-Lymphocyte Ratio (TLO) between the Epidural (+) and Epidural (-) groups.



Comparison of Other Parameters

As shown in Table 2, demographic and clinical parameters such as age, gravida, parity, abortus, BMI, hemoglobin (Hb), and platelet counts did not differ significantly between the two groups ($p > 0.05$).

Table 2. Comparison of Parameters Between Groups

Parameter	Group 1 Mean	Group 1 Std	Group 2 Mean	Group 2 Std	T-Statistic	P-Value	Significance
Age	30.52	4.75	31.2	4.76	-0.715	0.476	No
Gravity	2.04	1.38	2.28	0.88	-1.034	0.304	No
Parity	0.76	0.94	0.98	0.68	-1.339	0.184	No
Abortus	0.28	0.64	0.3	0.46	-0.179	0.858	No
BMI	25.62	2.97	25.96	2.88	-0.588	0.558	No
WBC	16.5	3.71	14.44	3.79	2.751	0.007	Yes
Hemoglobin	10.92	1.19	11.21	1.27	-1.193	0.236	No
Platelet	215.52	44.29	211.84	59.47	0.351	0.726	No
Weight	3366.3	366.81	3223.6	391.95	1.88	0.063	No
Labor duration	8.66	4.73	3.88	2.98	6.048	0.0	Yes

Group 1: Epidural (+) group, Group 2: Epidural (-) group, BMI: Body mass index, WBC: White blood cells

• WBC Count: WBC levels were significantly higher in the epidural group ($p = 0.007$). This supports the hypothesis that epidural analgesia may trigger an inflammatory response.

• Labor Duration: Labor duration was significantly longer in the epidural group ($p < 0.001$). This may be associated with the effects of epidural analgesia on muscle activity and pushing force.

The bar plots in Figure 2 present the mean values of other parameters for both groups. The differences in labor duration and WBC are particularly notable.

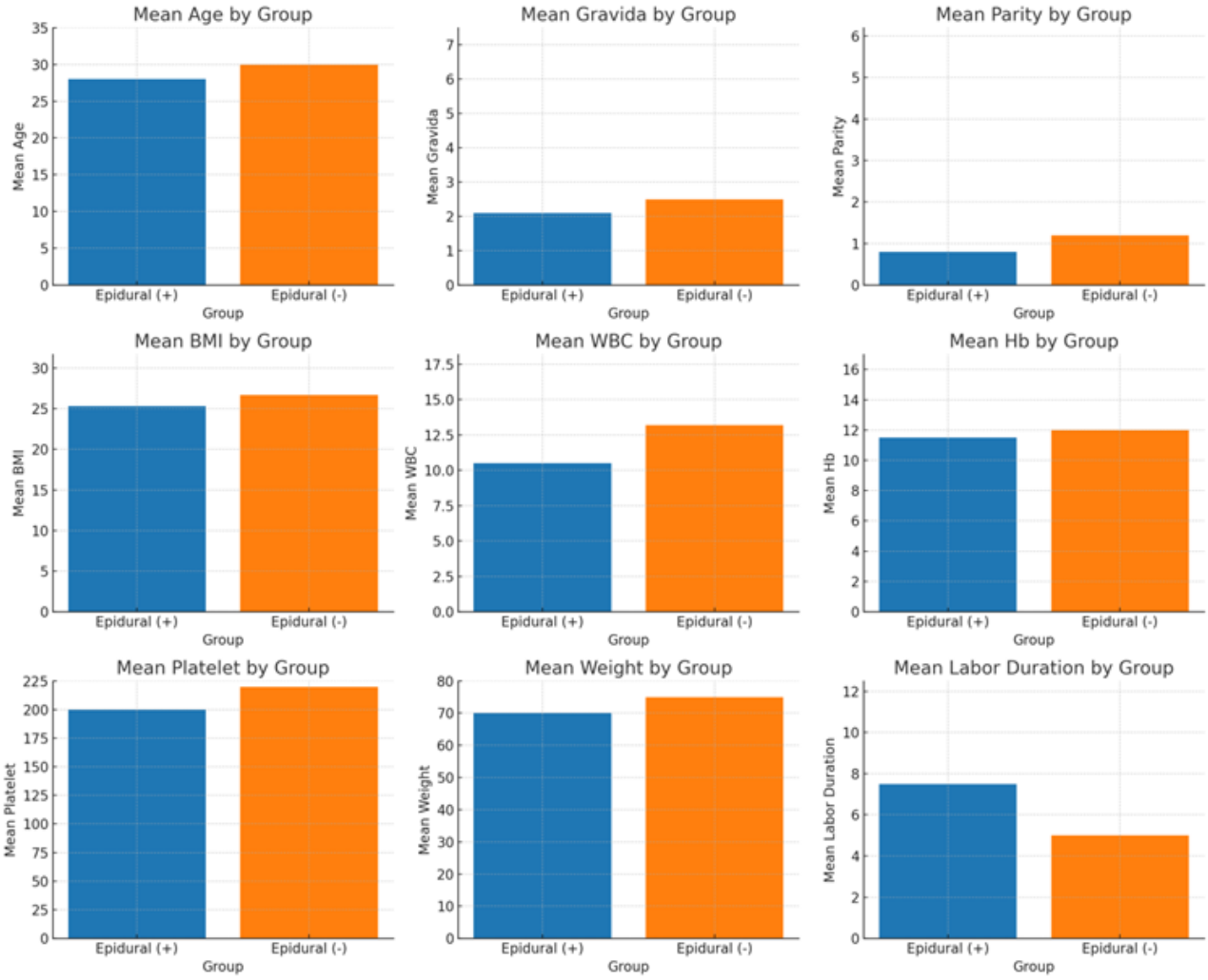
Discussions

This study contributes to the growing body of evidence regarding the effects of epidural analgesia on maternal inflammatory markers and labor outcomes. Epidural analgesia is widely used for pain management during vaginal delivery, yet its potential impact on systemic inflammation remains an area of active investigation.

The finding of no significant difference in NLR and PLR values between epidural and non-epidural groups aligns with previous studies suggesting that epidural analgesia does not significantly alter systemic inflammatory markers (8, 9). For instance, it's reported that NLR and PLR values were consistent across different modes of analgesia during labor, indicating that the physiological stress of labor itself might overshadow any minor effects of analgesia on these markers (10).

In the obstetrics field, several studies have examined the association between maternal WBC count and maternal or neonatal adverse outcomes (11-13). Shigemi et al. investigated the association between maternal WBC count on the day after operative vaginal delivery and sequential maternal adverse events during hospitalization (14). In this study, there was no significant association of WBC count on the day after operative vaginal delivery with maternal adverse outcomes. The observed increase in WBC levels

Figure 2. The following bar plots show the mean values of various parameters (Age, Gravida, Parity, BMI, WBC, Hb, Platelet, Weight, LaborDuration) between the Epidural (+) and Epidural (-) groups.



in the epidural group warrants further exploration. While elevated WBC levels could be indicative of an inflammatory response triggered by epidural administration, it is also possible that this reflects a stress-related physiological adaptation rather than pathological inflammation. Similar findings by Zhang et al. suggest that WBC elevations in epidural groups may not necessarily correlate with adverse maternal or neonatal outcomes, but rather reflect transient responses to procedural stress (15).

Prolonged labor duration in the epidural group is a well-documented phenomenon. A Cochrane review by Anim-Somuah et al. found that epidural analgesia is associated with a modest increase in the duration of both the first and second stages of labor, potentially due to reduced maternal pushing efforts and altered uterine contractility (16). The current study's findings are consistent with this literature and further emphasize the need for monitoring and supportive interventions to mitigate potential delays in labor progression.

In light of these findings, the potential immunological implications of epidural analgesia during labor merit further attention. Hawkins et al. (17) demonstrated that epidural analgesia may attenuate the systemic release of pro-inflammatory cytokines, potentially reducing the risk of excessive inflammatory responses. This could explain the lack of significant differences in NLR and PLR observed in this study, as epidural analgesia might modulate systemic inflammation without overtly impacting hematological markers. Moreover, the observed increase in WBC levels in our study might reflect a localized stress or inflammatory reaction, aligning with the hypothesis that the procedure triggers a transient physiological response

rather than a pathological one. This modulation of maternal inflammatory and stress responses could have important clinical implications, particularly in high-risk pregnancies where exaggerated inflammatory states may exacerbate complications such as preeclampsia or fetal distress. Future research should explore these mechanisms in greater depth to enhance our understanding of epidural analgesia's impact on labor outcomes and recovery.

The clinical implications of these findings are significant. Epidural analgesia remains a safe and effective method for pain relief during labor. However, the observed changes in WBC levels and labor duration underscore the importance of individualized patient care. Future research should focus on elucidating the mechanisms underlying these observations and exploring whether specific patient populations may require tailored management strategies.

Some potential confounding factors like maternal BMI and gestational age can change the results of our study. When the Table 2 examination, we see the same BMI results for both groups. In future studies, including patients in the same gestational week may increase the scientific power of the study.

This study has several limitations. First, the retrospective nature of the study, which may introduce biases in data collection and patient selection. Second, a limited sample size, potentially restricting the ability to detect subtle differences in inflammatory markers. Third, The absence of data on potential confounding factors, such as nutritional status, comorbidities, or subclinical conditions, that could influence the results and finally, the lack of evaluation of long-term maternal or neonatal outcomes related to the observed changes in inflammatory markers and labor duration. Future prospective, multicenter studies with larger sample sizes are needed to validate these findings and explore underlying mechanisms in greater detail.

In conclusion, epidural analgesia effectively reduces labor pain while having minimal effects on inflammatory markers. However, the associated prolongation of labor duration should be carefully monitored. These findings provide encouraging evidence for the safe use of epidural analgesia in obstetric practice.

Funding

This study received no funding.

Conflict of interest

The authors report no conflict of interest.

References

1.Halliday L, Nelson SM, Kearns RJ. Epidural analgesia in labor: A narrative review. Int J Gynaecol Obstet. 2022 Nov;159(2):356-364. doi: 10.1002/ijgo.14175. Epub 2022 Mar 21. PMID: 35277971.

2. Ata N, Kulhan M, Kulhan NG, Turkler C. Can neutrophil-lymphocyte and platelet-lymphocyte ratios predict threatened abortion and early pregnancy loss? Ginekol Pol. 2020;91(4):210-215. doi: 10.5603/GP.2020.0042. PMID: 32374021.

3. Esercan A, Demir I. Neutrophil/Lymphocyte and Platelet/ Lymphocyte Ratio in Preterm Premature Rupture of Membranes. Cureus. 2023 May 7;15(5):e38664. doi: 10.7759/ cureus.38664. PMID: 37163192; PMCID: PMC10164351.

4. Verit FF, Cetin O, Yildirim O, Keskin S, Yucel O, Yalcinkaya S. Neutrophil to lymphocyte ratio is superior to platelet to lymphocyte ratio as an early predictor of moderate/severe ovarian hyperstimulation syndrome. J Obstet Gynaecol. 2014; 34(7): 639–643, doi: 10.3109/01443615.2014.920792, indexed in Pubmed: 24911966.

5. Ilhan G, Atmaca FFV, Altan E, Zebitay AG, Sozen H, Akyol H, et al. Evaluation of Neutrophil-Lymphocyte Ratio, Platelet-Lymphocyte Ratio and Red Blood Cell Distribution Width-Platelet Ratio for Diagnosis of Premature Ovarian Insufciency. J Family Reprod Health. 2016; 10(4): 211–216, indexed in Pubmed: 28546821.

6. Lin L, Lin G, Lian H, Chen Q, Huang P, Lin S, et al. Preoperative Neutrophil-to-Lymphocyte Ratio Level is a Predictor of Postoperative Fertility in Infertile Patients with Ovarian Endometrioma. Reprod Sci. 2022 Apr;29(4):1145-1155. doi: 10.1007/s43032-021-00782-1. Epub 2021 Nov 2. Erratum in: Reprod Sci. 2022 Apr;29(4):1156. doi: 10.1007/s43032-022-00847-9. PMID: 34729718.

7. Siddik-Sayyid SM, Taha SK, Azar MS, Hakki MA, Yaman RA, Baraka AS, et al. Comparison of three doses of epidural fentanyl followed by bupivacaine and fentanyl for labor analgesia. Acta Anaesthesiol Scand. 2008 Oct;52(9):1285-90. doi: 10.1111/j.1399-6576.2008.01765.x. PMID: 18823470.

8. Sargın MA, Yassa M, Taymur BD, Celik A, Ergun E, Tug N. Neutrophil-to-lymphocyte andplatelet-to-lymphocyte ratios: are they useful for predicting gestationaldiabetes mellitus during pregnancy? Ther Clin Risk Manag. 2016; 12:657–665, doi: 10.2147/TCRM.S104247, indexed in Pubmed: 27217758.

9. Serin S, Avcı F, Ercan O, Köstü B, Bakacak M, Kıran H. Is neutrophil/lymphocyte ratio a useful markerto predict the severity of pre-eclampsia? Pregnancy Hypertens. 2016; 6(1): 22–25, doi: 10.1016/j.preghy.2016.01.005, indexed in Pubmed: 26955767.

10. Gökkaya Ş, Yılmaz İ, Erdemir F. The effects of epidural analgesia on systemic inflammatory markers during labor: A comparative study. Int J Obstet Anesth. 2021;46:102960. doi:10.1016/j.ijoa.2021.102960.

11. Chen YY, Chen CP, Sun FJ, Chen CY. Factors associated with neonatal outcomes in preterm prelabor rupture of membranes after cervical cerclage. Int J Gynaecol Obstet. 2019 Dec;147(3):382-388. doi: 10.1002/ijgo.12974. Epub 2019 Oct 9. PMID: 31529463.

12. Harrison MS, Thorsten VR, Dudley DJ, Parker CB, Koch MA, Hogue CJR, et al. Stillbirth, Inflammatory Markers, and Obesity: Results from the Stillbirth Collaborative Research Network. Am J Perinatol. 2018 Sep;35(11):1071-1078. doi: 10.1055/s-0038-1639340. Epub 2018 Apr 2. PMID: 29609190; PMCID: PMC6436964.

13. Musilova I, Pliskova L, Gerychova R, Janku P, Simetka O, Matlak P, et al. Maternal white blood cell count cannot identify the presence of microbial invasion of the amniotic cavity or intra-amniotic inflammation in women with preterm prelabor rupture of membranes. PLoS One. 2017 Dec 12;12(12):e0189394. doi: 10.1371/journal.pone.0189394. PMID: 29232399; PMCID: PMC5726631.

14. Shigemi D, Yasunaga H. Association of white blood cell count after operative vaginal delivery with maternal adverse outcome: A retrospective cohort study. Ann Clin Epidemiol. 2023 Jul 13;5(4):113-120. doi: 10.37737/ace.23015. PMID: 38504951; PMCID: PMC10944988.

15. Zhang L, Li J, Zhang J, Wang Y, Liu H. The impact of epidural analgesia on white blood cell levels during labor: A retrospective cohort study. BMC Pregnancy Childbirth. 2020;20(1):55. doi:10.1186/s12884-020-2745-7.

16. Anim-Somuah M, Smyth RM, Cyna AM, Cuthbert A. Epidural versus non-epidural or no analgesia for pain management in labour. Cochrane Database Syst Rev. 2018 May 21;5(5):CD000331. doi: 10.1002/14651858.CD000331.pub4. PMID: 29781504; PMCID: PMC6494646.

17. Hawkins JL, Bucklin BA, Gambis ML. Epidural analgesia and systemic cytokine modulation during labor: A systematic review. Anesth Analg. 2019;129(5):1234-1242. doi:10.1213/ANE.0000000000004356.

Received: 27 Aug 2024 | **Accepted:** 21 Feb 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 352-361
DOI: 10.54005/geneltip.1539354

ORIGINAL ARTICLE

The Relationship Between Cyber Wellness and Psychological Resilience in Children: A Cross-Sectional Study

Çocuklarda Siber Sağlık ve Psikolojik Sağlamlık Arasındaki İlişki: Kesitsel Bir Araştırma

[1]Aylin Kurt, [2]Ismail Berat Uzun, [1]Beyza Nur Acici, [1]Ahmet Can Tunc, [1]Beritak Buyukatar

[1]Department of Nursing, Faculty of Health Sciences, Bartın University, Bartın, Türkiye
[2]Department of Child Development, Faculty of Health Sciences, Bartın University, Bartın, Türkiye

Correspondence

Aylin Kurt, Assist. Prof.
Bartın University Faculty of Health Science, Agdacı Campus, 74100 Bartın, Türkiye

E-Mail: aylinkurt67@gmail.com

How to cite ?

Kurt A, Uzun IB, Acici BN, Tunc AC, Buyukatar B. The Relationship Between Cyber Wellness and Psychological Resilience in Children: A Cross-Sectional Study. Genel Tıp Derg. 2025;35 (2): 352-361

ABSTRACT

Aim: This study aimed to examine the relationship between cyber health and psychological resilience among children.
Methods: A cross-sectional study design was employed, with data being collected from a sample of 420 middle school students. The Student Cyber Health Scale (SCHS) and the Child and Adolescent Psychological Resilience Scale (CAPRS) were utilized as data collection instruments.
Results: The study revealed that 87.1% of the children accessed the internet through their phones, with an average usage time of 2.75 ± 2.16 hours. The study found a positive correlation between psychological resilience scores and various cyber health sub-dimensions. Specifically, a series of significant positive correlations were identified, with psychological resilience scores demonstrating positive associations with various aspects of cyber health, including awareness of internet addiction ($r=0.385$, $p<0.001$), online courtesy ($r=0.414$, $p<0.001$), online privacy ($r=0.384$, $p<0.001$), online safety ($r=0.493$), cyberbullying awareness ($r=0.534$, $p<0.001$), and online inappropriate content awareness ($r=0.450$, $p<0.001$). An increase of one unit in psychological resilience level was associated with a corresponding increase of 0.534 in cyberbullying awareness score, 0.414 in online kindness awareness score, 0.386 in online privacy awareness score, 0.450 in online inappropriate content awareness score, and 0.443 in online safety awareness score.
Conclusion: It is imperative to educate children from an early age about the risks and responsibilities associated with online interactions. It is imperative to inculcate a sense of awareness regarding cyber health from the onset of the academic year. To this end, the development and implementation of psychoeducation programs and group training on topics such as media literacy and online privacy protection is recommended.

Keywords: Children and youth, cyber wellness, psychological resilience

ÖZ

Amaç: Bu araştırmanın amacı, çocuklar arasında siber sağlık ile psikolojik sağlamlık arasındaki ilişkiyi incelemektir.
Yöntem: Kesitsel bir araştırma olarak gerçekleştirilen bu çalışmada, 420 ortaokul öğrencisinin verileri toplanmıştır. Veri toplama araçları olarak "Öğrenci Siber Sağlık Ölçeği" ve "Çocuk ve Genç Psikolojik Sağlamlık Ölçeği" kullanılmıştır.
Bulgular: Araştırma sonuçlarına göre, çocukların %87,1'i internete telefon aracılığıyla girmekte ve ortalama internet kullanım süresi 2.75±2.16 saattir. Psikolojik sağlamlık puanları ile siber sağlık alt boyutları arasında pozitif ilişkiler bulunmuştur. Özellikle, psikolojik sağlamlık ile internet bağımlılığı farkındalığı ($r=0.385$, $p<0.001$), çevrimiçi nezaket farkındalığı ($r=0.414$, $p<0.001$), çevrimiçi mahremiyet farkındalığı ($r=0.384$, $p<0.001$), çevrimiçi güvenlik farkındalığı ($r=0.493$), siber zorbalık farkındalığı ($r=0.534$, $p<0.001$) ve çevrimiçi uygunsuz içerik farkındalığı ($r=0.450$, $p<0.001$) arasında anlamlı pozitif korelasyonlar tespit edilmiştir. Psikolojik sağlamlık düzeyindeki her 1 birimlik artış, siber zorbalık farkındalığı puanında 0.534, çevrimiçi nezaket farkındalığı puanında 0.414, çevrimiçi mahremiyet farkındalığı puanında 0.386, çevrimiçi uygunsuz içerik farkındalığı puanında 0.450 ve çevrimiçi güvenlik farkındalığı puanında ise 0.443'lük bir artışa yol açmıştır.
Sonuç: Çocukların okul yılı başından itibaren siber sağlığa duyarlı hale getirilmesi önemlidir. Bu amaçla, medya okuryazarlığı ve çevrimiçi mahremiyetin korunması gibi konularda psikoeğitim programları ve grup eğitimlerinin planlanması önerilmektedir.

Anahtar kelimeler: Çocuk ve genç, psikolojik sağlamlık, siber sağlık

Introduction

The advent of the digital age has precipitated a period that has exerted a profound influence on numerous facets of children's lives. This period has afforded children numerous opportunities in various domains, including education, entertainment, socialization, and access to information (1). Therefore, it is imperative to acknowledge the effective utilization of technology by children in these domains. However, the increase in time spent in the digital world introduces potential risks (2). In this context, the concepts of cyber health and psychological resilience have emerged as significant determinants of children's physical and psychological well-being (3).

The concept of cyber health encompasses the secure, ethical, and informed utilization of digital technologies, playing a pivotal role in the development of contemporary youth. The cultivation of cyber health awareness and the development of relevant skills

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

in children is instrumental in empowering them to safeguard their well-being against potential threats and hazards encountered in the digital landscape (4). The phenomenon of bullying on online platforms has been shown to have detrimental effects on children, including the development of psychological trauma (5). Sarcastic comments, threats, and experiences of exclusion, especially on social media platforms, have the potential to engender long-term mental health problems in children (6). Furthermore, children may encounter harmful content online, which can have a detrimental impact on their mental well-being. Content containing violence, hate speech, or misinformation can have a detrimental effect on children's mental development (7). Moreover, excessive screen time can lead to various physical health concerns, such as eye strain and a sedentary lifestyle. Additionally, this excessive screen time can result in social isolation(8). The development of addiction to digital games and social media platforms has the potential to adversely impact children's academic achievement and real-world relationships (9). The depiction of idealized lifestyles on social media platforms has the potential to adversely impact children's self-esteem. Consequently, this may result in the development of social anxieties, jealousy, and a negative body perception (10).

Psychological resilience is defined as a set of skills that enhance an individual's ability to cope with challenging life circumstances, leading to personal growth and strength (11). In the contemporary digital landscape, children are particularly vulnerable to the challenges posed by online negativity, underscoring the necessity for this skill (12). Psychological resilience equips children with the capacity to effectively cope with the stress they encounter in the online environment. For instance, in the context of online bullying, a child possessing this skill set can rationalize the incident and seek support when necessary (13). The cultivation of psychological resilience in children has been shown to foster the development of empathy and a more profound understanding of their own emotional experiences (14). These competencies serve as effective instruments for managing adversity in online interactions. Children who possess a robust psychological foundation are better equipped to navigate online environments with confidence. These individuals possess the capacity to articulate their thoughts and feelings with confidence, enabling them to adopt a more assertive stance when confronted with challenging situations (13).

Children may be exposed to problematic behaviors, such as cyberbullying, which can result in psychological, social, and academic negativity (15). For children who have been exposed to negative experiences, psychological resilience is a crucial factor in their ability to recover and cope with these challenges in a healthy manner (16). It is therefore proposed that psychological resilience may be an effective variable in the context of cyber health. A review of the literature revealed no research examining the relationship between the concepts of cyber health and psychological resilience. The concept of cyber health is a significant and timely issue in Turkey. However, the notion of cyber health is addressed based on more specific concepts, such as internet/game addiction, cyberbullying, online kindness, online privacy, online inappropriate content, copyright, and online safety (17,18). It is important to note that cyber health is not studied as a general concept; rather, it is introduced as an important concept in Turkey. In light of these considerations, the objective of this study is to ascertain whether psychological resilience constitutes a significant predictor of cyber health in children, encompassing domains such as internet/game addiction, cyberbullying, online kindness, online privacy, inappropriate content, copyright, and online safety. In line with this general objective, the research questions are as follows:

1) Does a significant relationship exist between children's cyber health concepts, including but not limited to internet/game addiction, cyberbullying, online kindness, online privacy, online inappropriate content, copyright, and online safety, and their psychological resilience levels?

2) Does psychological resilience act as a significant predictor of cyber health, including such factors as internet/game addiction, cyberbullying, online kindness, online privacy, online inappropriate content, copyright, and online safety, in children?

Material and Methods

Design and Participants

The cohort of this cross-sectional study consisted of a total of 1800 students attending three different secondary schools in a city center in western Turkey during the spring semester of the 2023-2024 academic year. To enhance the heterogeneity of the sample and ensure the generalizability of the findings, schools from diverse socioeconomic backgrounds were purposively selected. The sample size was determined according

to a 5% margin of error and 95% confidence interval, and the probability of occurrence (p) was taken as 0.5 and the probability of non-occurrence (q) as 0.5 to ensure maximum variance. According to these parameters, it was determined that a sample of 317 students would be sufficient for the study. However, the final sample size was 420 secondary school students, which was done to ensure a more comprehensive representation. To ensure a diverse sample, a stratified random sampling method was employed for participant selection. This method aimed to ensure a balanced representation of demographic variables, such as school type and socioeconomic level. The age distribution of the selected students ranged between 10-14 years, and the gender distribution was balanced (52% girls, 48% boys). While the majority of the participants hailed from middle-income families, the study also included students from low and high-income groups. The inclusion criteria for students in the study were as follows: (1) Enrollment in a secondary school (2) Obtaining written parental consent for participation (3) Engaging in data collection sessions organized during the research process (4) Not being in a situation to affect the applicability of the study, such as a communication disorder or cognitive impairment. The students meeting the criteria completed the data collection tools applied within the scope of the study. The representativeness of the study population, both in terms of demographic characteristics and size, enhances the generalizability and validity of the results obtained.

Data Collection

Between January and April of 2024, the current study was carried out in three secondary schools located in a western Turkish city center. The consent form was given to the adolescents' parents in an envelope along with interviews explaining the study's purpose and scope after ethical approval and necessary permissions were obtained from the pertinent institutions. In this manner, the children were extended an invitation to participate. The data were collected using the Student Cyber Health Scale (SCHS) and the Child and Adolescent Psychological Resilience Scale (CAPRS). The data were collected by the researchers on the days and at the times specified by the students' course schedules.

Introductory Information Form

The form examines a range of characteristics on children, including age, gender, the device used to access the Internet, daily Internet usage time, the presence of an Internet connection at home, the purpose of connecting to the Internet, the practices employed to reduce Internet use, and the effect of Internet use on academic performance.

Child and Adolescent Psychological Resilience Scale (CAPRS)

CAPRS was utilized to assess psychological resilience in adolescents. The scale's original 28-item form was developed based on data collected from 11 countries and consists of three subscales (19). In the context of this study, the scale underwent adaptation. The scale was initially translated into Turkish by Arslan (2015) and subsequently translated back into English by two faculty members from the field of Educational Sciences. The final version of the scale was then determined by comparing the translations of a third faculty member, who possesses proficiency in both languages. Following the translation of the scale, the final version was administered to 422 high school students (mean age = 15.42 years, standard deviation [SD] = 1.48 years, 39.9% female, 48.7% male) aged between 12 and 18 years. The factor structure was examined by confirmatory factor analysis, which indicated that the three-factor structure of the scale produced good fit values. The range of standardized regression values was from 0.37 to 0.74, and the total internal consistency coefficient was 0.92. The range of item-total correlation values was from 0.43 to 0.65, and the internal consistency coefficients for the subscales ranged from 0.80 to 0.82. The analysis demonstrated that the scale is a valid and reliable measurement tool for assessing psychological resilience in adolescents (20).

Student Cyber Health Scale (SCHS)

A psychometric tool called SCHS was created to evaluate middle school students' levels of cyber health. The scale was created to evaluate middle school pupils' levels of cyber health. This scale, which is a four-point Likert-type and self-report-based measurement tool, was developed by Mıhçı and Kılıç Çakmak (21). SCHS was deemed to be a valid and reliable instrument comprising seven distinct scales and a total of 54 items. The scales are as follows: Internet addiction awareness, cyberbullying awareness, online courtesy awareness, online privacy awareness, inappropriate content awareness, copyright awareness, and online safety awareness. Participants who obtained a score of 22 or lower on

the Internet Addiction sub-dimension were classified as "Not Aware"; those who obtained a score between 22 and 33 were classified as "Moderately Aware"; and those who obtained a score of 33 or higher were classified as "Highly Aware". The Cyberbullying Scale, which is comprised of eight items, consists exclusively of positive statements. Participants who attained a score of 16 points or less on the Cyberbullying dimension were designated as "Not Aware"; those who scored between 16 and 24 points were classified as "Moderately Aware"; and those who scored 24 points or more were labeled as "Highly Aware". The Online Courtesy sub-dimension, which comprises eight items, is characterized by positive connotations. Participants who attained a score of 16 or less on the Online Civility sub-dimension were designated as "Not Aware"; those who scored between 16 and 24 were labeled as "Moderately Aware"; and those who scored 24 or more were categorized as "Highly Aware." The Online Privacy sub-dimension consists of 4 items, all of which have a positive meaning. Participants who obtained a score of 8 or less on the Online Privacy sub-dimension were classified as "Not Aware"; those who obtained a score between 8 and 12 were classified as "Moderately Aware"; and those who obtained a score of 12 or higher were classified as "Highly Aware". The Inappropriate Online Content sub-dimension consists of seven items, all of which have positive meanings. Participants who obtained a score of 14 points or less on the Online Inappropriate Content sub-dimension were designated as "No Awareness"; those obtaining between 14 and 21 points were classified as "Moderately Aware"; and those attaining 21 points or more were labeled as "Highly Aware". The Copyright sub-dimension, which comprises six items, also manifests positive connotations. Participants who obtained a score of 10 points or less on the Copyright sub-dimension were designated as "Not Aware"; those who attained scores between 10 and 15 points were classified as "Moderately Aware"; and those who achieved scores of 15 points or higher were labeled as "Highly Aware". The Online Safety Scale is comprised of 11 items, with items 3, 5, 6, 8, 9, and 10 exhibiting reversed meanings. These items are scored by reversing them. Consequently, students who attained a score of 22 points or less on the Online Safety dimension were categorized as "Not Aware"; those who scored between 22 and 33 points were designated as "Moderately Aware"; and students who achieved a score of 33 points or more were labeled as "Highly Aware". The Cronbach Alpha coefficients for each scale are reported to be as follows: 0.82, 0.81, 0.61, 0.60, 0.72, 0.75, and 0.81, respectively. As the scale scores increase, awareness also increases (21). In this study, the Cronbach alpha coefficients were determined to be 0.87, 0.87, 0.74, 0.74, 0.72, 0.72, 0.78, 0.79, and 0.84, respectively.

Statistical Analysis

The analysis of the data was conducted using the Statistical Package for the Social Sciences (SPSS) version 22 in a computerized environment. Descriptive statistics were presented, including the mean, standard deviation, median, minimum, maximum, and percentage values. To assess the normality of the data, the Kolmogorov-Smirnov test was applied. In cases where the data conformed to a normal distribution, pairwise comparisons were performed using a Student's t-test. The Pearson correlation test was utilized to explore the relationships between continuous variables, such as scale scores. Additionally, simple regression analysis was employed to investigate the relationship between psychological resilience and cyber health. A significance threshold of $p < 0.05$ was established as acceptable.

Ethics

The study was carried out in compliance with the ethical guidelines established by the XXX University Social and Human Sciences Ethics Committee (Protocol No. 2024-SBB-0001, Date: 01/02/2024). Authorization for the research was obtained from the Provincial Directorate of National Education. The authors were approached through email to seek permission for the utilization of the scales used in the research. The participating families have thoroughly explained the purpose and method of the research, that participation was voluntary, and that participation or non-participation would not have any negative consequences. The families were informed about how the confidentiality of the data to be collected during the research would be protected and would only be used for scientific purposes. The families were informed that participation in the study was completely voluntary and were given time to address any questions or concerns they might have had. Both written and verbal consent were obtained, with a standard consent form being utilized for the written component. This form explicitly delineated the specifics of the research and the participants' rights. Participants and their families were reminded that they had the right to terminate their participation at any time.

Results

The mean age of the children was 13.76±4.20 years (range 8-12 years), and 51.4% were female. A total of 87.1% of the students accessed the Internet via their mobile phones, with an average daily usage time of 2.75±2.16 hours. Eighty percent of the students had access to the Internet at home. The primary objective of accessing the Internet was to obtain information, as reported by 25.7% of respondents. Twenty-five percent of the students engaged in activities with their families to reduce their Internet usage, while 48.6 percent believed that the Internet had a beneficial impact on their academic performance (Table 1).

Table 1. Characteristics of children (n=420)

	n	%
Age	**Mean±SD=**13.76±4.20	**Range=**8-12
Gender		
Girl	216	51.4
Male	204	48.6
Device accessing the Internet		
Telephone	366	87.1
Computer	45	10.7
Television	9	2.1
Daily Internet usage time (hours)	**Mean±SD=**2.75±2.16	**Range=**1-12
Presence of Internet connection at home		
Yes	336	80.0
No	84	20.0
Purposes for connecting to the Internet		
Obtaining information	108	25.7
Playing games	93	22.1
Social media	90	21.4
Watching educational videos	57	13.6
Wasting time aimlessly	72	17.1
The most common practices to reduce or cut Internet use		
Spending time with family	105	25.0
Studying	96	22.9
Talking to my friends	72	17.1
Reading a book	63	15.0
All of them	51	12.1
Eating food	33	7.9
Impact of Internet use on lessons		
Positive	204	48.6
No impact	147	35.0
Negative	69	16.4

SD: Standard deviation

The mean score on CAPRS was found to be significantly correlated with SCHS sub-dimensions of Internet addiction awareness (r=0.385, p<0.001), online courtesy awareness (r=0.414, p<0.001), online privacy awareness (r=0.384, p<0.001), online safety awareness (r=0.493), cyberbullying awareness (r=0.534, p<0.001), and online inappropriate content awareness (r=0.450, p<0.001) (Table 2).

The results of the regression analysis indicated that, except for the Internet addiction and copyright models, all models were statistically significant ($p < 0.05$) when the corresponding F-value significance level was examined. An examination of the beta coefficient value, t-value, and significance level of the independent variable reveals that the psychological resilience score has a statistically significant effect on cyberbullying (t=6.856, p<0.001), online courtesy (t=4.871, p<0.001), online privacy (t=4.540, p<0.001), online inappropriate content (t=5.378, p<0.001), and online safety (t=5.283, p<0.001) scores (Table 3).

The present study sought to investigate the relationship between psychological resilience and children's cyber health awareness levels. Specifically, a one-unit increase in the psychological resilience score was associated with a 0.534-unit increase in the cyberbullying awareness score (Table 3). This finding suggests that individuals with high resilience possess the capacity to more effectively recognize online bullying incidents and cope with such situations. This finding lends further support to the notion that an individual's capacity to resist bullying is directly related to their emotional resilience. An increase of 0.414 units in online kindness awareness suggests that children with high resilience are more inclined to demonstrate positive and constructive communication in online environments (Table 3). The increase of 0.386 units in online privacy awareness demonstrates a correlation between resilience level and individuals' awareness of protecting their digital identities (Table 3). This suggests that enhancing individuals' psychological resilience can equip them with better tools to navigate and withstand the potential risks they may encounter in online spaces. The findings further indicate that individuals with higher resilience demonstrate a greater propensity to adhere to online ethical and safety standards, as evidenced by the increases in awareness of inappropriate content sharing (0.450 units) and online safety awareness (0.443 units) (Table 3). These findings underscore the critical role of psychological resilience in effectively managing online risks and cultivating safe digital habits.

Discussion

The objective of this study was to determine whether psychological resilience serves as a significant predictor

Table 2. The relationship between children's mean scores on the sub-dimensions of the Student Cyber Health Scale and the total scores of the Child and Adolescent Resilience Scale (n=420)

Scales	Mean±SD1	1	2	3	4	5	6	7	8
SCH- Internet addiction awareness (1)	25.12±6.03	1							
SCH- Cyberbullying awareness (2)	25.25±4.42	0.004	1						
SCH- Awareness of online courtesy (3)	23.20±3.51	0.082	0.558*	1					
SCH-Online privacy awareness (4)	12.04±2.11	0.015	0.508*	0.511*	1				
SCH- Awareness of inappropriate content online (5)	21.28±3.76	0.054	0.486*	0.349*	0.512*	1			
SCH-Copyright awareness (6)	14.59±2.96	0.056	0.547*	0.505*	0.430*	0.622*	1		
SCHS-Online safety awareness (7)	26.16±4.40	0.374*	0.300*	0.445*	0.420*	0.372*	0.402*	1	
CYPR (8)	38.10±6.35	0.385*	0.534*	0.414*	0.386*	0.450*	0.443*	0.493*	1

SCHS: Student Cyber Health Scale, CYPR: Child and Youth Psychological Resilience Scale, SD: Standard deviation

*p<0.001

Table 3. Regression analysis results for the level of psychological resilience predicting cyber health (n=420)

Model	Variable	B	SE	β	t	p	Model analysis
Internet addiction awareness	**Consent**	27.197	3.368		8.075	<0.001	R=0.060 R^2=0.005 F=0.424 p=0.516
	Psychological resilience	0.057	0.087	0.060	0.651	0.516	
Cyberbullying awareness	**Consent**	10.959	2.112		5.188	<0.001	R=0.534 R^2=0.279 F=47.007 p<0.001
	Psychological resilience	0.374	0.055	0.534	6.856	<0.001	
Online politeness awareness	**Consent**	14.448	1.816		7.956	<0.001	R=0.414 R^2=0.164 F=23.723 p<0.001
	Psychological resilience	0.229	0.047	0.414	4.871	<0.001	
Online privacy awareness	**Consent**	7.128	1.092		6.529	<0.001	R=0.386 R^2=0.141 F=20.608 p<0.001
	Psychological resilience	0.128	0.028	0.386	4.540	<0.001	
Awareness of inappropriate content online	**Consent**	11.318	1.884		6.006	<0.001	R=0.450 R^2=0.195 F=28.924 p<0.001
	Psychological resilience	0.261	0.049	0.450	5.378	<0.001	
Copyright Awareness	**Consent**	21.506	2.505		8.584	<0.000	R=0.178 R^2=0.022 F=3.439 p=0.066
	Psychological resilience	0.121	0.065	0.178	1.855	0.066	
Online safety awareness	**Consent**	6.886	1.478		4.660	<0.001	R=0.443 R^2=0.190 F=27.911 p<0.001
	Psychological resilience	0.203	0.038	0.443	5.283	<0.001	

of cyber health, which encompasses various aspects such as awareness of Internet and gaming addiction, cyberbullying, online kindness, privacy issues, inappropriate content, copyright concerns, and the safety of children in online environments. The findings indicated that fostering positive behaviors related to cyber health correlates with an enhancement in psychological resilience. This correlation was evidenced by a reduction in the recognition of cyberbullying incidents, an increase in acts of online kindness, an expansion of privacy measures, a decline in the dissemination of inappropriate content, and an improvement in online safety protocols. Within the realm of cyber health, psychological resilience is posited as a robust predictor and a protective factor (22). SCHC is utilized as a tool for assessing awareness in specific domains pertinent to cyber health (21). As psychological resilience increases, it can be inferred that awareness of positive behaviors linked to cyber health also improves or develops (22). For example, it can be proposed that children with elevated levels of psychological resilience demonstrate a heightened awareness of cyberbullying, which may serve as a protective mechanism against the associated risks (4).

The research demonstrated a notable positive relationship between children's psychological resilience and their understanding of cyberbullying. Additionally, psychological resilience emerged as a crucial predictor of awareness regarding cyberbullying.

In a similar vein, Kabadayı and Sarı(22) examined the influence of psychological resilience on children's experiences with cyberbullying and victimization. Their results corroborate our findings, indicating that psychological resilience is negatively and significantly associated with both cyberbullying and victimization, and it can serve as a significant predictor of cyberbullying. Thus, psychological resilience may act as a strong protective factor against the impacts of cyberbullying (23).

A salient finding of this study is that enhancing psychological resilience among adolescents is associated with an increased awareness of cyberbullying. This finding suggests that individuals with high psychological resilience possess the capacity to more effectively recognize online bullying incidents and develop effective coping strategies. Psychological resilience is defined as an individual's capacity to maintain emotional balance and cope with adversity in stressful situations. The present study's findings are consistent with those of previous research in this field. A study by Güçlü and Çam (24) demonstrated that psychological resilience is associated with a reduced likelihood of individuals becoming victims of cyberbullying, suggesting that those with high resilience are less susceptible to online threats. Likewise, Yiğit and Seferoğlu's (25) study underscored the significance of strategies aimed at enhancing cyberbullying awareness, demonstrating that these strategies facilitate heightened awareness of online bullying incidents among individuals. These studies underscore the protective role that educational programs and interventions aimed at enhancing psychological resilience can play at both the individual and societal levels.

The research revealed a significant positive relationship between children's psychological resilience and their awareness of online privacy. Psychological resilience was identified as a crucial predictor of online privacy awareness. Online privacy refers to an individual's ability to control the degree to which others can access personal information that has been shared online (26). In today's digital landscape, the importance of privacy is increasingly pronounced, as potential violations of online privacy can significantly impact individual behavior (27). Consequently, it is essential to enhance our understanding of individuals' psychological resilience concerning online privacy breaches (28). Psychological resilience may serve as a valuable tool for fostering the ability to manage the sharing of personal information (23).

The research indicated a positive relationship between children's recognition of inappropriate online content and their psychological resilience levels. Psychological resilience was identified as a crucial predictor of awareness regarding online inappropriate content. This term refers to any material that negatively affects a child's development, such as offensive language, pornographic images, and videos (29). Exposure to such content can lead to harmful effects (27). For instance, many adolescents who encounter sexual imagery online do not report feeling distressed as a result (30). Psychological resilience serves as an essential protective mechanism, reducing the probability of negative emotional responses that may arise from unfavorable online encounters (4). Furthermore, children and adolescents who demonstrate elevated levels of psychological resilience are likely to be less prone to participating in behaviors linked to inappropriate online material, as they possess the capacity to effectively navigate and cope with the challenging situations they encounter (31,32).

The research revealed a notable positive relationship between children's psychological resilience and their awareness of online safety. As the levels of psychological resilience in children increased, so too did their awareness regarding online safety issues. Given that children and adolescents have expanded opportunities to interact with the digital landscape, they are concurrently more susceptible to encountering potentially harmful content (33). Psychological resilience, which is characterized by the ability to effectively navigate online risks and manage the negative repercussions associated with online safety challenges, can act as a protective mechanism against the detrimental emotional effects that may follow an encounter with online risks (34). Children and adolescents exhibiting higher levels of psychological resilience are less prone to experiencing negative outcomes after facing online risks compared to their peers with lower resilience levels (35). This phenomenon can be attributed to their ability to undertake more intentional measures to ensure their safety (4).

In recent years, the relationship between cyber health and psychological resilience has been the subject of increased investigation in Turkey. According to the studies conducted on this subject, individuals with high levels of psychological resilience exhibit greater resistance to online threats and possess a stronger capacity to cope with negative online situations,

such as cyberbullying. Güçlü (36) underscored the correlation between exposure to cyberbullying in adolescents and psychological resilience, asserting that adolescents with high resilience demonstrate superior coping mechanisms in the face of such bullying. Sabancı's (37) examination of adolescents' coping strategies with cyberbullying and their psychological resilience levels further corroborates this finding, asserting that psychological resilience serves as a mitigating factor in the effects of online victimization. The findings of these studies are consistent with the results of the present study.

It has been demonstrated that deliberate actions and coping mechanisms in the digital domain are efficacious in fortifying the association between cyber health and psychological resilience. Çelik and Yılmaz's (38) study, which examined the mediating role of psychological resilience in the relationship between social media addiction and emotional eating, asserted that the level of resilience is a crucial factor in coping with online addiction and emotional difficulties. Moreover, Çekirdekçi and Yılmaz (39) investigated the function of psychological resilience as a protective factor in coping with negative emotional states, such as depression and anxiety. Their findings revealed that the level of resilience also provides significant protection against online safety risks. These findings underscore the necessity of integrating cyber health and psychological resilience training into the education system in Turkey. The integration of strategies aimed at enhancing psychological resilience within the framework of cyber health education programs is poised to empower young individuals, enabling them to navigate the digital landscape with greater safety and well-being (40).

Limitations

The notion of cyber health has emerged as a pertinent topic in Turkey, and the robustness of this research enhances the current body of literature on the subject. Additionally, the application of predictive factors and regression analyses serves as a notable methodological advantage. However, despite these strengths, the study does have its limitations. The sample was limited to three secondary schools within a single urban area, which may restrict the generalizability of the findings to a wider population. Moreover, the dependence on self-reported data constitutes a considerable limitation of the research.

Conclusion

This study demonstrates that children's psychological resilience is a critical factor in safeguarding their cyber health. It plays a protective role in various domains, including online safety, privacy, and coping with cyberbullying. Observations have revealed that children who possess high psychological resilience demonstrate a greater capacity to withstand online risks and can mitigate these risks by engaging in conscious behaviors. This underscores the significance of imparting media literacy and online safety education from an early age, a strategy that has been demonstrated to foster children's cyber health.

The findings of this study provide concrete recommendations for educators, parents, and policymakers. Educators are encouraged to incorporate media literacy and ethical Internet use into their curricula, while also providing guidance and counseling to support the development of psychological resilience in children. Parents, too, should receive training to raise awareness and model appropriate behavior, thereby facilitating the safe management of their children's online activities. Additionally, the development and implementation of national cyber health policies can contribute to enhancing online safety within educational institutions and throughout society.

Finally, the implementation of psychoeducational programs designed to enhance children's psychological resilience is strongly advocated. These programs can be implemented through school-based activities and gamified content on digital platforms. The development of projects in collaboration with local governments and communities has the potential to empower children and families to navigate the online landscape with greater awareness and safety. These recommendations offer a framework for mitigating online risks and empowering children to securely reap the benefits of the digital world.

Declaration of conflicting interests

The author declared the following potential conflicts of interest concerning the research, authorship, and/or publication of this article: The author is currently in the process of setting up a social enterprise aiming to provide digital solutions for managing outbreaks of communicable diseases.

Funding

None

References

1.Panjeti-Madan VN, Ranganathan P. Impact of screen time on children's development: cognitive, language, physical, and social and emotional domains. Multimodal Technol Interact. 2023;7:52.

2.Johnston K. Engagement and immersion in digital play: Supporting young children's digital wellbeing. Int J Environ Res Public Health. 2021;18(19):10179.

3.Las-Hayas C, Mateo-Abad M, Vergara I, Izco-Basurko I, González-Pinto A, Gabrielli S, et al. Relevance of well-being, resilience, and health-related quality of life to mental health profiles of European adolescents: results from a cross-sectional analysis of the school-based multinational UPRIGHT project. Soc Psychiatry Psychiatr Epidemiol. 2022;57(2):279–91.

4.Pan Q, Lan M, Tan CY, Tao S, Liang Q, Law N. Protective factors contributing to adolescents' multifaceted digital resilience for their wellbeing: A socio-ecological perspective. Comput Human Behav [Internet]. 2024;155:108164. Available from: https://doi.org/10.1016/j.chb.2024.108164

5.Al-Turif GAR, Al-Sanad HAR. The repercussions of digital bullying on social media users. Front Psychol. 2023;14:1–12.

6.Blanchard L, Conway-Moore K, Aguiar A, Önal F, Rutter H, Helleve A, et al. Associations between social media, adolescent mental health, and diet: A systematic review. Obes Rev. 2023;24(S2):1–15.

7.Castaño-Pulgarín SA, Suárez-Betancur N, Vega LMT, López HMH. Internet, social media, and online hate speech. Systematic review. Aggress Violent Behav. 2021;58:101608.

8.Pardhan S, Parkin J, Trott M, Driscoll R. Risks of digital screen time and recommendations for mitigating adverse outcomes in children and adolescents. J Sch Health. 2022;92(8):765–73.

9.Anjum R, Nodi NH, Das PR, Roknuzzaman ASM, Sarker R, Islam MR. Exploring the association between online gaming addiction and academic performance among school-going adolescents in Bangladesh: A cross-sectional study. Heal Sci Reports. 2024;7(9):e70043.

10.Merino M, Tornero-Aguilera JF, Rubio-Zarapuz A, Villanueva-Tobaldo CV, Martín-Rodríguez A, Clemente-Suárez VJ. Body perceptions and psychological well-being: a review of the impact of social media and physical measurements on self-esteem and mental health with a focus on body image satisfaction and its Relationship with Cultural and Gender Factors. Healthc. 2024;12(14):1396.

11.Baker FRL, Baker KL, Burrell J. Introducing the skills-based model of personal resilience: Drawing on content and process factors to build resilience in the workplace. J Occup Organ Psychol. 2021;94(2):458–81.

12.Gao AZ, Chen WC. The association between Internet use and cognitive ability among rural left-behind children in China. Front Public Heal. 2023;11:1–10.

13.Meng Q, Yan Z, Abbas J, Shankar A, Subramanian M. Human-computer interaction and digital literacy promote educational learning in pre-school children: the mediating role of psychological resilience for kids' mental well-being and school readiness. Int J Hum Comput Interact [Internet]. 2023; Article in. Available from: https://doi.org/10.1080/10447318.2023.2248432

14.Üzar-Özçetin YS, Çelik S, Özenç-Ira G. The relationships among psychological resilience, intercultural sensitivity and empathetic tendency among teachers of Syrian refugee children in Turkey. Heal Soc Care Community. 2022;30(2):e410–9.

15.Erbiçer ES, Ceylan V, Yalçın MH, Erbiçer S, Akın E, Koçtürk N, et al. Cyberbullying among children and youth in Türkiye: A systematic review and meta-analysis. J Pediatr Nurs. 2023;73:184–95.

16.Hinduja S, Patchin JW. Bullying, cyberbullying, and suicide. Arch Suicide Res. 2010;14(3):206–21.

17.Aslan O, Topuz İ, Eldeleklioğlu J. Investigating the mediating role of digital game addiction in the relationship between adolescents' school belonging and resilience. Educ Dev Psychol. 2024;42(1):37–49.

18.Yıldırım M, Çiçek İ. Fear of COVID-19 and smartphone addiction among Turkish adolescents: mitigating role of resilience. Fam J. 2022; Article in.

19.Liebenberg L, Ungar M, Leblanc JC. The CYRM-12: A Brief Measure of Resilience. Can J Public Heal. 2013;104(2):e131–5.

20.Arslan G. Psychometric Properties of Child and Youth Resilience Measure (CYRM-12): The study of reliability and validity. Ege Eğitim Derg 2015. 2015;2015(16):1–12.

21.Mıhçı P, Kılıç Çakmak E. A Study on Student Cyberwellness Scales Development. GEFAD / GUJGEF. 2017;37(2):457–91.

22.Kabadayi F, Sari S V. What is the role of resilience

in predicting cyberbullying perpetrators and their victims? J Psychol Couns Sch. 2018;28(1):102–17.

23.Bui MV, McInnes E, Ennis G, Foster K. Resilience and mental health nursing: An integrative review of updated evidence. Int J Ment Health Nurs. 2023;32(4):1055–71.

24.Güçlü G, Çam S. Investigation of resilience in according exposure to cyberbullying in adolescents. Cukurova Univ Fac Educ J. 2022;51(3):1584–609.

25.Yiğit MF, Seferoğlu SS. A review of cyberbullying-related factors and possible solutions was suggested. Online J Technol Addict Cyberbullying [Internet]. 2017;4(2):13–49. Available from: https://dergipark.org.tr/tr/pub/ojtac/issue/33736/350465

26.Finkelhor D, Jones L, Mitchell K. Teaching privacy: A flawed strategy for children's online safety. Child Abus Negl. 2021;117:105064.

27.Matz SC, Appel RE, Kosinski M. Privacy in the age of psychological targeting. Curr Opin Psychol [Internet]. 2020;31(2):116–21. Available from: https://doi.org/10.1016/j.copsyc.2019.08.010

28.Park J, Akter M, Ali NS, Agha Z, Alsoubai A, Wisniewski P. Towards resilience and autonomy-based approaches for adolescents online safety. SSRN Electron J. 2023;

29.Jevremovic A, Veinovic M, Cabarkapa M, Krstic M, Chorbev I, Dimitrovski I, et al. Keeping children safe online with limited resources: analyzing what is seen and heard. IEEE Access. 2021;9:132723–32.

30.Smahel D, Machackova H, Mascheroni G, Dedkova L, Staksrud E, Ólafsson K, et al. EU Kids Online 2020: Survey results from 19 countries. EU Kids Online. 2015;

31.Martzoukou K. "Maddie is online": an educational video cartoon series on digital literacy and resilience for children. J Res Innov Teach Learn. 2022;15(1):64–82.

32.Tang ACY, Lee RLT. Effects of a group mindfulness-based cognitive program on smartphone addictive symptoms and resilience among adolescents: study protocol of a cluster-randomized controlled trial. BMC Nurs. 2021;20(1):1–13.

33.Zhu C, Huang S, Evans R, Zhang W. Cyberbullying among adolescents and children: a comprehensive review of the global situation, risk factors, and preventive measures. Front Public Heal. 2021;9:634909.

34.Vissenberg J, D'haenens L. Protecting youths' wellbeing online: Studying the associations between opportunities, risks, and resilience. Media Commun. 2020;8(2):175–84.

35.El-Asam A, Lane R, Katz A. Psychological distress and its mediating effect on experiences of online risk: the case for vulnerable young people. Front Educ. 2022;7(August):772051.

36.Güçlü G. Investigation of resilience in adolescents by exposure. Çukurova University; 2019.

37.Taştekin E, Bayhan P. Examination of cyberbullying and victimization among adolescents. Online J Technol Addict Cyberbullying [Internet]. 2018;5(2):21–45. Available from: https://dergipark.org.tr/tr/pub/ojtac/issue/41898/392522

38.Çelik M, Yılmaz M. The mediating role of psychological resilience in the relationship between social media addiction and emotional eating. J Dicle Univ Ziya Gökalp Fac Educ. 2021;37:1–15.

39.Çekirdekçi A, Yılmaz M. The relationship between depression, panic disorder generalized anxiety disorder, and psychological resilience. J Posit Psychol Wellbeing. 2020;4(2):1–12.

40.İnayet A. Ethical issues in educational technology. Kastamonu Educ J. 2024;32(1):861–81.

Received: 04 Feb 2025 | **Accepted:** 24 Mar 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 362-368
DOI: 10.54005/geneltip.1632967

ORIGINAL ARTICLE

Determining the Psychological Resilience and Secondary Trauma Stress Levels of Surgical Nurses Caring for Earthquake Victims

Deprem Mağdurlarına Bakım Veren Cerrahi Hemşirelerinin Psikolojik Dayanıklılık ve İkincil Travma Stres Düzeylerinin Belirlenmesi

[1]Hamide Şişman, [2]Şeyma Yurtseven, [3]Dudu Alptekin

[1]Selcuk University Aksehir Kadir Yallagöz Health College, Aksehir, Türkiye
[2]Cukurova University Faculty of Medicine Balcalı Hospital, Adana, Türkiye
[3]Cukurova University Abdi Sütcü Health Services Vocational School, Adana, Türkiye

Correspondence

Hamide ŞİŞMAN
Selçuk University Akşehir Kadir Yallagöz Health College, Akşehir, Konya, Türkiye

E-Mail: busrasolmaz0038@gmail.com

How to cite ?

Solmaz B, Özaydın T. The Comparison of Body Mass Indexes, Dietary Habits, and Physical Activity Attitudes of Refugee and Turkish Adolescents. Genel Tıp Derg. 2025;35 (2): 362-368

ABSTRACT

Aim: This study aimed to determine the psychological resilience and secondary traumatic stress levels of surgical nurses experiencing an earthquake and providing care to earthquake victims and to draw attention to this issue.
Materials and Methods: The study with a descriptiveand cross-sectional design was conducted with 370 surgical nurses from a university hospital experiencing the earthquake and providing care to victims between May and July 2023. Data were collected by the researcher through face-to-face interviews using the Personal Information Form, the Psychological Resilience Scale(PRS), and the Secondary Traumatic Stress Scale Turkish Form (STSS).
Results: The nurses scored 55.1±9.9 (min: 9, max: 83) on PRS, with sub-dimension scores of 17.8±3.9 (min: 2, max: 28) for commitment, 17.4±3.4 (min: 5, max: 27) for control, and 20.4±4.5 (min: 1, max: 29) for challenge. The STSS score was 54±12.3 (min: 17, max: 85). A weak, negative, and significant correlation was found between STSS levels (54±12.3) and PRS levels (r=-0.131, p<0.05).
Conclusions: The study found high levels of secondary traumatic stress in surgical nurses who were earthquake victims and provided care to other earthquake victims. Higher stress levels were associated with lower levels of psychological resilience.

Keywords: Earthquake, earthquake victims, resilience level, secondary traumatic stress, surgical nurses

ÖZ

Amaç: Bu araştırma, depremi yaşayan ve depremzedelere bakım veren cerrahi hemşirelerin psikolojik dayanıklılık ve ikincil travma stres seviyelerini belirlemek ve bu konuya dikkat çekmek amacıyla yapılmıştır.
Gereç ve Yöntemler: Tanımlayıcı ve kesitsel olarak planlanan çalışma, Mayıs-Temmuz 2023 tarihleri arasında bir üniversite hastanesinde çalışan, depremi deneyimleyen ve depremzedelere bakım veren 370 cerrahi hemşiresi ile yürütülmüştür. Veriler araştırmacı tarafından literatür veri tabanında bulunan "Kişisel Bilgi Formu", "Psikolojik Dayanıklılık Ölçeği" ve "İkincil Travma Stres Ölçeği Türkçe Formu" kullanılarak yüz yüze görüşme yoluyla toplanmıştır.
Bulgular: Hemşirelerin dayanıklılık toplam puan ortalaması 55.1±9.9 (min: 9, maks: 83), bağlılık alt boyut puan ortalaması 17.8±3.9 (min: 2, maks: 28), kontrol alt boyut puan ortalaması 17.4±3.4 (min:5, maks:27), zorluk alt boyut puan ortalaması 20.4±4.5 (min:1, maks:29) ve ikincil travmatik stres toplam puan ortalaması 54±12.3 (min:17, maks:85) olarak bulunmuştur. İkincil travmatik stres düzeyleri (54±12.3) ile psikolojik dayanıklılık düzeyleri arasında zayıf düzeyde negatif yönde anlamlı bir ilişki bulunmuştur (r=-131, p<0.05).
Sonuçlar: Deprem mağduru olan ve depremzede hastalara bakım veren cerrahi hemşirelerinde sekonder travmatik stres düzeylerinin yüksek olduğu, stres düzeyleri arttıkça psikolojik dayanıklılık düzeylerinin azaldığı bulunmuştur.

Anahtar Kelimeler: Deprem, deprem mağduru, hemşire, dayanıklılık düzeyi, ikincil travmatik stres

Introduction

Earthquakes represent frequent natural disasters in our country, causing significant losses and presenting multidimensional psychological, social, and economic challenges. These events lead to various forms of devastation, including mortality, bereavement, physical injuries, property destruction, and compromised sense of security (1). While residents of earthquake zones and direct survivors experience the most profound emotional impact, relief workers, volunteers, and support personnel operating in affected regions are similarly vulnerable to psychological consequences (2). Existing research suggests that healthcare workers with prior trauma exposure may experience exacerbated psychological symptoms and elevated STSS levels (3).

The role of healthcare professionals becomes particularly critical during disasters (4). Many face personal losses while simultaneously confronting the trauma of treating victims, witnessing catastrophic events, and absorbing patients' distressing narratives (5). Numerous studies document that professionals providing comprehensive support to disaster victims frequently develop symptoms including anhedonia, dysphoria, depressive states, existential distress, and secondary traumatic stress (6,7). The earthquakesof Kahramanmaraş on 6th February 2023 (magnitudes

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

7.7 and 7.6) exemplify this phenomenon, affecting 11 provinces and resulting in thousands of casualties (8). The mass casualty event created extraordinary demands on healthcare systems, exposing workers to extreme operational conditions (9). Healthcare professionals face compounded risks from excessive workloads, sleep deprivation, exhaustion, and chronic stress, all contributing to mental and physical health deterioration (10). Among these occupational hazards, secondary traumatic stress emerges as a particularly concerning psychological outcome (11).

This condition develops through intense empathic engagement with victims' trauma narratives and the psychological burden of reconciling these experiences with reality (12). Trauma-exposed professionals remain especially vulnerable (13), with certain personality traits (e.g., perfectionism, pessimism, excessive need for control) potentially exacerbating susceptibility (14). For nurses, secondary traumatic stress carries significant professional and personal consequences, including diminished work motivation, career changes, and overall health decline (15). While debate continues regarding optimal timing for post-disaster psychosocial interventions, consensus emphasizes the importance of pre-disaster mental health preparedness. This study consequently examines psychological resilience and secondary traumatic stress levels among surgical nurses providing earthquake victim care, aiming to illuminate this critical occupational health issue.

Materials and Methods

This descriptive, cross-sectional study was conducted from May to July 2023 with nurses in the surgical departments of a university hospital. Of the 432 nurses employed in the hospital's surgical clinics, 370 met the inclusion criteria: earthquake exposure, continued employment, provision of care to earthquake victims, and willingness to participate. All nurses received comprehensive information about the study, and written informed consent was obtained before data collection. The researcher collected the data following approval from the Ethics Committee (Decision No: 07/04/2023/64). The study adhered to the principles outlined in the Declaration of Helsinki.

Personal Information Form

The researcher-developed Personal Information Form, informed by a literature review, included 14 questions designed to collect the following information from the nurses: gender, education level, marital status, age, number of children, years of professional experience, work unit, history of earthquake exposure, location at the time of the earthquake, extent of housing damage, experience of losing relatives, accommodation after the earthquake, level of separation anxiety from family/children during work hours, and degree of fear regarding earthquake recurrence (16, 17).

Psychological Resilience Scale(PRS)

PRS" was used to assess nurses' resilience. Developed bylsık in 2016, the scale demonstrated adequate validity and reliability for measuring psychological resilience. This 21-item scale comprises three sub-dimensions: dedication (7 items), control (7 items), and challenge (7 items), with items rated on a 5-point Likert scale. Items are scored from 0 (lowest) to 4 (highest), yielding a total score range of 0 to 84. Response options include: (0) Strongly Disagree, (1) Disagree, (2) Neither Agree nor Disagree, (3) Agree, and (4) Strongly Agree. Items 2 and 15 are reverse-scored (4-3-2-1-0). Higher scores indicate greater resilience (18).

Secondary Traumatic Stress Scale Turkish Form(STSS)

The Turkish version of STSS was used to measure the nurses' traumatic stress.STSS was developed by Bride et al. in 2004, and the Turkish version of STSS was performed by Kahil,anexpert psychologist and psychological counselor,in 2016. The scale consists of 17 items, and the questions are in a 5-point Likert-type format.The scale consists of 17 items, and the questions are in a 5-point Likert type. The scale assesses symptoms experienced in the past 7 days, with items rated as: (1) Never, (2) Rarely, (3) Sometimes, (4) Often, and (5) Very Often.The scale has a possible score range of 17 to 85, where higher scores indicate higher stress levels.

Statistical analysis

SPSS version 22.0 software (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. Categorical variables are summarized using frequency and percentage distributions, and continuous variables are described using means and standard deviations. Group mean comparisons were performed using independent samples t-tests (for two groups) and ANOVA (for three or more groups). When ANOVA results were significant, Bonferroni corrections were used for posthoc comparisons. Pearson correlation analysis was conducted to determine the correlations between scale scores. Statistical significance was set at a p-value of <0.05.

Results

Table 1 presents the participants' demographic

characteristics and average scale scores. Among the participants, 73.2% were women, 50.8% had undergraduate degrees, and 66.5% were married. The mean age was 34±7.8 years (range: 20 to 64), and the mean working time was 12.4±10 years (range: 1 to 45). Before the study, 61.6% of the participants had experienced an earthquake, 81.4% were at home during the earthquake, 68.9% reported no damage to their homes, and 35.4% had lost relatives. The mean total score of PRS was 55.1±9.9 (min: 9, max: 83), with sub-dimension scores of 17.8±3.9 (min: 2, max: 28) for dedication, 17.4±3.4 (min: 5, max: 27) for control, and 20.4±4.5 (min: 1, max: 29) for challenge. The mean STSS score was 54±12.3 (min: 17, max: 85) (Table 1).

Table 1. Demographics of subjects (n=370)

Variables	n	%
Gender		
Female	271	73.2
Male	99	26.8
Education		
High School	113	30.5
AssociateDegree	45	12.2
License	188	50.8
Graduate	24	6.5
Maritalstatus		
Single	124	33.5
Married	246	66.5
Have you experienced an earthquake before?		
Yes	228	61.6
No	142	38.4
Where were you caught in the earthquake?		
House	301	81.4
Hospital	69	18.6
Damage status of your house		
Undamaged	255	68.9
LessDamaged	99	26.8
HeavilyDamaged	14	3.8
Demolished	2	0.5
Did you lose your relative in the earthquake?		
Yes	131	35.4
No	239	64.5
Do you have a hospital disaster plan?		
Yes	210	56.8
No	54	14.6
I don't know	106	28.6
Have you received disaster training?		
Yes	290	78.4
No	80	21.6
	mean±SD	**Min-Max**
Age(years)	34±7.8	20-64
Operation time	12.4±10	1-45
Resilience Scale Sub-Dimensions (PRS)		
Dedication	17.8±3.9	2-28
Control Size	17.4±3.4	5-27
Challenge	20.4±4.5	1-29
Total ScaleScore	55.1±9.9	9-83
Secondary Traumatic Stress Scale Score (ITSS)	54±12.3	17-85

*Data are expressed as numbers (n), frequency (%), mean±SD, and min-max.PRS: Psychological Resilience Scale, SD: Standard deviation,

Table 2 presents findings related to the post-earthquake period. 40.8% of the participants stayed in their own homes, while 33.5% stayed with relatives.While 65.1% of participants reported significant anxiety about leaving their families at home to work, 46% reported occasional earthquake anxiety, and 23% reported constant earthquake anxiety.Furthermore, 83% of the participants felt that their workplace hospital was unsafe (Table 2).

Table 2. Variables Related to the Post-Earthquake Process

Variables	n	%
Where Did You Stay After the Earthquake?		
House	151	40.8
Tent	30	8.1
Dormitory/Guesthouse	26	7
In a Relative's house	124	33.5
Car	39	10.5
Does leaving your family at home while coming to work cause you to feel anxious?		
No	19	5.1
Lowlevel	28	7.6
Medium-level	82	22.2
Toomuch	241	65.1
Do you have anxietyabout an earthquake?		
No	42	11.4
Sometimes	171	46.2
Often	72	19.5
Continually	85	23
Do you think the hospital you work in is safe?		
Yes	63	17
No	307	83

*Data are expressed as numbers (n) and frequency (%)

Table 3 compares participants' characteristics with mean STSS and PRS scores. Educational level was significantly correlated with mean STSSs (F=3.35, p=0.01). Bonferroni posthoc analysis indicated that high school graduates exhibited the highest mean STSS score (53.8±12.7), while postgraduate students exhibited the lowest (46.6±8.8). Previous earthquake experience was negatively correlated with participants' mean PRS scores (t=-2.22, p=0.02), with participants who had experienced an earthquake demonstrating higher mean PRS scores (56±9.2) than those without (53.7±10.8). Mean PRS scores were significantly correlated with participants' residence during the post-earthquake period (F=5.55, p=0.02). Bonferroni posthoc analysis revealed that participants staying with relatives had the highest mean PRS scores (57.4±8.8), whereas those staying in tents had the lowest (48.5±13.1). Both mean PRS and STSS scores were significantly correlated with participants' anxiety levels about leaving their families to work (F=3.39, p=0.01; F=23.5, p<0.001, respectively). Specifically, the Bonferroni posthoc analysis showed that the mean PRS score was highest for those reporting no anxiety (60.7±7.1) and lowest for those reporting low anxiety (54.1±8.6), while participants with high anxiety had the highest mean STSS score (57.5±11.3) and those with minimal anxiety had the lowest (43.2±14.4). The level of earthquake anxiety was significantly correlated with participants' mean STSS scores (F=6.45, p<0.001). Bonferroni posthoc analysis indicated that participants experiencing frequent fears of earthquakes had the highest mean score (55.2±9.0), and those not experiencing anxiety had the lowest

Table 3. Comparison of Individual Resilience and Secondary Traumatic Stress Scores with Individual Characteristics of Participants

Variables	n (%)	PRS Mean±SD (%)	STSS Mean±SD (%)
Educational Status			
High School (1)	113	53.5±10.8	53.8±12.7
Associate (2)	45	56.3±12	55.5±11.2
Bachelor (3)	188	55.8 ±8.6	54 ±12.3
Graduate (4)	24	54.9 ±9.9	46.6±8.8
	Analysis Possibility	F= 1.48, p=0.21	F= 3.35, **p=0.01***
	Significant Difference		2>3>1>4
Have You Experienced an Earthquake Before?			
No (1)	142	53.7±10.8	55.2±11.6
Yes (2)	228	56±9.2	53.2±12.7
	Analysis Possibility	t= -2.22 **p=0.02****	t= 1.49, p=0.13
	Significant Difference	2>1	
Where Did You Stay After the Earthquake?			
Home (1)	151	55.2±9.9	52.7±12.6
Tent (2)	30	48.5±13.1	54.8±13.2
Dormitory/Guesthouse (3)	26	53.4±9.9	53.8±12.8
Relative (4)	124	57.4±8.8	54±11.9
Car (5)	39	53.8±7.7	58.3±11.2
	Analysis Possibility	F= 5.55 **p=0.02***	F= 1.64, p=0.16
	Significant Difference	4>1>5>3>2	
Does Leaving Your Family At Home While Coming to Work Cause You Anxiety?			
No (1)	19	60.7±7.1	43.2±14.4
Low (2)	28	54.1±8.6	46±12.1
Intermediate (3)	82	56.6±8.8	48.9±10.2
Toomuch (4)	241	54.3±10.4	57.5±11.3
	Analysis Possibility	F= 3.39 **p=0.01***	F= 23.5, **p=0.00***
	Significant Difference	1>3>>4>2	4>3>2>1
Do You Have Anxiety About An Earthquake?			
No (1)	42	56.1±9.5	46.3±13.1
Sometimes (2)	171	54.9±8.9	54.9±13.2
Often (3)	72	55±9.9	55.2±9
Continuous (4)	85	55±11.9	54.9±11.2
	Analysis Possibility	F= 0,16 p=0,92	F= 6.45, **p=0.00***
	Significant Difference		3>2=4>1
Have you received Disaster Training?	290	55.5±9.8	52.9±11.9
Yes (1)	80	53.9±10.3	57.9±13.2
No (2)			
	Analysis Possibility	t= 1.25 p=0.21	t= -3.2, **p=0.00****
	Significant Difference		2>1
Do you think the hospital you work in is safe?			
Yes (1)	63	56.6±11.2	49.9±13.9
No (2)	307	54.8±9.6	54.9±11.8
	Analysis Possibility	t= 1.33 p=0.18	t= -2.9, **p=0.00****
	Significant Difference		2>1

Data are expressed as numbers (n), mean±SD, OneWay ANOVA**and Student t test*.PRS: Psychological Resilience Scale, SD: Standard deviation, STSS: Secondary Traumatic Stress Scale Turkish Form

(46.3±13.1). Disaster education was significantly and negatively correlated with mean STSS scores (t=-3.2, p<0.001), with participants who received training having lower mean STSS scores (52.9±11.9) than those who did not (57.9±13.2). Finally, participants' perception of hospital safety during earthquakes was significantly and negatively related to their mean STSS scores (t=-2.9, p<0.001), with participants feeling their hospital was safe having lower mean scores (49.9±3.9) than those feeling it was unsafe (54.9±11.8) (Table 3).

Table 4 shows the correlation between participants' mean PRS and STSS scores. The analysis revealed a statistically significant, weak negative correlation between PRS and STSS (r=-0.131, p<0.05), suggesting that higher resilience is associated with lower secondary traumatic stress.

Table 4. Evaluation of the Relationship between the Resilience of the Participants and their Secondary Traumatic Stress

		Secondary Traumatic Stress Level
Resilience Level	Pearson r	-,131
	p	0.01
	n	370

*Thecorrelation is significant at the p<0.05 level.

Discussion

The devastating earthquake affected 11 provinces, including the hospital where this studywas performed. The experience of providing care to disaster victims, listening to harrowing accounts from those affected, witnessing numerous deaths, and facing the overwhelming inability to meet the needs of hundreds of individuals can induce significant secondary traumatization in nurses (20, 21). This study underscores the profound impact on surgical nurses, who were uniquely positioned as both earthquake victims and caregivers to fellow victims. These nurses demonstrated moderate PRS (55.1±9.9) and alarmingly high levels of STSS (54±12.3). Individuals with direct exposure to the earthquake's trauma, such as those trapped in the wreckage, those suffering the loss of relatives, those sustaining injuries, and those enduring major disruptions to their physical and social environments, are particularly vulnerable to emotional sequelae. Moreover, a substantial segment of the community involved in the disaster response, encompassing witnesses, officials, volunteers, and aid providers, is also affected (2). Immediate responses may manifest as reliving the event, vivid flashbacks, intrusive imagery, recurrent nightmares, acute anxiety, intense fear, and physical symptoms including breathing difficulties and palpitations. Prolonged reactions to such losses frequently include avoidance of trauma reminders, emotional numbing, impaired concentration, hyperarousal, heightened startle response, irritability, persistent anxiety, and profound grief (22). In the current study, a significant majority (65%) of participants reported considerable anxiety related to leaving their families to attend work, nearly a quarter (23%) reported persistent worry about the threat of aftershocks, and a large majority (83%) expressed serious concerns regarding the safety of their workplace hospital. These findings strongly suggest that, despite the consistency with expected post-earthquake responses, the participants experienced a clinically significant degree of anxiety.

The increased demands placed on health workers during disasters can lead to significant stress and psychological problems. For nurses directly involved in disaster response, this can result in physical health issues, workforce shortages, and a decline in professional practice standards (21). Disasters can also cause nurses to experience profound loneliness, burnout, and despair due to the disruption of their families and living environments (20). Disaster settings present a heightened risk of burnout, as many healthcare workers and their families are directly affected by events such as earthquakes through hospital damage or destruction and increased workloads. To mitigate the increased working hours, fear, anxiety, and worry experienced by healthcare professionals, it is crucial to establish safe and supportive working environments for all professionals in the affected region, including support staff. Furthermore, secondary traumatization exacerbates the risk of burnout (23). In line with the study's findings, nurses' diminished PRS and heightened STSScorrelate with leaving their families to work and perceiving their workplace as unsafe. Consequently, it is recommended that all health personnel receive comprehensive disaster health services training through various courses, training programs, and practical exercises, both during and after their professional training. The responsibilities of health professionals in disaster situations, their interprofessional communication, and the availability of essential medical supplies should be clearly defined in advance (24). Notably, in this study, nurses receivingeducation fordisaster demonstrated lower levels of secondary psychological stress, consistent with findings in the broader literature. This reduction is likely attributable to the increased clarity regarding

roles, responsibilities, material supply protocols, and communication strategies facilitated by the education.

To promote workers' psychological well-being and ensure effective psychosocial interventions, the literature suggests further studies on preventing secondary trauma, both in the immediate aftermath of a disaster and in the long term (22). Given that psychological resilience is a key protective factor for individuals working in high-risk environments (25), initial support following a disaster should prioritize psychological first aid over psychotherapy or medication, even if trauma-related symptoms appear shortly after the event (2). In this study, a weak negative correlation ($r = -0.131$, $p < 0.05$) was found between surgical nurses' PRS and STSS levels. Aligning with existing literature, higher psychological resilience was associated with lower secondary traumatic stress. Consequently, these findings underscore the importance of enhancing psychological resilience to mitigate secondary traumatic stress, thus highlighting the necessity of relevant interventions.

Conclusion

This study revealed that surgical nurses both enduring the earthquake and subsequently providing care to victims demonstrated elevated levels of secondary traumatic stress. In line with this, increased stress was associated with decreased psychological resilience. Earthquakes have a detrimental impact on societal mental well-being, affecting not only those directly impacted but also the nurses delivering care. The severity of the earthquake, coupled with inadequate resources and damage to healthcare facilities, may result in the neglect of secondary psychological trauma. Accordingly, it is crucial to evaluate nurses exposed to the earthquake and to provide essential psychological support.

Limitations of the Study

The findings of this study may not be generalizable to all nurses, as the research was conducted with nurses working in the surgical departments of a single hospital in the earthquake-affected province.

Conflict of Interest

The authors declare no potential conflicts of interest regarding the research, authorship, and/or publication of this article.

Financial Support

No financial support was received for the conduct of this research or the preparation of this article.

Acknowledgment

The authors would like to thank all the participants.

References

1.Güre, MDP. How to help those who help: ıntegrative group therapy applications with disaster professionals. J Soc Work. 2021;6(1):29-40https://dergipark.org.tr/en/download/article-file/2345302

2.Yıldırım, M. Early Influence in Mass Traumas. Guide to the Prevention, Intervention, and Treatment of Mental Illnesses in Mass Traumas and Disasters, Ş Yüksel, A Başterzi (Ed). Turkish Psychiatric Association Publications, Ankara, 2021.

3.Şeker, Z. Investigation of Vicarious Traumatization, Compassion Level and Fatigue, Psychological Resilience and Post-Traumatic Growth in Occupational Groups Exposed to Psychological Trauma through History and Physical Contact, Doctoral Thesis, Kocaeli University Institute of Health Sciences, 2021.

4.Dinçer İ, Akin KM, Akin M. ve ark. February 6, 2023,Kahramanmaraş earthquakes. Konuralp Med J. 2023;14(1):1-16.

5.Dinçer S & Kumru S. Preparedness of health personnel for disasters and emergencies. Gümüşhane University Journal of Health Sciences. 2021; 10(1): 32-43. https://doi.org/10.37989/gumussagbil.790884

6.Pak, M. D., Özcan, E., & Çoban, A. İ. Secondary Traumatic Stress Level of Emergency Service Workers And Psychological Resilience. Journal Of International Social Research. 2017; 10(52). http://dx.doi.org/10.17719/jisr.2017.1923

7.Çalık Var, E.,& Büyükbodur, A. Çetinkaya. (2017). Secondary traumatic stress in social workers;p> Journal of Human Sciences. 2017; 14(4): 3676–3689.http://orcid.org/0000-0002-8042-4174

8.Gözükızıl C. A. & Tezcan S. Disasters in Turkey in the Centennial of the Republic: February 6, 2023, Kahramanmaraş Earthquakes. City Academy Journal. 2023; 97-114. https://doi.org/10.35674/kent.1353445

9.Kahve AC, Aydın S & Er GD. Approach to Post-Earthquake Psychological Problems in Trauma-Exposed Individuals and Healthcare Workers. TOTBID Derg. 2023; 22: 642-651. https://doi.org/10.5578/totbid.dergisi.2023.94

10.Guo C, Li S & Chan SS. Long-Term Effects Of Disaster

Exposure On Health Care Workers' Resilience: A Comparison Of The Wenchuan Earthquake-Exposed And Unexposed Groups. Int J Disaster Risk Reduct. 2022;67:102658.

11.Şeremet GG, & Ekinci N. Compassion Fatigue, Compassion Satisfaction and Fear of Compassion in Healthcare Workers. Süleyman Demirel University Visionary Journal. 2021; 12(29): 330-344. https://doi.org/10.21076/vizyoner.722874

12.Kahil A ve Palabıyıkoğlu NR. Secondary Traumatic Stress. Curr Approaches Psychiatry., 2018; 10(1): 59-70. https://doi.org/10.18863/pgy.336495

13.Ludick, M.,& Figley, C. R. Toward A Mechanism for Secondary Trauma Induction and Reduction: Reimagining A Theory of Secondary Traumatic Stress. Traumatology. 2017; 23(1): 112. https://doi.org/10.1037/trm0000096

14.Işıkhan, V. Strengthening Disaster Response Relief Personnel. Natural Disasters and Environment Journal. 2021; 7(2): 399-406. DOI: 10.21324/dacd.893075

15.Machado, M. Secondary traumatic stress among emergency department nurses. Published Master Dissertation. Rhode Island College. 2018. https://doi.org/10.28971/532018MM74)

16.Erdener, M. Investigation of psychological resilience and secondary traumatic stress levels of professionals working in the field of disaster (Master's thesis), Institute of Social Sciences, 2016.

17.Aktan K. F. T.C. Evaluation of Individual Earthquake Preparedness and Related Factors of Employees of Sakarya University Training and Research Hospital, Ministry of Health. (Medical Specialization Thesis). Sakarya University Faculty of Medicine, Sakarya, 2019. https://tez.yok.gov.tr/UlusalTezMerkezi/tezDetay.id=87WkzKCB1SRHy2V1ADLNQw&no=c3q8QECqoj_d77Qi9YEuMg

18.Işık, Ş. (2016). Development of the Resilience Scale: Validity and Reliability Study. The Journal of Happiness & Well-Being, 4(2), 165-182. https://avesis.gazi.edu.tr/yayin/55c9a659-3478-4528-b111-50d47923e679/

19.Kahil, A. Investigation of Secondary Traumatic Stress Levels of Professionals and Volunteers who Helped Individuals with Traumatic Experiences. Master Thesis, Ufuk University, Ankara, 2016.

20.Taskıran, G., Baykal, U. T. Nurses' preparedness for disasters in Turkey: A literature review. New Trends and Issues Proceedings on Humanities and Social Sciences. 2017; 4(2): 47-56. DOI: 10.5222/SHYD.2017.079

21.VanDevanter, N., Raveis, VH., Kovner, CT., McCollum, M., Keller, R. (2017). Challenges and Resources for Nurses Participatingin a Hurricane Sandy Hospital Evacuation. J Nurs Scholarsh. 49(6), 635-643. DOI: 10.1111/jnu.12329

22. Yıldız, M. İ., Başterzi, A. D., Yıldırım, E. A., Yüksel, Ş., Aker, A. T., Semerci, B., ... & Hacıoğlu Yıldırım, M. Preventive and Therapeutic Mental Health Service in the Early Period After the Earthquake, Expert Opinion of the Turkish Psychiatric Association. Turkish Journal of Psychiatry, 2023; 34(1). https://doi.org/10.5080/u27305

23.Kucukparlak, I. Second Traumatization and Burnout in Mass Traumas. Prevention, Intervention, and Treatment of Mental Illnesses in Mass Traumas and Disasters, A Başterzi, Ş Yüksel (Ed), Ankara, Turkish Psychiatric Association Publications, 2021.

24.Demirbaş,H., Sezer, A., Ergun, A. The Role of the Public Health Nurse in Disaster Management and Responsibilities. Florence Nightingale J Nurs. 2013; 21(2): 122-128. Retrieved from https://dergipark.org.tr/en/pub/fnjn/issue/9010/112445

25.Chang, K.,& Taormina, R. J. Reduced Secondary Trauma Among Chinese Earthquake Rescuers:A Test of Correlates and Life Indicators. J Loss Trauma. 2011; 16(6): 542-562. https://doi.org/10.1080/15325024.2011.600682

Received: 13 Feb 2025 | **Accepted:** 07 Apr 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 369-373
DOI: 10.54005/geneltip.1639378

ORIGINAL ARTICLE

The Diagnostic Role of PET/CT in Patients with Malignant Pleural Effusion

Malign Plevral Efüzyonu Olan Hastalarda PET / BT'nin Tanıdaki Rolü

[1]Süleyman Emre Akın, [1]Hasan Emre Yıldırım, [2]Samet Yağcı, [3]Umut Otlu, [1]Hasan Ekrem Çamas, [2]Mehmet Erdoğan, [1]İsa Döngel, [2]Sevim Süreyya Şengül, [1]Rasih Yazkan

[1]Suleyman Demirel University, Faculty of Medicine, Thoracic Surgery Department, Isparta, Türkiye
[2]Suleyman Demirel University, Faculty of Medicine, Nuclear Medicine Department, Isparta, Türkiye
[3]Manisa Demirci District Health Directorate, Manisa, Tükriye

Correspondence

Assist. Prof. Suleyman Emre AKIN
Suleyman Demirel University, Medical Faculty Department of Thoracic Surgery, 32260, Isparta, Türkiye

E-Mail: suleymanemreakin@yahoo.com

How to cite ?

Akın SE, Yıldırım HE, Yagcı S, Otlu U, Çamas HE, Erdoğan M, Döngel İ, Şengül SS, Yazkan R. The Diagnostic Role of PET/CT in Patients with Malignant Pleural Effusion. Genel Tıp Derg. 2025;35 (2): 369-373

ABSTRACT

Background: Malignant pleural effusion (MPE) is defined as the presence of malignant cells in pleural effusion (PE) or biopsy specimens and occurs in 15% of all cancer patients. The most common cause is lung cancer in men and breast cancer in women. The reason for hospital admission is usually shortness of breath. The main goal of treatment is to relieve symptoms and prevent recurrence. PET/CT is an imaging system that combines the metabolic properties of PET with the morphologic properties of computed tomography. The patient can be managed more rapidly if malignant effusion can be detected on PET/CT. In this study, we aimed to predict the diagnostic impact of metabolic uptake of fluid in patients with malignant pleural effusion.
Methods: In our study, we aimed to find the contribution of PET/CT to the diagnosis of malignant pleural effusion by examining patients between 18 and 90 years of age who had malignancy as a result of pleural cytology and who underwent PET/CT with a primary diagnosis of malignancy. 26 patients were evaluated. The values analyzed were; the presence of PE FDG uptake, the presence of single or double uptake in PE, the presence of multiple pulmonary nodules, the presence of pleural thickness (PT) increase, PT diameter, the presence of FDG uptake in PT, primary pathology being lung or other organ, PE Standardized Uptake Value (SUV) max, PE SUVmax/ Med SUVmax, PE SUVmax/ Liver SUVmax, PE SUVmax/ primary tumor SUVmax, primary tumor SUV values.
Results: 6 of 26 patients had bilateral effusions and 12 patients had FDG uptake. 5 patients had pleural thickening and 4 of them had pleural uptake. In the ROC analysis, PE SUVmax, PE SUV / Med SUV, PE SUV / Liver SUV, and PE SUV / Primary tumor SUV values were found to be significant in terms of predicting PE FDG uptake, while PT diameter was not significant.
Conclusions: Patients with MPE have a short life expectancy. Diagnosis and treatment management of patients should be performed effectively and rapidly. PET/CT can be used as a noninvasive diagnostic method for this purpose. Therefore, if further studies are performed, PET/CT in the diagnosis of MPE will contribute to patient management.

Keywords: malignant pleural effusion, PET/CT, 18F-fluorodeoxyglucose, cancer, pleural metastasis

ÖZ

Giriş: Malign plevral efüzyon (MPE) , plevral efüzyon (PE) veya biyopsi örneklerinde malign hücrelerin varlığı olarak tanımlanır ve tüm kanser hastalarının %15' inde görülür. Erkeklerde en sık sebep akciğer kanseri iken kadınlarda meme kanseridir. Hastaneye başvuru sebebi genelde nefes darlığıdır. Tedavide ana hedef semptomları ortadan kaldırmak ve tekrarlamasını önlemektir. PET/BT, PET' in metabolik özellikleri bilgisayarlı tomografinin morfolojik özelliklerini birleştiren görüntüleme sistemidir. PET/BT' de malign efüzyon tespit edilebilirse hastanın yönetimi daha hızlı yapılabilir. Biz bu çalışmada malign plevral efüzyon olan hastalarda sıvının metabolik tutulumunun tanıdaki etkisini öngörmeyi amaçladık.
Materyal-Metod: Çalışmamızda plevral sitoloji sonucu malignitesi olup primer malignite tanısı olan PET/BT çekilmiş 18-90 yaş aralığında hastaları inceleyerek malign plevral efüzyon için PET/BT'nin tanıya katkısını bulmayı amaçladık. 26 hastayı değerlendirmeye aldık. Analize tabi tutulan değerler; PE FDG tutulumu varlığı, PE'de tek ya da çift taraflı tutulum olması, çoklu pulmoner nodül varlığı, plevral kalınlık (PK) artışı varlığı, PK çapı, PK'da FDG tutulumu varlığı, primer patolojinin akciğer veya diğer organ olması, PE Standardized Uptake Value (SUV) max, PE SUVmax/ Mediastinal (med) SUVmax, PE SUVmax/ Karaciğer SUVmax, PE SUVmax/ primer tümör SUVmax, primer tümör SUV değerleridir.
Bulgular: 26 hastanın 6'sında efüzyon çift taraflıydı ve 12 hastanın efüzyonunda FDG tutulumu vardı. 5 hastada plevral kalınlaşma vardı bunların 4'ünde plevra tutulumu mevcuttu. Yapılan ROC analizinde PE FDG tutulumunu tahmin bakımından; PE SUVmax, PE SUV / Med SUV, PE SUV / Karaciğer SUV, PE SUV / Primer tümör SUV değerlerinin anlamlı olduğu, PK çapının anlamlı olmadığı görülmüştür.
Sonuç: MPE hastalarında kısa bir yaşam süresi söz konusudur. Hastaların tanı ve tedavi yönetiminin etkin ve hızlı bir şekilde yapılması gerekmektedir. PET/BT bu amaçla noninvaziv bir tanı yöntemi olarak kullanılabilir. Bu nedenle ileri çalışmaların yapılması halinde malign plevral efüzyon tanısında PET/BT' nin hasta yönetimine katkısı olacaktır.

Anahtar kelimeler: malign plevral efüzyon, PET/BT, 18F-florodeoksiglukoz, kanser, plevral metastaz

Introduction

In healthy individuals, there is 0.1-0.3 ml/kg fluid between the visceral and parietal pleura surrounding the lungs. Abnormal accumulation of this fluid, which allows the pleural leaves to move freely during respiration, can be defined as pleural effusion (PE) (1). Congestive heart failure, pulmonary embolism, pulmonary hypertension, gastrointestinal system diseases, liver diseases, renal diseases, infection, rheumatologic diseases, use of certain drugs such as amiodarone, methotrexate, different benign pathologies as well as malignancy may lead to this condition. This wide spectrum can make diagnosis and effective treatment difficult. Considering that pleural effusions have high mortality and morbidity, noninvasive methods and rapid diagnostic methods gain more importance in terms of the prognosis of the disease, especially in patients with malignant disease

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

(2).

MPE is defined as the presence of malignant cells in pleural fluid or pleural biopsy specimens and occurs in 15% of all cancer patients. The most common causes include malignancies such as lung cancer, breast cancer, malignant lymphoma, ovarian cancer, and gastrointestinal cancers (3). Malignant tumors invade the pleura directly or indirectly and cause pleural effusion. It is thought that malignancy-related pleural effusions develop due to increased fluid passage into the pleural cavity and/or impaired lymphatic drainage (4). Malignant effusions have a higher recurrence rate, duration of hospitalization, and financial and emotional burden on the physician, patient, and hospital compared to other benign effusions. Therefore, early and effective diagnosis becomes more important.

Diagnostic methods in MPE include invasive procedures such as thoracentesis, pleural biopsy, thoracoscopy, and thoracotomy as well as radiologic imaging. These methods include chest radiography, computed tomography (CT), thoracic ultrasonography, thoracic magnetic resonance imaging, and positron emission tomography. Fluorine-18-fluorodeoxyglucose (18F FDG) positron emission tomography/computed tomography (PET/CT) is an integrated imaging modality that combines the metabolic properties of PET with the morphologic properties of CT and provides significant guidance (5).

If malignant effusion can be detected on PET/CT, patients can be managed more quickly and easily. The role of PET/CT in the diagnosis of MPE has not yet been fully elucidated due to significant heterogeneity and discrepancies between existing studies. In this study, we aimed to predict MPE in patients with pleural effusion based on metabolic uptake of the fluid using PET/CT.

Materials And Methods

After the approval of the local ethics committee dated 18.11.2022 and numbered 323, the data, PET/CT images, and pathology parameters of 26 patients in the digital archive of our hospital were retrospectively analyzed. Patients between the ages of 18-90 years with effusion and malignancy who could be evaluated in our study and who underwent PET-CT were included. Patients younger than 18 years and older than 90 years with no pleural cytology results and patients with benign cytology results were excluded from the study. Values subjected to analysis were the presence of PE FDG uptake, the presence of single or double uptake in PE, presence of multiple pulmonary nodules, presence of pleural thickness (PT) increase, PT diameter, presence of FDG uptake in PT, primary pathology being lung or other organ, PE Standardized Uptake Value (SUV) max, PE SUVmax/ Med SUVmax, PE SUVmax/ Liver SUVmax, PE SUVmax/ primary tumor SUVmax, primary tumor SUV values.

18F FDG PET/CT images were acquired with a Philips GEMINI TF PET/CT scanner with TOF imaging (Philips Medical Systems, Cleveland, Ohio, USA) and a 64-slice CT scanner. 18F FDG uptake in pleural effusion was evaluated. SUVmax was calculated if uptake was present. Mediastinum (aortic arch), liver, and primary tumor basal FDG uptake values were recorded as SUVmax. A quantitative value was then obtained by dividing the pleural fluid FDG uptake rate by the mediastinum, liver, and primary tumor uptake rates, respectively. In patients with pleural effusion, we drew a region of interest (ROI) of 1 cm3 and looked for FDG uptake in this area. While doing this, we ensured no hypermetabolic lesion or pleural focus in the neighborhood. We also tried to get maximum ROI in patients with effusion smaller than 1 cm3.

Statistical analyses were performed using the IBM SPSS Statistics 25 software program. Compliance of the parameters with normal distribution was evaluated by Kolmogorov-Smirnov test. One Way Anova test was used to compare quantitative data for normally distributed parameters and Mann-Whitney U-test was used to compare non-normally distributed parameters. The chi-square test was used to compare quantitative data. $P < 0.05$ was accepted to indicate statistical significance.

Reslts

Sixteen of our patients were female and ten were male. Approximately 46% of our patients had 18F-FDG uptake in PE (Figure 1,2) and 77% had unilateral effusion. When we examined the pleura, approximately 20% of the patients had increased PT, while 15% had 18F-FDG uptake in PT. The diagnosis of 5 patients was made by thoracoscopy, the others were confirmed by cytologic examination of thoracentesis fluid. The primary malignancy diagnoses of the patients were as follows: 9 lung adenocarcinoma, 2 mesothelioma, 2 small cell lung cancer, 2 breast cancer, 1 bladder cancer, 1 malignant mesenchymal tumor, 2 plasma cell myeloma, 2 lymphoma, 1 renal cell cancer, 2 ovarian cancer, 1 colon adenocarcinoma, 1 mixed

müllerian tumor. PE SUVmax, PE SUVmax/ Med SUV, PE SUVmax/ Liver SUVmax, and PE SUVmax/ primary tumor SUVmax values were correlated with each other as expected. No correlation was observed between PT diameter and SUVmax values (p>0.05).

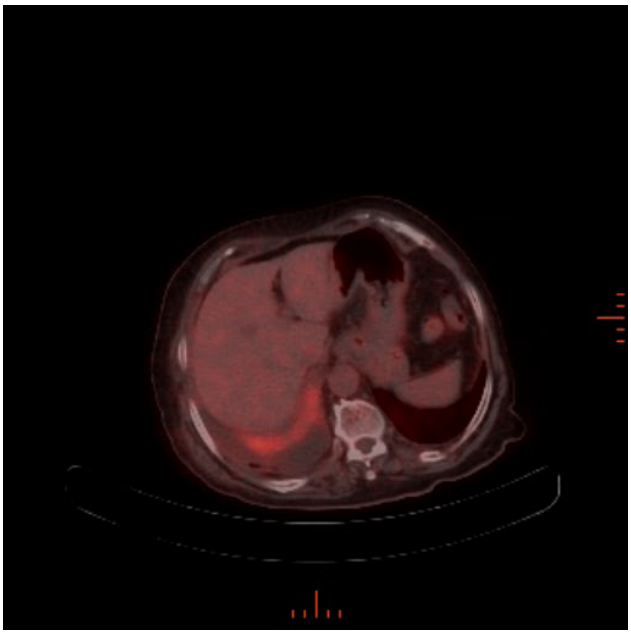


Figure 1. ROC analysis graph

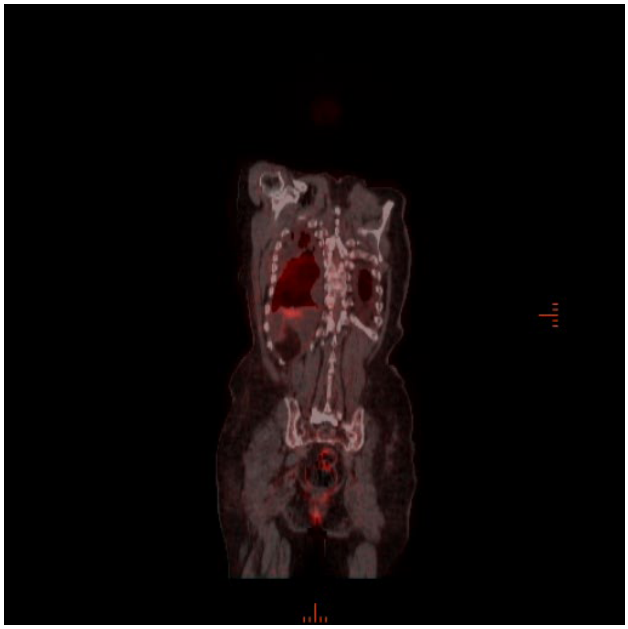


Figure 2. Axial cross-sectional PET/CT image of a patient with high SUV uptake in pleural effusion.

The presence of PE FDG uptake was correlated with higher SUVmax values (PE SUVmax, PE SUVmax/ Med SUV, PE SUVmax/ Liver SUVmax, PE SUVmax/ primary tumor SUVmax) (p<0.001). On the other hand, the presence of PE FDG uptake was not associated with PT diameter and primary tumor SUVmax (p>0.05). Single or double uptake in PE was not associated with SUVmax values and PT diameter (p>0.05). There was no correlation between the presence of PT enhancement and SUVmax values (p>0.05). The presence of FDG uptake in PT was associated with increased PT diameter (p<0.001).

There was no correlation between the primary pathology being lung or other organs and the parameters considered in our study (p>0.05). There was no correlation between the presence of multiple pulmonary nodules and the parameters considered in our study (p>0.05).

In terms of the association with the presence of PE FDG uptake, it was evaluated according to the presence of single-double nodules, the presence of increased PT, the presence of FDG uptake in PT, the presence of multiple pulmonary nodules and whether the primary pathology was lung or not, and it was found that there was no association with these parameters.

In the ROC analysis, PE SUVmax, PE SUVmax / Med SUV, PE SUVmax / Liver SUVmax, and PE SUVmax / Primary tumor SUVmax values were found to be significant in terms of predicting PE FDG uptake, while PT diameter was not significant (Table 1) (Figure 3).

Table 1. Prediction of PE FDG uptake in ROC analysis.

Parameter	Significance Level	Area Under Curve (AUC)	Cut-off Value
PE SUVmax	p<0,001	0,976	1,50
PE SUV / Med_SUV	p<0,001	0,911	0,94
PE SUV / Liver_SUV	p<0,001	0,935	0,77
PE SUV / Primer_Tm_SUV	p<0,001	0,881	0,23
PT diameter	p>0,1	-	-

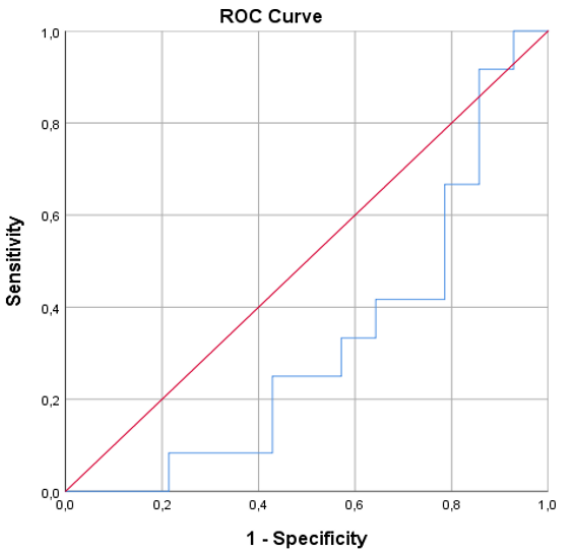


Figure 3. Coronal cross-sectional PET/CT image of a patient with high SUV uptake in pleural effusion

Discussion

In cancer patients, the diagnosis of MPE indicates advanced disease and poor prognosis. It changes and complicates the treatment approach. In patients with PE with primary malignancy, rapid characterization by PET/CT without invasive procedures may facilitate patient management. Many studies have shown the usefulness of PET/CT in the differential diagnosis of pleural diseases in patients with cancer (6). However, there is still no consensus on this issue. PET/CT is an effective method for the detection of cancerous cells with high glucose uptake. The sensitivity and specificity of MPE detection with this method vary between 89-100% and 67-94%, respectively (7, 8). Our study shows similar results to other studies.

Simsek et al. (9) evaluated the efficacy of PET/CT in the evaluation of PE using 23 parameters. According to their results, none of these parameters provided sufficient clinical benefit when used alone. Therefore, they created a combined approach. These parameters are; 1) Diffuse-nodular/nodular pleural thickening, 2) Post-obstructive atelectasis, 3) nodule/mass in the lung with SUVmax > 2.5, and 4) multiple pulmonary nodules. The accuracy rate was approximately 90% and the positive predictive value (PPV) was 100%. In their study, the cut-off value for PE SUVmax was >1.3, while in our study it was 1.50. The cut-off value of PE SUVmax/Liver SUVmax was 0.65 whereas it was 0.77 in our study (9).

On the other hand, various parameters have been examined in many studies. The size, location, side of effusion, lymph node involvement, and metastasis status of PT are some of these parameters (10-12). Nakajima et al. reported 100% sensitivity, 56% PPV, and 69% accuracy for PE with SUVmax > 1.39 and found that SUV uptake was higher in MPE compared to benign effusions (6, 13). Sun et al. (14) suggested pleural glucose metabolism and PT to differentiate MPE from benign effusion. Zhang et al. (15) determined false negativity on PET/CT imaging in 18 patients with MPE. Most of these patients did not have an underlying atelectasis, consolidation, and inflammation. In another study, 27 patients with MPE and 6 patients with benign effusion were analyzed. Among these, PET/CT gave false positive results in one patient with tuberculous pleurisy (16).

SUVmax is a PET/CT parameter used to detect malignancy, predict prognosis, and evaluate invasion and metastasis. Li et al. found significant differences in this value in differentiating MPE and benign effusion but did not consider them as independent factors in predicting MPE. However, they determined SUVmax > 2.5 as a predictive factor and revealed that PE SUVmax value is an important parameter in defining MPE (5). Porcel et al. (17) performed a meta-analysis study to evaluate the effectiveness of PET/CT in the diagnosis of MPE. In this analysis, they examined 407 patients with MPE and 232 patients with benign effusion. They found a sensitivity of 83.3% and specificity of 92.2%. In a different study, PET/CT was found to be effective in excluding MPE from tuberculous pleurisy and other benign effusions (12).

The limitations of this study are the retrospective analysis of the data, the single-center nature of the study, and the limited number of patients. Some of the parameters we studied were found to be significant in the characterization of PE and the diagnosis of MPE, and we think that they will facilitate diagnosis and treatment in the future.

In conclusion, PET/CT is an effective and non-invasive method for the differential diagnosis of MPE in patients with PE in other radiologic imaging studies. Increased pleural FDG uptake and pleural thickening indicate pleural metastases. Such studies may increase patient comfort by reducing unnecessary invasive procedures in the diagnosis of MPE and may also lead to the decision of pleurodesis by making an accurate diagnosis. Therefore, if multicenter, prospective studies with a larger number of patients are conducted, the efficacy of PET/CT in the diagnosis of MPE will be clarified more clearly and will contribute to patient management.

Declarations

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

This study was approved by the local ethics committee (Dated: 18.11.2022; Approval Number: 323)

References

1.Poyraz N, Kalkan H, Ödev K, Ceran S. Imaging of pleural diseases: evaluation of imaging methods based on chest radiography. Tuberk Toraks. 2017;65(1):41-55.

2.Light RW. Pleural effusions. Med Clin North Am. 2011;95(6):1055-70.

3.Yazkan R. Malign plevral efüzyon. Turk J Clin Lab. 2016;7(1):19-22.

4.Yüksel M, Balcı AA. Göğüs Cerrahisi:" Kırmızı Kitap". İstanbul: Nobel Tıp Kitabevi; 2015.

5.Li Y, Mu W, Li Y, Song X, Huang Y, Jiang L. Predicting the nature of pleural effusion in patients with lung adenocarcinoma based on (18)F-FDG PET/CT. EJNMMI Res. 2021;11(1):108.

6.Nakajima R, Abe K, Sakai S. Diagnostic Ability of FDG-PET/CT in the Detection of Malignant Pleural Effusion. Medicine (Baltimore). 2015;94(29):e1010.

7.Erasmus JJ, McAdams HP, Rossi SE, Goodman PC, Coleman RE, Patz EF. FDG PET of pleural effusions in patients with non-small cell lung cancer. AJR Am J Roentgenol. 2000;175(1):245-9.

8.Toaff JS, Metser U, Gottfried M, Gur O, Deeb ME, Lievshitz G, et al. Differentiation between malignant and benign pleural effusion in patients with extra-pleural primary malignancies: assessment with positron emission tomography-computed tomography. Invest Radiol. 2005;40(4):204-9.

9.Simsek FS, Yuksel D, Yaylali O, Aslan HS, Kılıçarslan E, Bir F, et al. Can PET/CT be used more effectively in pleural effusion evaluation? Jpn J Radiol. 2021;39(12):1186-94.

10.Hooper C, Lee YC, Maskell N, Group BTSPG. Investigation of a unilateral pleural effusion in adults: British Thoracic Society Pleural Disease Guideline 2010. Thorax. 2010;65 Suppl 2(Suppl 2):ii4-17.

11.Porcel JM, Esquerda A, Vives M, Bielsa S. Etiology of pleural effusions: analysis of more than 3,000 consecutive thoracenteses. Arch Bronconeumol (English Edition). 2014;50(5):161-5.

12.Yang MF, Tong ZH, Wang Z, Zhang YY, Xu LL, Wang XJ, et al. Development and validation of the PET-CT score for diagnosis of malignant pleural effusion. Eur J Nucl Med Mol Imaging. 2019;46(7):1457-67.

13.Arnold DT, De Fonseka D, Perry S, Morley A, Harvey JE, Medford A, et al. Investigating unilateral pleural effusions: the role of cytology. Eur Respir J. 2018;52(5).

14.Sun Y, Yu H, Ma J, Lu P. The Role of 18F-FDG PET/CT Integrated Imaging in Distinguishing Malignant from Benign Pleural Effusion. PLoS One. 2016;11(8):e0161764.

15.Zhang W, Liu Z, Duan X, Li Y, Shen C, Guo Y, Yang J. Differentiating malignant and benign pleural effusion in patients with lung cancer: an 18F-FDG PET/CT retrospectively study. Front Oncol. 2023;13:1192870.

16.Liao R, Yang X, Wang S, Zhou Q, Nie Q, Zhong W, et al. [Clinical role of F-18 FDG PET/CT in differentiating malignant and benign pleural effusion in patients with lung cancer]. Chin J Lung Cancer. 2012;15(11):652-5.

17.Porcel JM, Hernandez P, Martinez-Alonso M, Bielsa S, Salud A. Accuracy of fluorodeoxyglucose-PET imaging for differentiating benign from malignant pleural effusions: a meta-analysis. Chest. 2015;147(2):502-12.

Received: 04 May 2024 | **Accepted:** 15 Apr 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 374-381
DOI: 10.54005/geneltip.1476892

ORIGINAL ARTICLE

The Protective Effect of Sildenafil on Colon Anastomosis in a Rat Model Undergoing Hyperthermic Intraperitoneal Chemotherapy

Hipertermik İntraperitoneal Kemoterapi Uygulanan Sıçan Modelinde Sildenafilin Kolon Anastomozunu Koruyucu Etkisi

[1]Ahmet Başak, [2]Mehmet Timuçin Aydın, [2]Mehmet Mahir Fersahoğlu, [2]İksan Taşdelen, [3]Adnan Somay, [4]Emre Teke, [5]Erdem Durum, [2]Kemal Memişoğlu

[1]Department of General Surgery ,Erzurum Regional Training and Research Hospital, Erzurum, Türkiye
[2]Department of General Surgery, Fatih Sultan Mehmet Training and Research Hospital, İstanbul, Türkiye
[3]Department of Pathology, Fatih Sultan Mehmet Training and Research Hospital, İstanbul, Türkiye
[4]Department of General Surgery, Gaziantep City Hospital, Gaziantep, Türkiye
[5]Department of General Surgery, Dr. Ersin Arslan Training and Research Hospital, Gaziantep, Turkiye

Correspondence

Ahmet Başak,
Erzurum Regional Training and Research Hospital, Erzurum, Türkiye

E-Mail: abasak54@yandex.com

How to cite ?

Başak A, Aydın MT, Fersahoğlu MM, Taşdelen İ, Somay A, Teke E, Durum E, Memişoğlu K. The Protective Effect of Sildenafil on Colon Anastomosis in a Rat Model Undergoing Hyperthermic Intraperitoneal Chemotherap. Genel Tıp Derg. 2025;35 (2): 374-381

ABSTRACT

Aim: This study aimed to investigate the effects of sildenafil on colonic anastomosis healing in rats treated with hyperthermic intraperitoneal chemotherapy (HIPEC).
Method: In our study, 30 Wistar-albino rats were used. 30 rats were divided into 3 groups: the sildenafil, control, and sham groups. Left colon anastomosis was performed on rats in all three groups. The HIPEC procedure was applied to the sildenafil group and control group. During the postoperative period, sildenafil was given orally to the sildenafil group. On the 7th day, the anastomotic loop was excised, and bursting pressure, and adhesion were evaluated. The anastomotic loop was evaluated histopathologically. The results were compared statistically.
Results: When the results were evaluated considering bursting pressure, and adhesion between the sildenafil group and control group, there was no difference. Considering adhesion, the sham group was superior to the other two groups. Histopathological examination reveals that the sham group was significantly superior to the other two groups in terms of anastomotic re-epitelization and muscle separation. There was a significant difference between the sildenafil group and the control group in terms of fibrosis and granulation.
Conclusion: On colon anastomosis performed together with HIPEC application, histopathologically positive effects of sildenafil were observed. The burst pressure of colon anastomosis was not significantly different.

Keywords: Anastomosis healing, colonic anastomosis, hyperthermic intraperitoneal chemotherapy, sildenafil

ÖZ

Amaç: Çalışmanın amacı hipertermik intraperitoneal kemoterapi uygulanan sıçanlarda kolon anastomozu iyileşmesi üzerine sildenafilin etkilerini araştırmaktır.
Gereç ve Yöntemler: Çalışmamızda 30 adet Wistar-albino cinsi sıçan kullanılmıştır. Sildenafil, kontrol ve sham grubu olmak üzere 3 grupta 10'ar sıçan kullanılmıştır. Tüm gruptaki sıçanlara sol kolon anastomozu yapıldı. Sildenafil grubu ve kontrol grubuna HIPEK işlemi uygulandı. Sildenafil grubuna postoperatif oral sildenafil verildi. 7. gün anastomoz ansı eksize edilerek patlama basıncı ve adezyon değerlendirildi. Anastomoz ansı histopatolojik olarak değerlendirildi. Sonuçlar istatistiksel olarak karşılaştırıldı.
Bulgular: Sonuçlar değerlendirildiğinde patlama basıncı ve adezyon açısından sildenafil grubu ile kontrol grubu arasında fark saptanmamıştır. Sham grubu ise adezyon açısından diğer iki gruba üstün görülmüştür. Histopatolojik incelemede ise sham grubunun anastomoz re-epitelizasyonu ve kas ayrışması açısından diğer iki gruba karşı anlamlı olarak üstün olduğu görülmüştür. Fibrosis ve granülasyon açısından sildenafil grubu ile kontrol grubu arasında anlamlı olarak farklılık saptanmıştır.
Sonuçlar: HIPEK uygulaması ile beraber yapılan kolon anastomozu üzerinde sildenafilin histopatolojik olarak olumlu etkileri görülmüştür. Kolon anastomozu patlama basınç açısından ise fark görülmemiştir.

Anahtar Kelimeler: Anastomoz iyileşmesi, hipertermik intraperitoneal kemoterapi, kolon anastomozu, sildenafil

Introduction

Anastomotic leakage after colorectal surgery is an important cause of mortality, morbidity, and prolonged hospital stays. Perioperative mortality is often caused by septicemia and peritonitis (1). The main causes of anastomotic leak are thought to be anatomical mismatch and suboptimal blood supply (2). In addition, surgical technique, intestinal integrity, anastomotic tension, drugs, and comorbid diseases can be considered. Even under optimal conditions, there is a significant risk of leakage in left colon and rectum surgeries (3).

Colorectal cancer with peritoneal metastasis is considered stage 4. The dose of medication required for the treatment of peritoneal metastases via intravenous chemotherapy is much greater than the normal dose. When the dose is administered intraperitoneally, it has a sufficient effect on tumor cells up to a sufficient tissue depth by diffusion, and systemic toxicity is avoided. Therefore, hyperthermic intraperitoneal chemotherapy (HIPEC) and cytoreductive surgery are among the best treatment options for such patients (4).According to previous studies, the anastomotic burst pressure and collagen ratio in anastomotic tissue decrease when

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

HIPEC is applied with mitomycin (3). Therefore, the risk of anastomotic leakage is predicted to increase in patients undergoing HIPEC.
Oral administration of sildenafil in anastomosed rats increases the strength of the anastomosis and increases burst pressure by affecting NO metabolism, which reduces oxidative stress by vasodilation and activates the nitrate-nitrite oxide pathway, one of the wound healing pathways (5-7).

In our study, the effectiveness of sildenafil citrate, which has previously been shown to increase tissue nitric oxide levels and increase anastomotic burst pressure and which is effective for enhancing anastomotic strength and burst pressure, on colon anastomosis, which is assumed to be weakened by HIPEC treatment, was questioned (5,7). It was thought that sildenafil would increase anastomotic blood flow by providing vascular vasodilation and increase anastomotic strength under HIPEC treatment by reducing microangiopathic damage due to hyperthermia and chemotherapy agents combined with HIPEC treatment.

Material and methods

Ethical Approval and Animal Subjects

In the present study, 30 female Wistar-Albino rats with an average weight of 250-300 grams and aged 20-28 weeks, and no history of medical treatment or surgical procedure were used. GPower 3.1 software was used for sample size calculation. All necessary approval was obtained from the institutional ethical review board (Approval no: 2021/11-6), and the research procedures complied with established ethical standards to safeguard the well-being of the animals involved. The rats were divided into three main groups, each containing 10 rats, which were the study group and given sildenafil citrate the control group, and the sham group.

Housing and Animal Care

Throughout the entire experiment, The rats in the same study group were monitored in separate cages in groups of 4. The rat pellet was provided both before and after the surgical procedure, and water was supplied ad libitum. All animals were housed and fed under controlled conditions with a 12-hour light/12-hour dark cycle at a room temperature of 24°C.

Experimental Groups and Study Design

Group 1 (Study group): After bowel anastomosis, HIPEC containing mitomycin C was performed via the closed method. Sildenafil citrate (10 mg/kg) was given orally by gavage for three days.

Group 2 (Control group): After bowel anastomosis, HIPEC containing mitomycin C was performed via the closed method.

Group 3 (Sham group): Only bowel anastomosis was performed.

Surgical Procedure

After the midline incision in the abdomen was made, the colon was found and 1 cm of the colon was resected 3 cm proximal to the peritoneal reflection without disturbing the vascularization of the left colon. The proximal end and distal ends were sutured with 7.0 prolene suture as a single-layer inverting suture and end-to-end anastomosis was achieved. Mitomycin C was applied for HIPEC according to the methods of Molyneux et al. (8). The drainage catheters were removed. The abdomen was closed with 5.0 silk sutures over a double layer.

HIPEC Administration

Mitomycin C was prepared at a dose of 15 mg/m2 after dilution with 20 mg. Half of the dose was placed in 100 mL of physiological saline. The fluid, which was brought to a temperature of 43°C with a heater, was infused into the abdomen with the help of a subdiaphragmatic catheter. Fluid from the drainage catheter was collected. The collected perfusate was rewarmed and reinfused with the help of infusion through the subdiaphragmatic catheter. Processing was continued for 30 minutes. The remaining dose was placed in two parts in another 100 mL of physiological saline. The same process was repeated twice for 30 min. The intraperitoneal temperature was measured during the procedure with a thermometer placed in the rectovesical area. The infusion temperature was changed to maintain the temperature between 40.5 and 41.5°C. After the procedure, the abdomen was opened and washed with physiological saline for 10 minutes. The drainage catheters were removed. The abdomen was closed with 5.0 silk sutures over a double layer. (Figure 1)

Sildenafil Administration

Sildenafil (10 mg/kg; dissolved in pH 4 water) was administered via orogastric gavage for three days, the first of which was administered at the 2nd postoperative hour.

Postoperative Evaluation and Sacrifice

Seven days after the procedure, the rats were

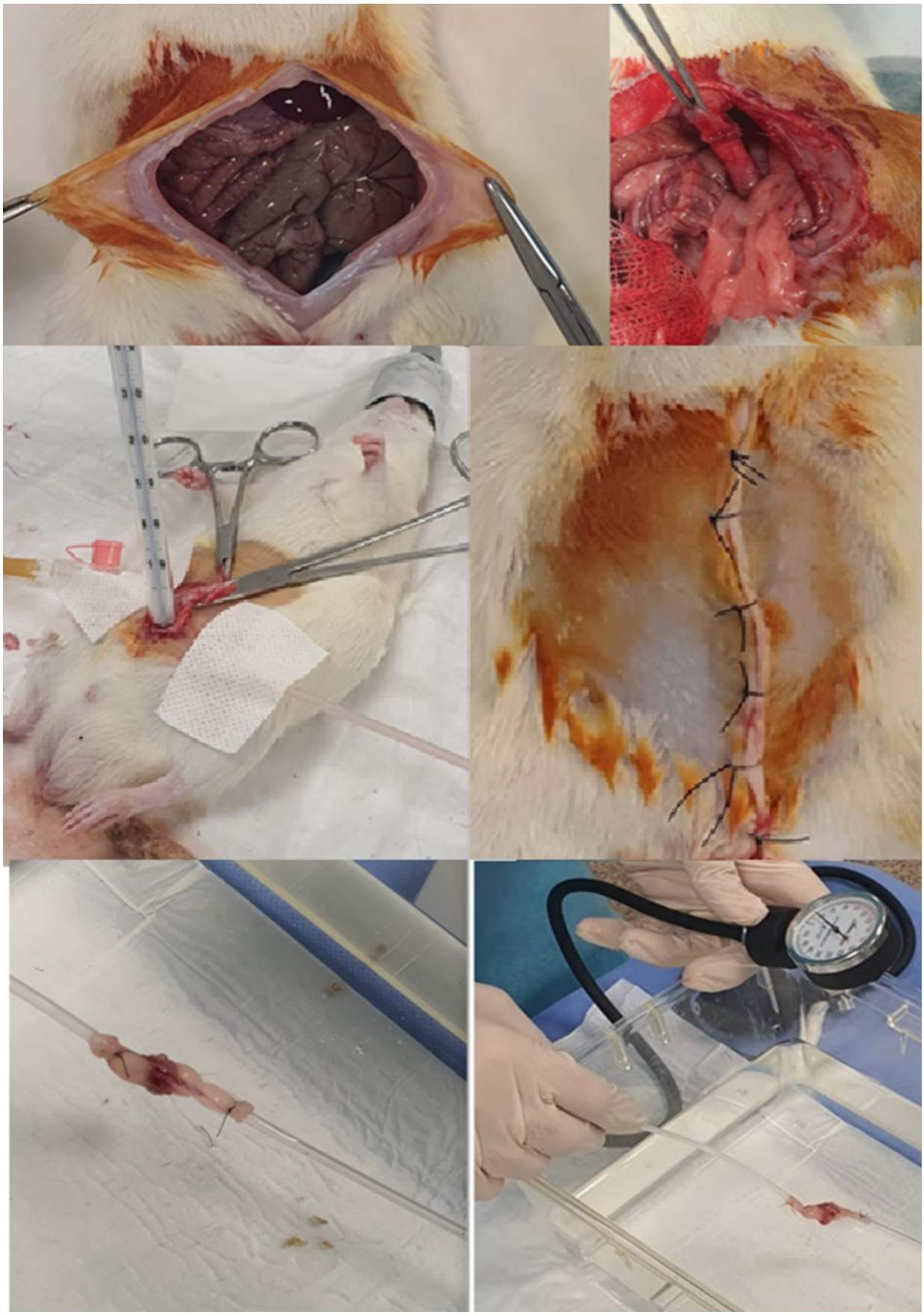


Figure 1. A) Rat abdomen undergoing laparotomy, **B)** Left colon after anastomosis, **C)** HIPEC process and peritoneal temperature measurement, **D)** Sutured abdomen with a silk suture, **E)** Burst pressure measuring setup, **F)** Burst pressure measuring with a sphygmomanometer

sacrificed by administering a high dose of anesthetic. The abdomen was opened and the anastomosis line was evaluated for adhesion. The anastomosis line was graded according to the adhesion around it. While the evaluation was carried out without the knowledge of the groups, data were collected by the researcher.

Measurement of Anastomotic Burst Pressure

The anastomotic loop was excised by extending 1 cm from the proximal and distal ends. The proximal end was threaded and ligated with an inflation device and the distal end was threaded and ligated with a sphygmomanometer. The loop was placed in a tub filled with water. The loop was inflated with air and pressure was measured with a sphygmomanometer. The integrity of the anastomosis was disrupted, air bubbles appeared and a sudden decrease in the sphygmomanometer was recorded by measuring the pressure. This pressure was accepted as the burst pressure.

Histopathological Examination

After the operation, the colon resection material of each rat was sampled by a pathologist, cassetteed, and paraffin blocked. The slides were prepared and stained with hematoxylin-eosin and Masson-Trichrome stains. Colon perforation, serosal inflammation, the presence of fibroblasts, mononuclear cells, and neovascularization were noted during the examination. Inflammatory granuloma and granulation tissue formation, fibrosis formation, inflammatory cell infiltration, and neovascularization were determined according to Ehrlich and Hunt's numerical scale modified by Phillips et al (9).

Statistical analysis

The Number Cruncher Statistical System (NCSS) (Utah, USA) program was used for statistical analysis. While evaluating the study data, descriptive statistical methods (mean, standard deviation, median, IQR, frequency, ratio) as well as the Shapiro-Wilk test and box plot graphics were used for assessing the compliance of the variables with a normal distribution. The Kruskal-Wallis test was used for the comparisons of the variables that were not normally distributed, and the Dunn test was used to determine whether the group was significantly different. The Fisher–Freeman Halton test was used to compare qualitative data. Significance was evaluated at the $p<0.05$ level.

Results

In the present study, there were two deaths in the study and control groups and one death in the sham group. New subjects were added to the study to complete the number instead of the number of dying subjects. One rat from the control group died on the 3rd postoperative day. In the sham group, two rats died on the 1st postoperative day and one rat died on the 2nd postoperative day. After sacrifice, the area around the anastomosis was evaluated for adhesion. There was a significant difference in adhesion between the sham group, sildenafil group ($p=0.001$), and control group ($p=0.026$) (Table 1).

Table 1. Perianastomotic adhesion

	Grade 0	Grade 1	Grade 2	Grade 3	Total	Median (IQR)
Sildenafil Group	0	2	3	5	10	2.5 (1-3)
Control Group	0	5	3	1	9	1 (1-3)
Sham Group	3	4	0	0	7	0 (0-1)
p						0.001**
Post hoc						$P_{1\&3}$=0.001** $P_{2\&3}$=0.026*

Kruskal Wallis test & post hoc Dunn test, *p<0.0, **p<0.01, IQR: 25%-75%

Anastomotic burst pressures were measured one by one. For five rats in the sildenafil group and four rats in the control group, measurements could not be performed because of point perforation or full-thickness separation. When the measured animals were evaluated, there was no significant difference among the three groups ($p>0.05$) (Table 2).

Table 2. Anastomosis Bursting Pressure

	Mean±SD	Median (IQR)	p
Sildenafil Group	160±23.45	150 (145-180)	
Control Group	150±8.16	150 (142.5-157.5)	**0.648**
Sham Group	179.68±71.61	200(125-250)	

Kruskal Wallis test, IQR: 25%-75%, SD: Standard deviation

Inflammatory granuloma and granulation tissue formation were compared between the groups. The inflammatory cell grades in the sham group were significantly lower than those in the sildenafil group ($p=0.025$) and control group ($p=0,006$) (Table 3).,

Table 3. Formation of inflammatory granuloma and granulation tissue

	Sildenafil Group	Control Group	Sham Group	p
Fibroblastic Proliferation				
Minimum	0	0	0	
Mild	1	4	4	
Moderate	4	5	1	
Intense	5	0	2	
Median (IQR)	3.5 (3-4)	3 (2-3)	2 (2-4)	0.025*
			Post Hoc	$P_{1\&2}$=0.003** $P_{1\&3}$=0.042* $P_{2\&3}$=0.878
Fibrosis formation				
Minimum	1	6	1	
Mild	3	3	5	
Moderate	6	0	1	
Intense	0	0	0	
Median (IQR)	3 (2-3)	1 (1-2)	2 (2-2)	0.000**
			Post Hoc	$P_{1\&2}$=0.001** $P_{1\&3}$=0.031* $P_{2\&3}$=0.001**
Giant cells				
Minimum	1	8	6	
Mild	8	1	1	
Moderate	1	0	0	
Intense	0	0	0	
Median (IQR)	2 (2-2)	1 (1-1)	1 (1-1)	0.001**
			Post Hoc	$P_{1\&2}$=0.001** $P_{1\&3}$=0.099 $P_{2\&3}$=0.006**
Neovascularization				
Minimum	1	8	6	
Mild	8	1	1	
Moderate	1	0	0	
Intense	0	0	0	
Median (IQR)	2 (2-2)	1 (1-1)	1 (1-1)	0.001**
			Post Hoc	$P_{1\&2}$=0.001** $P_{1\&3}$=0.099 $P_{2\&3}$=0.770

Kruskal Wallis test & post hoc Dunn test, *p<0.05, **p<0.01

When fibrosis formation was examined, fibrosis formation was significantly greater in the sildenafil group than in the control group and sham group (p=0.001; p=0.031). Fibrosis formation was significantly lower in the control group than in the sham group (p=0.001). Analysis of inflammatory infiltration revealed that the inflammatory infiltration in the sham group was significantly lower than that in the sildenafil group (p=0.002) and the control group (p=0.001).

Anastomotic wound inflammatory cell infiltration was compared between the groups. The values in the sham group were significantly lower than those in the sildenafil group (p=0.037) and the control group (p=0.001).

The histiocyte infiltration grade in the control group was significantly lower than that in the sildenafil group (p=0.001) and the sham group (p=0.006) (Table 4).

Table 4. Anastomotic inflammatory cell infiltration

	Sildenafil Group	Control Group	Sham Group	P
Histiocyte Infiltration				
Minimum	0	1	0	
Mild	4	8	5	
Moderate	6	0	2	
Intense	0	0	0	
Median (IQR)	3 (2-3)	2 (2-2)	2 (2-3)	0.001**

Kruskal Wallis test & post hoc Dunn test, *p<0.05, **p<0.01

In terms of giant cells, the histiocyte infiltration grades of the control group were found to be significantly lower than those of the sildenafil group (p=0.001).

Upon examining the neovascularization grades, no significant difference was observed between the sildenafil group and the control group (p=0.408).

Discussion

In colorectal cancers with peritoneal involvement, HIPEC is applied as a treatment in suitable patients (10,11). It has been shown that HIPEC application increases colorectal anastomotic leakage (12). There are few studies in the literature showing that sildenafil application increases the strength of colon anastomosis (5,13,14).

In our study, the death of five rats was observed during surgical intervention. These deaths were thought to be related to the effects of anesthesia. Replacement rats were included in the study to compensate for these losses. Additionally, four rat deaths were recorded during the follow-up period. These deaths were attributed to the effects of chemotherapy or a possible anastomotic leak.

Anastomotic leakage after HIPEC is a clinically important condition. In a study, rectal anastomotic leakage was observed in nine (22%) of 41 patients not undergoing the diverting ileostomy, and the mortality rate within 90 days was 7.1%(15). In another study, the rate of enteric fistula and leakage was 10.5% (16). Therefore, increasing the anastomotic strength and reducing the possibility of leakage without an invasive procedure such as a protective ileostomy are important in terms of clinical improvement and overall cost. Oral and topical agents are being used to prevent anastomotic leakage. For example, studies have shown that platelet-rich plasma applied topically to the anastomosis in rats treated with 5-fluorouracil and

HIPEC strengthens tissue healing (17,18). Sildenafil was used similarly in our study. In the rat model, the effects of sildenafil citrate on the physical resistance and histopathology of the anastomosis, which is assumed to be weakened by HIPEC, were examined.

There were no drug-related side effects or immune reactions throughout the study. In the present study, there were two deaths in the study and control groups and one death in the sham group. New subjects were added to the study to complete the number instead of the number of dying subjects. One rat from the control group died on the 3rd postoperative day. In the sham group, two rats died on the 1st postoperative day, and one rat died on the 2nd postoperative day. Intraoperative deaths were thought to be due to anesthesia-related complications, and postoperative deaths were thought to be due to sepsis. The limited number of rats used was a limitation of our study since the minimal number of rats recommended by the power analysis results was used.

In our study, there was no significant difference between the sildenafil group and the control group in terms of intra-abdominal adhesion. There was a significant difference between the Sham group and both groups. It has been shown in the literature that intraperitoneal chemotherapy causes adhesion (19). The difference with the Sham group is also in line with these results. In a study conducted in the rat anastomosis model in 2008, it was observed that intra-abdominal adhesions were significantly less in rats administered intraperitoneal sildenafil in the exploration performed on the 7th postoperative day (20). Contrary to oral administration in our study, intraperitoneal administration was performed. Although the dose of 8 mg/kg sildenafil given intraperitoneally during the operation was less than the daily dose of 10 mg/kg sildenafil given in our study, it was thought that it may have provided a higher effect in terms of bioavailability. Burst pressure could not be measured effectively in five rats in the sildenafil group and four rats in the control group. Anastomotic leakage occurred in nine rats that underwent HIPEC There was no difference in the number of rats that could be measured between the sildenafil group and the control group. According to various publications in the literature, sildenafil has positive effects on anastomotic burst pressure (13, 20). The reason why no difference was observed in our study is that the negative effect of HIPEC on anastomosis outweighs the effect of sildenafil. There was no significant difference in burst pressure between the sham group and the sildenafil and control groups. Since the burst pressure of the rats could not be measured during the statistical analysis, it was thought that there was no significant difference. In addition, meaningful results can be found in a study by using a larger sample of rats.

When the inflammatory granuloma and granulation tissue formation were examined, significant differences were observed between the sham group and the sildenafil and control groups in terms of the presence of inflammatory cells, and a more intense inflammatory response was observed in the HIPEC-treated rats. In terms of neovascularization, a significant difference was observed between the sham group and the control group, while a statistically insignificant difference was observed between the sham group and the sildenafil group. There was a significant difference between the sildenafil group and the control group in terms of fibroblastic proliferation and fibrosis formation. In a study conducted in canine open wounds in 2002, it was stated that fibroblastic proliferation increased in response to sildenafil and this change accelerated wound healing (21). Although sildenafil has been shown to reduce pulmonary fibrosis, it accelerates wound healing by increasing epithelial fibrosis during wound healing (22).

In our study, no significant difference was observed between the sildenafil group and the other groups in terms of neutrophil or lymphocyte infiltration or anastomotic inflammatory infiltration and neovascularization. While there was a significant difference between the sildenafil group and the control group in terms of histiocytes, a significant difference was observed between the sildenafil group and both groups in terms of giant cells. Giant cells and histiocytes play important roles in the granulation that occurs during wound healing. Consequently, sildenafil is expected to increase granulation.

In the meta-analysis of studies on anastomosis resistance, positive effects of many agents on anastomosis were observed. In addition, agents whose effectiveness has been proven in many studies have not been proven to have a significant effect (23-27). In our study, sildenafil increased fibrosis and granulation. However, there was no difference in burst pressure or adhesion, as were the differences in the agents used in other studies.

Study Limitations

A prominent limitation of this study is the lack of compatibility between the animal model and the

human model. When extrapolating chemical dosages from humans to rodents, an appropriate dosage cannot be established. Additionally, the limited similarity of wound healing between rodents and humans restricts the applicability of findings. Beyond these concerns, animal sampling may not be sufficient for producing statistically meaningful results.

Conclusion

On colon anastomosis performed together with HIPEC application, histopathologically positive effects of sildenafil were observed. The burst pressure of the colon anastomosis was not significantly different.

Disclosure Statement: The authors declare that they have no relevant or material financial interests that relate to the research described in this paper.

Statements and Declarations

1. Conflict of Interest Statement: The authors declare that they have no conflicts of interest regarding the publication of this paper.

2. Funding Statement: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

3. Ethical Approval: This research adhered to the ethical standards outlined in "The Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH), ensuring the appropriate care and use of animals. Additionally, international, national, and institutional guidelines relevant to the ethical treatment of animals in research were strictly followed. The study was conducted under the principles of "The International Guiding Principles for Biomedical Research Involving Animals." All necessary approval was obtained from the institutional ethical review board, and the research procedures complied with established ethical standards to safeguard the well-being of the animals involved.

References

1.Bruce J, Krukowski ZH, Al-Khairy G, Russell EM, Park KGM. A systematic review of the definition and measurement of anastomotic leak after gastrointestinal surgery. British Journal of Surgery [Internet]. 2001;88:1157–68. Available from: www.bjs.co.uk

2.Moran H, Moran BJ, Heald RJ. Anastomotic Leakage After Colorectal Anastomosis. Vol. 18, Seminars in Surgical Oncology. 2000.

3.Pelz JOW, Doerfer J, Decker M, Dimmler A, Hohenberger W, Meyer T. Hyperthermic intraperitoneal chemoperfusion (HIPEC) decrease wound strength of colonic anastomosis in a rat model. Int J Colorectal Dis. 2007 Aug;22(8):941–7.

4.Turaga K, Levine E, Barone R, Sticca R, Petrelli N, Lambert L, et al. Consensus guidelines from the American Society of Peritoneal Surface Malignancies on standardizing the delivery of hyperthermic intraperitoneal chemotherapy (HIPEC) in colorectal cancer patients in the United States. Ann Surg Oncol. 2014;21(5):1501–5.

5.Uzun H, Konukoglu D, Nuri MK, Ersoy EY, Özçevik S, Yavuz N. The effects of sildenafil citrate on ischemic colonic anastomotic healing in rats: Its relationship between nitric oxide and oxidative stress. World J Surg. 2008 Sep;32(9):2107–13.

6.Lee RH, Efron D, Tantry U, Barbul A. Nitric oxide in the healing wound: A time-course study. In: Journal of Surgical Research. Academic Press Inc.; 2001. p. 104–8.

7.Hasanoğlu Adnan, Erkan Serkan, Temel Selim, Urhan M. Kemal, Güler Osman. Effect of sildenafil citrate on healing of colonic anastomoses. Turkish Medical Journal. 2007;1:66–75.

8.Molyneux G, Gibson FM, Gordon-Smith EC, Pilling AM, Liu KC, Rizzo S, et al. The haemotoxicity of mitomycin in a repeat dose study in the female CD-1 mouse. Vol. 86, Int. J. Exp. Path. 2005.

9.Phillips JD, Kim CS, Fonkalsrud EW, Zeng H, Dindar H. Effects of Chronic Corticosteroids and Vitamin A on the Healing of Intestinal Anastomoses. The American Journal of Surgery. 1992 Jan;163:71–7.

10.NCCN Clinical practice guidelines in oncology, Colon Cancer Version 1.2022.

11.Schneebaum S, Arnold MW, Staubus A, Young DC, Dumond D, Martin EW. Intraperitoneal Hyperthermic Perfusion with Mitomycin C for Colorectal Cancer with Peritoneal Metastases. Vol. 3, Annals of Surgical Oncology. 1996.

12.López-López V, Lynn PB, Gil J, García-Salom M, Gil E, González A, et al. Effect of Paclitaxel-based Hyperthermic Intraperitoneal Chemotherapy (HIPEC) on colonic anastomosis in a rat model. Clinical and Translational Oncology. 2019 Apr 9;21(4):505–11.

13.Hasanoğlu Adnan, Erkan Serkan, Temel Selim, Urhan M. Kemal, Güler Osman. Effect of sildenafil citrate on healing of colonic anastomoses. Turkish Medical Journal. 2007;(1):66–75.

14.Cakir T, Ozer I, Bostanci EB, Keklik TT, Ercin U, Bilgihan A, et al. Increased collagen maturity with sildenafil citrate: Experimental high-risk colonic anastomosis model. International Journal of Surgery. 2015 Jan 1;13:152–6.

15.Whealon MD, Gahagan J v., Sujatha-Bhaskar S, O'Leary MP, Selleck M, Dumitra S, et al. Is Fecal Diversion Needed in Pelvic Anastomoses During Hyperthermic Intraperitoneal Chemotherapy (HIPEC)? Ann Surg Oncol. 2017 Aug 1;24(8):2122–8.

16.Piso P, Nedelcut SD, Rau B, Königsrainer A, Glockzin G, Ströhlein MA, et al. Morbidity and Mortality Following

Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: Data from the DGAV StuDoQ Registry with 2149 Consecutive Patients. Ann Surg Oncol. 2019 Jan 15;26(1):148–54.

17.Gorur M, Sozutek A, Irkorucu O, Karakaya B. The influence of platelet-rich plasma (PRP) on colonic anastomosis healing is impaired by intraperitoneal 5-fluorouracil application. An experimental study. Acta Cir Bras. 2020;35(5):1–9.

18.Buk OF, Ocak S, Genc B, Avcı B, Uzuner HO. Is platelet-rich plasma improves the anastomotic healing in hyperthermic intraperitoneal chemotherapy with oxaliplatin: An experimental rat study. Ann Surg Treat Res. 2020;98(2):89–95.

19.Jacquet P. Sugarbaker PH. Abdominal adhesions causing intestinal obstruction following cytoreductive surgery and early postoperative intraperitoneal chemotherapy. Acta Chir Austriaca. 1995;2.

20.Ayten R, Çetinkaya Z, Girgin M, Ozercan I, Ustundag B, Aygen E. The effects of intraperitoneal sildenafil administration on healing of left colonic anastomoses and intra-abdominal adhesion formation in the presence of intra-abdominal infection. Dis Colon Rectum. 2008 Dec;51(12):1837–41.

21.Taş A, Atasoy N, Özbek H, Aslan L, Yüksel H, Ceylan E, et al. The effects of sildenafil citrate (viagra) in the early phase of the healing process in open wounds in dogs. Acta Veterinaria Brno. 2003;72(2):273–7.

22.David A. Zisman, Marvin Schwarz. A Controlled Trial of Sildenafil in Advanced Idiopathic Pulmonary Fibrosis. New England Journal of Medicine [Internet]. 2010 Aug 12 [cited 2022 May 1];363(7):620–8. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMoa1002110

23.Øines MN, Krarup PM, Jorgensen LN, Ågren MS. Pharmacological interventions for improved colonic anastomotic healing: A meta-analysis. Vol. 20, World Journal of Gastroenterology. WJG Press; 2014. p. 12637–48.

24.Karahasanoğlu T, Altınlı E, Hamzaoğlu İ. Effect of growth hormone treatment on the healing of left colonic anastomoses in protein-malnourished rats. British Journal of Surgery. 1998;85:931–3.

25.Moran M, Ozmen MM, Duzgun AP, Gok R, Renda N, Sedan S, et al. The effect of erythropoietin on healing of obstructive vs nonobstructive left colonic anastomosis: An experimental study. World Journal of Emergency Surgery. 2007;2(1).

26.Dauser B, Heitland W, Bader FG, Brunner W, Nir Y, Zbar AP. Histologic changes in early colonic anastomotic healing using autologous platelet-rich fibrin matrix. European Surgery - Acta Chirurgica Austriaca. 2020 Aug 1;52(4):155–64.

27.Sümer A, Altinli E, Senger S, Köksal N, Onur E, Ero□lu E, et al. Effect of pentoxifylline and vinpocetine on the healing of ischemic colon anastomosis: An experimental study. Ulusal Travma ve Acil Cerrahi Dergisi. 2011;17(6):482–7.

Received: 27 Sep 2024 | **Accepted:** 22 Mar 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 382-387
DOI: 10.54005/geneltip.1557225

ORIGINAL ARTICLE

Effects of Hydroxychloroquine Treatment on QTc Interval in COVID-19 Positive Patients with Schizophrenia

COVID-19 Pozitif Şizofreni Hastalarında Hidroksiklorokin Tedavisinin QTc Aralığı Üzerindeki Etkileri

[1]Beyazit Garip, [2]Şükran Tekin

[1]Gülhane Training and Research Hospital, Department of Psychiatry, Ankara, Türkiye
[2]LWL-Klinik Dortmund, Department of Psychiatry, Marsbruchstraße 179, 44287, Dortmund, Germany

Correspondence

Beyazit Garip, MD.
Gulhane Training and Research Hospital, General Tevfik Saglam Caddesi, Emrah Mahallesi No: 11 Room 2, Etlik-Ankara, Türkiye

E-Mail: beyazitgarip@gmail.com

How to cite ?

Garip B, Tekin Ş. Effects of Hydroxychloroquine Treatment on QTc Interval in COVID-19 Positive Patients with Schizophrenia. Genel Tıp Derg. 2025;35 (2): 382-387

ABSTRACT

Aim: The effect of hydroxychloroquine (HCQ) treatment on the corrected QT interval (QTc) in COVID-19-positive schizophrenia patients was a significant topic of discussion at the beginning of the pandemic. While the efficacy of HCQ remains controversial, severe cardiac side effects such as QTc prolongation can potentially lead to life-threatening arrhythmias. This study aims to investigate the potential impact of HCQ on QTc prolongation when used in combination with antipsychotic medications.
Materials and Methods: This retrospective study includes 25 schizophrenia patients diagnosed with COVID-19 and undergoing antipsychotic treatment. Electrocardiographic (ECG) data obtained during routine follow-up were retrospectively evaluated. The dose management of antipsychotic drugs during treatment was analyzed. A QTc interval of 500 ms or longer was considered the pathological threshold.
Results: A significant prolongation of the QTc interval was observed on the 3rd and 5th days of HCQ treatment, as well as on the first day after discontinuation, compared to the QTc intervals recorded at hospital admission ($p < 0.05$). Gender-based analysis revealed that significant QTc changes were observed only in female patients on the 2nd and 3rd days of HCQ treatment ($p < 0.05$). In cases where QTc prolongation occurred, no common characteristics were identified in terms of medications used, clinical diagnoses, or comorbid conditions.
Conclusion: The potential QTc prolongation associated with HCQ use is considered a significant risk factor for ventricular fibrillation and sudden cardiac arrest. The combination of HCQ with antipsychotic medications may lead to potentially life-threatening cardiac side effects. Therefore, regular monitoring of cardiac electrical activity, particularly QTc interval, is critically important.

Keywords: Antipsychotics, COVID-19, hydroxychloroquine, QTc interval, schizophrenia

ÖZ

Giriş: COVID-19 pozitif şizofreni hastalarında hidroksiklorokin (HCQ) tedavisinin corrected QT interval (QTc) aralığı üzerindeki etkisi, pandeminin başlangıcında önemli bir tartışma konusu olmuştur. HCQ'nun etkinliği halen tartışmalı olmakla birlikte, QTc uzaması gibi ciddi kardiyak yan etkileri potansiyel olarak hayatı tehdit eden aritmilere yol açabilmektedir. Bu çalışmanın amacı, HCQ'nun antipsikotik ilaçlarla birlikte kullanıldığında QTc uzaması üzerindeki potansiyel etkisini araştırmaktır.
Gereç ve Yöntemler: Bu retrospektif çalışma, COVID-19 tanısı almış ve antipsikotik tedavi gören 25 şizofreni hastasını içermektedir. Takip sürecinde rutin olarak elde edilen elektrokardiyografik (EKG) veriler retrospektif olarak değerlendirilmiştir. Tedavi sürecinde antipsikotik ilaçların doz yönetimi analiz edilmiştir. QTc aralığının 500 ms ve üzerinde olması patolojik sınır olarak kabul edilmiştir.
Bulgular: HCQ tedavisinin 3. ve 5. günlerinde ve tedavinin kesildiği ilk gün, hastaneye yatış sırasında kaydedilen QTc aralıklarıyla karşılaştırıldığında, QTc aralığında anlamlı bir uzama olduğu belirlenmiştir ($p < 0.05$). Cinsiyete göre yapılan analizde, QTc aralığında anlamlı değişiklik yalnızca kadın hastalarda HCQ tedavisinin 2. ve 3. günlerinde gözlemlenmiştir ($p < 0.05$). QTc uzaması gelişen olgularda, kullanılan ilaçlar, klinik tanı veya eşlik eden hastalıklar açısından ortak bir özellik saptanmamıştır.
Sonuç: HCQ kullanımına bağlı olası QTc uzaması, ventriküler fibrilasyon ve ani kardiyak arrest açısından önemli bir risk faktörü olarak değerlendirilmektedir. HCQ'nun antipsikotik ilaçlarla birlikte uygulanması, potansiyel olarak yaşamı tehdit edebilecek kardiyak yan etkilere yol açabilmektedir. Bu nedenle, özellikle QTc aralığı başta olmak üzere kardiyak elektriksel aktivitenin düzenli olarak izlenmesi kritik öneme sahiptir.

Anahtar Kelimeler: Antipsikotikler, COVID-19, hidroksiklorokin, QTc aralığı, şizofreni

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused a pandemic in 2019, leading to significant economic and social issues worldwide (1). At the beginning of the pandemic, the absence of a vaccine to prevent COVID-19 and the lack of an established treatment protocol led to the exploration of alternative therapeutic options. Among these alternatives, chloroquine (CQ) and hydroxychloroquine (HCQ), drugs that have been used for many years in the treatment of malaria, were reported as potentially good options that could be effective in treatment. Although primarily used to prevent and treat malaria, HCQ and CQ were also used in the treatment of rheumatoid arthritis, lupus, and porphyria cutanea tarda and were among the first off-label approved drugs for COVID-19 treatment. Regarding HCQ effectiveness and safety, a growing number of studies have been published with conflicting results (2).

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

The prolongation of the corrected QT interval (QTc), an electrocardiographic parameter reflecting ventricular repolarization, is a key indicator of cardiac risk. A prolonged QTc interval can result in severe consequences, including Torsades de Pointes, ventricular fibrillation, and sudden cardiac arrest. This risk may be further exacerbated when QTc-prolonging medications, such as certain first-generation antipsychotics, are used concurrently(3). The simultaneous use of antipsychotics and HCQ has raised concerns regarding proper management. While previous studies have primarily focused on the general cardiac side effects of HCQ, the specific risks in COVID-19-positive schizophrenia patients - a particularly vulnerable group - have not been thoroughly investigated. It is well established that antipsychotics, particularly first-generation agents such as chlorpromazine and haloperidol, negatively affect cardiac rhythm conduction and significantly prolong the QTc interval (3). In patients with pre-existing QTc prolongation, this can substantially increase the risk of life-threatening arrhythmias, including ventricular fibrillation(4).

The primary objective of this study is to assess the impact of HCQ treatment on QTc intervals in schizophrenia patients with COVID-19, particularly in combination with antipsychotics, and to evaluate the potential risks associated with QTc prolongation. Additionally, changes in QTc intervals following the concurrent use of antipsychotics with HCQ, azithromycin, and favipiravir were documented. The treatment strategy and COVID-19 management algorithm were retrospectively analyzed, taking into account comorbid conditions that could influence QTc intervals.

Materials and Methods

Subjects and Procedures

This retrospective study was conducted on patients with schizophrenia spectrum disorders (n=25), including 10 females and 15 males, diagnosed with COVID-19. Patients with other psychiatric comorbidities or conditions such as multi-organ failure, treatment-resistant electrolyte imbalances, known cardiac arrhythmia, heart failure, previous cardiac surgery, or those on ongoing antiarrhythmic medications were excluded from the study. Biochemical tests (whole blood and routine biochemistry) and radiological tests (chest computerized tomography) were conducted, and infection with the SARS-CoV-2 virus was confirmed via PCR testing during initial hospitalization.

Patients were categorized according to the World Health Organization (WHO) severity scale (mild, moderate, severe, critical). The association between disease severity and QTc prolongation was examined; however, no significant correlation was identified. Antipsychotic doses were managed based on chlorpromazine equivalent doses before the initiation of HCQ treatment. To prevent possible QTc prolongation, antipsychotic doses were reduced to half of the normal dose in hospitalized patients. All patients received five days of HCQ treatment according to the COVID-19 guidelines issued and updated by the Turkish Republic Ministry of Health Science Board. According to the guidelines, when additional treatment was required, azithromycin (n = 8) and favipiravir (n=1) were administered.

Electrocardiographic measurements were taken before treatment and during the five-day follow-up period using the same General Electric (GE) device (Model: MAC200), and again seven days after discontinuation of HCQ treatment. A follow-up ECG was performed on Day 7 after HCQ discontinuation as part of routine monitoring to evaluate potential late-onset QTc prolongation, per institutional protocol. QTc intervals of 470 ms in females and 450 ms in males were considered the upper limit, with longer QTc intervals considered pathological. QTc intervals of more than 500 ms were considered potentially life-threatening, possibly causing severe arrhythmias in both genders. QTc intervals measured before HCQ treatment were compared with those during the five-day treatment period and the seven days following the completion of HCQ treatment.

Statistical Analyses and Ethics

All data were expressed as mean ± standard error of the mean (SEM). QTc intervals were compared using Student's t-test for paired samples, and a Bonferroni correction was applied to account for experiment-wise error due to multiple comparisons. The correlations between daily QTc intervals and the chlorpromazine-equivalent doses of the antipsychotics were calculated using Pearson's test. The sample size was determined using G*Power v3.1.9.4, and it was estimated that 23 patients would be required to achieve adequate power (0.80) with an estimated effect size (d=0.82). Statistical significance was set at $p < 0.05$. The local institutional ethics board at Ankara City Hospital approved this study (June 25th, 2020,

#E1-20-773), and approval was obtained from the Turkish Ministry of Health (Approval certificate number: 2020-05-13T22-06-22).

Electrocardiographic Measurements

ECG measurements were obtained using a General Electric MAC200 device, which is known for its reliability and precision in capturing cardiac electrical activity. Standard settings for the device included a recording speed of 25 mm/s and an amplitude of 10 mm/mV, both of which are widely recognized for ensuring accurate waveform representation. The QTc intervals were calculated using Bazett's formula, a commonly used method for correcting the QT interval for heart rate. The visual showing the QTc measurement has been included in Figure 3.

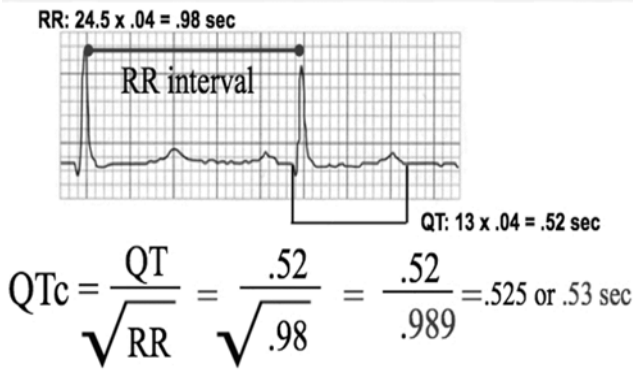


Figure 3. The visual shows the, P wave, QRS complex, and T wave, with markers highlighting the QT interval and the QTc calculation, including Bazett's formula

Results

The patients were 48.64±2.24 years old, with no significant difference in age between male and female patients (p >0.05; males: 51.27±3.03 vs females: 44.70±3.02 years). The patients were treated with several atypical antipsychotic drugs (n=11, olanzapine; n=6, risperidone; n=3, aripiprazole; n=3, quetiapine; n=1, clozapine; n=1, paliperidone). The mean chlorpromazine equivalent dose was calculated as 427.31±66.99 mg/day.

The results of the QTc intervals are presented in Table 1, and Figures 1 and 2. According to the data, QTc intervals exceeded the upper limit between the 3rd and 5th days of HCQ treatment, and on the first day after HCQ discontinuation, compared to the baseline QTc recorded at initial admission (p <0.05; Figure 1). Since the upper limits of QTc prolongation differ between men and women, these two groups were evaluated separately in the next stage. The QTc duration upper limits are 470 ms for women and 450 ms for men. HCQ treatment significantly increased QTc durations on the 2nd and 3rd days of the treatment period compared to baseline levels (p <0.05, Figure 2). The difference in QTc duration compared to baseline reached statistically significant levels only in women and on the 2nd and 3rd days of HCQ treatment (p <0.05, Figure 2).

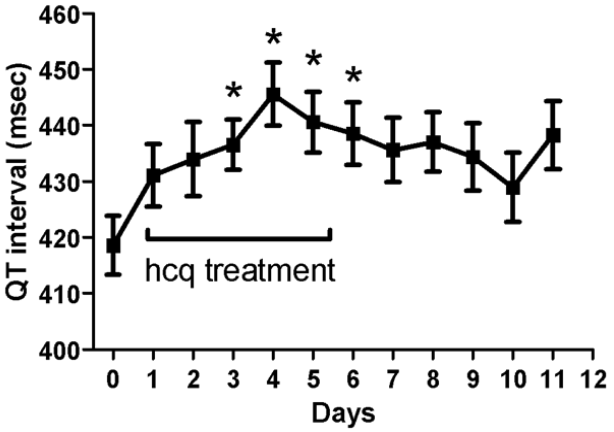


Figure 1. QTc intervals exceeded the upper limit between 3rd and 5th days

Table 1. QTc Interval (msec) of the patients categorized according to sex.

	All the patients (n=25)			Male (n=15)			Female (n=10)		
Days	Mean±SD	Median	Min-Max	Mean±S.D.	Median	Min-Max	Mean±SD	Median	Min-Max
0	418.56±26.28	415.0	355-469	414.60±26.57	410.0	355-460	424.50±24.67	419.5	391-469
1 (HCQ)	431.08±27.24	430.5	366-479	426.07±31.40	416.5	366-479	438.10±17.76	438.5	411-471
2 (HCQ)	433.96±33.04	438.0	349-492	427.73±29.01	433.0	378-478	443.30±36.36*	452.0	349-492
3 (HCQ)	436.54±21.96*	434.5	377-488	431.86±22.38	432.0	377-466	443.10±19.57*	435.0	421-488
4 (HCQ)	445.58±27.50*	447.5	385-497	440.36±23.58	447.5	385-473	452.90±30.74	457.5	402-497
5 (HCQ)	440.60±27.06*	443.0	393-492	433.07±23.82	432.0	393-486	451.90±27.67	453.0	400-492
6	438.52±26.75*	441.0	392-495	429.36±20.43	430.0	392 - 464	452.78±29.07	453.0	393-495
7	435.63±28.22	442.0	382-479	431.64±26.46	437.0	390-472	441.20±29.64	450.5	382-479
8	437.04±26.11	442.0	348-480	431.71±27.50	442.0	348-469	444.50±21.96	445.0	411-480
9	434.36±28.27	435.5	385-484	431.00±25.70	435.5	385-471	440.25±31.44	438.0	400-484
10	428.94±26.16	432.0	378-481	426.70±19.03	430.5	392-457	431.75±32.75	439.5	378-481
11	438.27±23.44	447.0	389-467	430.22±22.91	430.0	389-467	450.33±18.54	457.5	411-465

SD: Standard deviation, Min-Max: Minimum-Maximum. (HCQ, hydroxychloroquine treatment; *p <0.05, Student's t-test for paired samples).

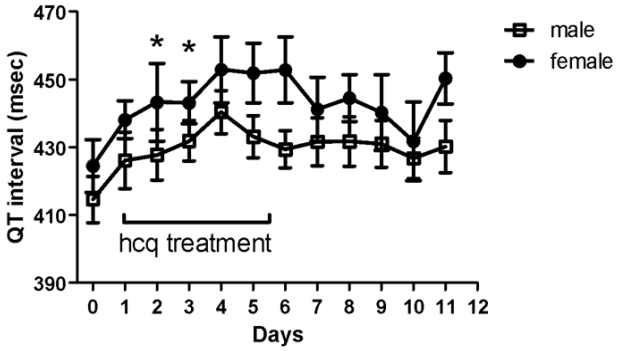


Figure 2. Significant difference in QTc durations on the 2nd and 3rd days after HCQ initiation

The mean±SEM values of QTc intervals did not exceed 450 ms in men or 470 ms in women while patients were followed up in the clinic. Upon individual analysis, cases that occasionally exceeded the borderline showed no common characteristics in terms of drug use, clinical diagnosis, or comorbidities, and these patients exhibited no clinical signs or symptoms. The correlations between QTc intervals and chlorpromazine equivalent doses are presented in Table 2. No significant correlations were observed between these variables.

Table 2. Correlation coefficients and significance levels between chlorpromazine equivalent doses of antipsychotic drugs and QTc intervals

	Days											
	0	1	2	3	4	5	6	7	8	9	10	11
r	0,264	-0,090	0,288	0,066	0,102	0,022	-0,071	0,005	-0,002	-0,429	0,129	0,301
p	0,212	0,682	0,173	0,763	0,643	0,918	0,754	0,982	0,991	0,053	0,623	0,295

Discussion

In the present study, we showed that QTc intervals exceeded the upper limit on the 3rd and 5th days of HCQ treatment, as well as on the first day after discontinuing HCQ, compared to QTc intervals recorded at initial hospital admission ($p < 0.05$). In addition to that significant difference in QTc intervals only in women was seen on the 2nd and 3rd days of HCQ treatment ($p < 0.05$). The present study indicated that patients need to be monitored more closely for QTc prolongation to prevent potential life-threatening side effects when HCQ treatment is administered alongside antipsychotic drugs. QTc prolongation may be associated with the number of antipsychotic drugs prescribed concurrently or with drugs that can cause QTc prolongation, such as HCQ. All drugs that prolong the QTc interval, when prescribed with antipsychotics, should be thoroughly evaluated. Dose adjustments and close monitoring are essential when concurrent use with HCQ is necessary, as failure to do so could lead to life-threatening problems such as ventricular fibrillation or death (5).

According to a randomized clinical study conducted on a large group of patients, a higher dose of HCQ is associated with potentially life-threatening QTc prolongation, especially when taken with azithromycin and oseltamivir (6). The potential risk factor for QTc prolongation with HCQ was identified as doses exceeding 1200 mg/day for 10 days. However, in the present study, HCQ was administered at a loading dose of 800 mg/day on the first day, followed by a reduced dose of 400 mg/day. Therefore, our procedure differed from the studies we compared with. Additionally, our study group consisted of younger patients (average age: 48.6 vs. 54.7 years).

Another study indicated that HCQ-induced QTc prolongation in COVID-19 patients, with 500 ms being considered the pathological limit. Takla & Jeevaratnam (7) reported that among the total studies investigating cardiac side effects, 44% identified an increased incidence of QTc prolongation and/or arrhythmias. Furthermore, the addition of azithromycin was associated with more pronounced changes in QTc. A recently published study demonstrated that HCQ/azithromycin treatment led to QTc interval prolongation, with a subset of patients developing a QTc interval exceeding 500 ms (8).

There is evidence suggesting that the effects of HCQ and azithromycin on QTc intervals vary by sex. In a study conducted by Grewal et al (9) female COVID-19 patients exhibited longer mean QTc intervals in two of the three cohorts analyzed. The greater QTc prolongation observed in female COVID-19 patients may be attributed to hormonal differences. Estrogen is known to influence cardiac repolarization, and it is hypothesized that the observed sex-related difference in QTc intervals may result from estrogen-mediated inhibition of potassium channels. The available data suggest that female COVID-19 patients may be more

susceptible to the effects of these drugs, with more pronounced QTc prolongation compared to their male counterparts.

In a separate study evaluating the safety of the azithromycin/ HCQ combination, it was reported that 21% of patients experienced QTc prolongation exceeding 500 ms. A retrospective analysis was performed to investigate the factors contributing to this increase in QTc interval, utilizing regression analyses to assess the potential influence of various variables. Factors associated with QTc prolongation ≥500 ms included age, body mass index (BMI) <30 kg/m², heart failure, elevated creatinine levels, and documented peak troponin levels (10). Notably, patients with underlying metabolic or cardiological conditions demonstrated a more substantial increase in QTc intervals. The study also found that none of the patients, regardless of the presence of underlying conditions, succumbed to life-threatening arrhythmias during the combination therapy. The results suggest that the azithromycin/HCQ combination does lead to QTc prolongation, with the effect being more pronounced in patients with cardiovascular, renal, and age-related issues.

The data regarding the safety of favipiravir and its effect on the QTc interval in COVID-19-positive patients are contradictory. In a study by Çap et al. (11), although HCQ was shown to prolong the QTc interval, no data were found indicating that favipiravir affects the QTc interval. On the other hand, another study by Sertbaş et al. (12) through a post hoc analysis of a subgroup of patients, reported limited statistical data suggesting that favipiravir may prolong the QTc interval. In our study, since only one patient received favipiravir, it was not possible to make any assessment regarding its effect on the QTc interval. While substantial data suggests that azithromycin prolongs the QTc interval, information on the potential effect of favipiravir on the QTc interval remains limited.

In the present study, none of the schizophrenia patients exhibited QTc prolongation beyond 500 ms during COVID-19 treatment. Unlike previous studies, no heart rhythm problems were observed in patients who were on both antipsychotics and the HCQ/ azithromycin combination. Thus, the concurrent use of antipsychotics with HCQ/azithromycin was found to be safe when accompanied by close electrophysiological monitoring. This may be attributable to the inclusion of only eight patients receiving the azithromycin/HCQ combination in our study. Additionally, one possible reason for the lack of observed differences could be the exclusion criterion in our study, which required patients to be free of underlying cardiological or metabolic conditions. While the azithromycin/HCQ combination does prolong the QTc interval, it is crucial to emphasize the need for comprehensive, multi-dimensional patient evaluation and close monitoring when administering this combination therapy.

In conclusion, schizophrenia patients are particularly vulnerable due to coexisting cardiologic and metabolic comorbidities. In cases of COVID-19 infection, it is essential to consider the potential side effects of drug-drug interactions, underlying metabolic abnormalities, and electrocardiographic effects, especially in mentally ill patients, such as those with schizophrenia or intellectual disabilities(13). The limited number of studies on schizophrenia patients makes the management of COVID-19 infection in this population more challenging at that time. One of the most important lessons to be learned from the COVID-19 pandemic is the need for a detailed evaluation of medications and comorbid diseases, particularly for sensitive groups like those with schizophrenia. This vulnerable group often has numerous comorbid pathologies, both mental and physical(14). While current antipsychotics and those used in the past for the treatment of schizophrenia have many side effects, particular attention should be paid to their tendency to prolong the QTc interval, especially when additional treatment is required.

Limitations

There are several limitations to this study. Firstly, the limited sample size (n=25) reduces the statistical power and effect size of the findings. Additionally, this study was conducted retrospectively, and due to the urgent nature of COVID-19 treatment protocols at the time, a control group could not be established, which constitutes another limitation. Future prospective studies, particularly in the event of a new pandemic, should incorporate a matched control group to facilitate a more robust comparative analysis. Furthermore, due to the absence of a control group, multiple comparisons to assess the specific effects of HCQ on QTc prolongation could not be performed.

Conflict of Interest

There is no conflict of interest between the authors.

Data Availability

All of the data related to the study are recorded in

the hospital's digital system. All of the data has been transferred from this system to an Excel file for study purposes. There is no ethical issue to access our data.

Role of funding source

No funding has been received for this study.

Acknowledgment

I would like to sincerely thank Dr. Hakan Kayir and Dr. Turan Ayidaga for their invaluable contributions, as well as all the patients who participated in our study.

References

1.Shamshirian A, Hessami A, Heydari K, Navaei RA, Ebrahimzadeh MA, Yip GW, et al. The Role of Hydroxychloroquine in COVID-19: A Systematic Review and Meta-Analysis. Ann Acad Med Singap. 2020 Oct;49(10):789–800.

2.Chen C, Pan K, Wu B, Li X, Chen Z, Xu Q, et al. Safety of hydroxychloroquine in COVID-19 and other diseases: a systematic review and meta-analysis of 53 randomized trials. Eur J Clin Pharmacol. 2021 Jan;77(1):13–24.

3.Etchegoyen CV, Keller GA, Mrad S, Cheng S, Di Girolamo G. Drug-induced QT Interval Prolongation in the Intensive Care Unit. Curr Clin Pharmacol. 2017;12(4):210–22.

4.Singh AK, Singh A, Singh R, Misra A. "Hydroxychloroquine in patients with COVID-19: A Systematic Review and meta-analysis.". Diabetes Metab Syndr. 2020;14(4):589–96.

5.van den Broek MPH, Möhlmann JE, Abeln BGS, Liebregts M, van Dijk VF, van de Garde EMW. Chloroquine-induced QTc prolongation in COVID-19 patients. Neth Heart J. 2020 Jul;28(7–8):406–9.

6.Gopinathannair R, Merchant FM, Lakkireddy DR, Etheridge SP, Feigofsky S, Han JK, et al. COVID-19 and cardiac arrhythmias: a global perspective on arrhythmia characteristics and management strategies. Journal of Interventional Cardiac Electrophysiology. 2020 Nov 3;59(2):329–36.

7.Takla M, Jeevaratnam K. Chloroquine, hydroxychloroquine, and COVID-19: Systematic review and narrative synthesis of efficacy and safety. Saudi Pharm J. 2020 Dec;28(12):1760–76.

8.Bernardini A, Ciconte G, Negro G, Rondine R, Mecarocci V, Viva T, et al. Assessing QT interval in COVID-19 patients: safety of hydroxychloroquine-azithromycin combination regimen. Int J Cardiol. 2021 Feb 1;324:242–8.

9.Grewal S, Jankelson L, van den Broek MPH, Cour M, Bachmann G, Kostis JB, et al. QTc Prolongation Risk Evaluation in Female COVID-19 Patients Undergoing Chloroquine and Hydroxychloroquine With/Without Azithromycin Treatment. Front Cardiovasc Med. 2020;7:152.

10.O'Connell TF, Bradley CJ, Abbas AE, Williamson BD, Rusia A, Tawney AM, et al. Hydroxychloroquine/Azithromycin Therapy and QT Prolongation in Hospitalized Patients With COVID-19. JACC Clin Electrophysiol. 2021 Jan;7(1):16–25.

11.Çap M, Bilge Ö, Işık F, Burak C, Karagöz A, İnci Ü, et al. The effect of favipiravir on QTc interval in patients hospitalized with coronavirus disease 2019. J Electrocardiol. 2020;63:115–9.

12.Sertbas Y, Ozdil K, Terzi S, Dagci S, Saylan B, Kizilay V, et al. The association between QT interval changes and the treatment protocols of COVID-19 patients. North Clin Istanb. 2022;9(3):199–206.

13.Fonseca L, Diniz E, Mendonça G, Malinowski F, Mari J, Gadelha A. Schizophrenia and COVID-19: risks and recommendations. Brazilian Journal of Psychiatry. 2020 Jun;42(3):236–8.

14.Javelot H, Straczek C, Meyer G, Gitahy Falcao Faria C, Weiner L, Drapier D, et al. Psychotropics and COVID-19: An analysis of safety and prophylaxis. Encephale. 2021 Dec;47(6):564–88.

Received: 04 Dec 2024 | **Accepted:** 28 Jan 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 388-392
DOI: 10.54005/geneltip.1595508

CASE REPORT

Surgical Repair of Multiple Superficial Femoral Artery Pseudoaneurysms Following Failed and Complicated Endovascular Interventions: A Case Report

Başarısız ve Erken Komplikasyon İzlenen Tekrarlayan Endovasküler Girişimler Sonucu Oluşan Çoklu Yüzeyel Femoral Arter Psödoanevrizmasının Cerrahi Onarımı: Olgu Sunumu

[1]Elgin Hacızade, [1]Cavid İbrahimov, [1]Memmed Jafarov, [2]Emre Kubat, [1]Nazim Hacıyev

[1]Central Military Hospital of the Ministry of National Defense of Azerbaijan, Bakü, Azerbaijan
[2]Gülhane Training and Research Hospital, Ankara, Türkiye

Correspondence

Elgin Hacızade M.D.
Central Military Hospital of the Ministry of National Defense of Azerbaijan, Bakü, Azerbaijan

E-Mail: elginhacızade@gmail.com

How to cite ?

Hacızade E, İbrahimov C, Jafarov M, Kubat E, Hacıyev N. Surgical Repair of Multiple Superficial Femoral Artery Pseudoaneurysms Following Failed and Complicated Endovascular Interventions: A Case Report. Genel Tıp Derg. 2025;35 (2): 388-392

ABSTRACT

In recent years, the rise in arterial endovascular procedures has led to an increase in associated complications. In this case, the example we present here demonstrates how an endovascular intervention can be traumatic and complication-prone for total occluded superficial femoral artery, which is their application for long segment total occlusions increase day by day.

Keywords: Complication, endovascular procedures, peripheric vascular diseases

ÖZ

Son yıllarda, arteriyel endovasküler prosedürlerdeki artış, ilişkili komplikasyonlarda bir artışa yol açmıştır. Bu durumda, burada sunduğumuz örnek, endovasküler bir müdahalenin, uzun segmentli total tıkanıklıklar için uygulamaları her geçen gün artan, total tıkalı süperfisyal femoral arter için ne kadar travmatik ve komplikasyona yatkın olabileceğini göstermektedir.

Anahtar Kelimeler: Endovasküler prosedürler, komplikasyon, periferik vasküler hastalıklar

Introduction

Peripheral artery disease (PAD) is characterized by the accumulation of plaques in the arteries of the extremities. It is estimated to affect between 4.3 and 5.9% of individuals aged between 40 years or older, and 14.5% of individuals aged between 70 and older (1). Without successful revascularization, peripheral arterial disease can result in significant morbidity, with a limb loss rate as high as 90% within one year (2). Managing occlusive lesions in the superficial femoral artery (SFA) is a matter of significant debate. Treatment has traditionally involved surgical bypass although endovascular treatment has gained widespread acceptance in recent years with similar outcomes for certain patients (2). Endovascular repair for long-segment occlusion often requires the use of stents. One of the infrequent complications is a stent fracture in SFA and the formation of associated pseudoaneurysms. Here, we report the first documented case of surgical correction of SFA stent fracture with multiple associated pseudoaneurysms following the failure of numerous endovascular treatments.

Case

A 68-year-old male patient with a history of coronary artery bypass surgery, femoropopliteal bypass surgery on the contralateral side, smoking, hyperlipidemia, and undergoing spine surgery was admitted to our clinic with swelling in the groin area, pain, and walking limitation. Initial arterial duplex ultrasound (US) demonstrated multiple SFA pseudoaneurysms due to the stent rupturing the femoral artery at previous interventions (Fig. 1). The patient had undergone left lower extremity

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

angiography and recanalization of the long segment of the left SFA CTO in another center 15 days before, fusiform aneurysms with a maximum diameter of 10 and 8 cm originating from the proximal and mid-portion of

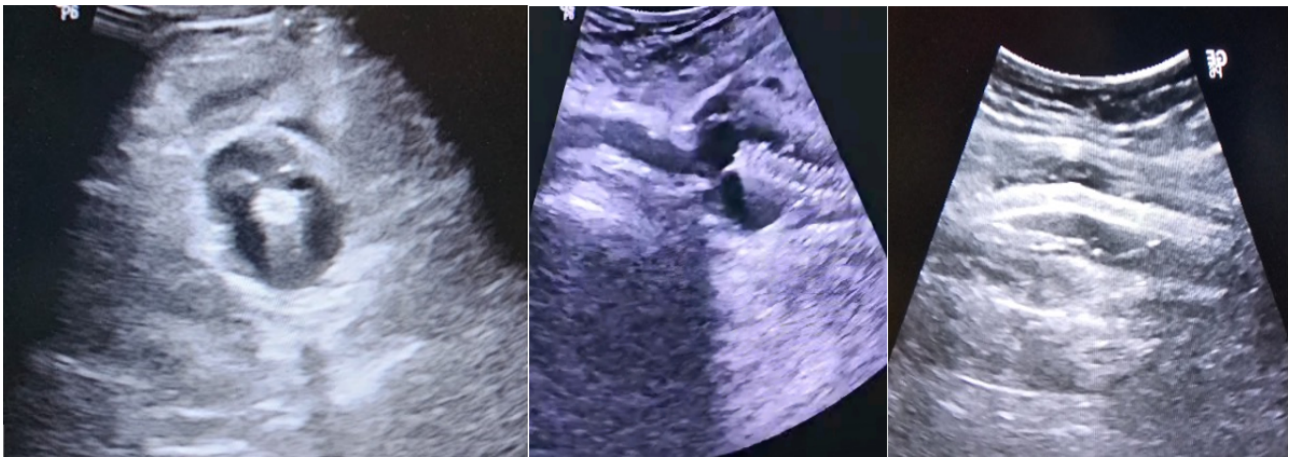


Figure 1. The Doppler ultrasound reveals a distal pseudoaneurysm caused by the rupturing of the distal SFA stent.

applying to us. After reviewing the procedure images, we noticed that two stents had been initially placed. However, after 10 days, they became thrombosed and required reintervention. When the images from the second procedure were examined, we concluded that the stent ruptured the femoral artery due to balloon tension, resulting in the formation of pseudoaneurysms in the proximal and mid-segments between the two stents (Fig. 2).

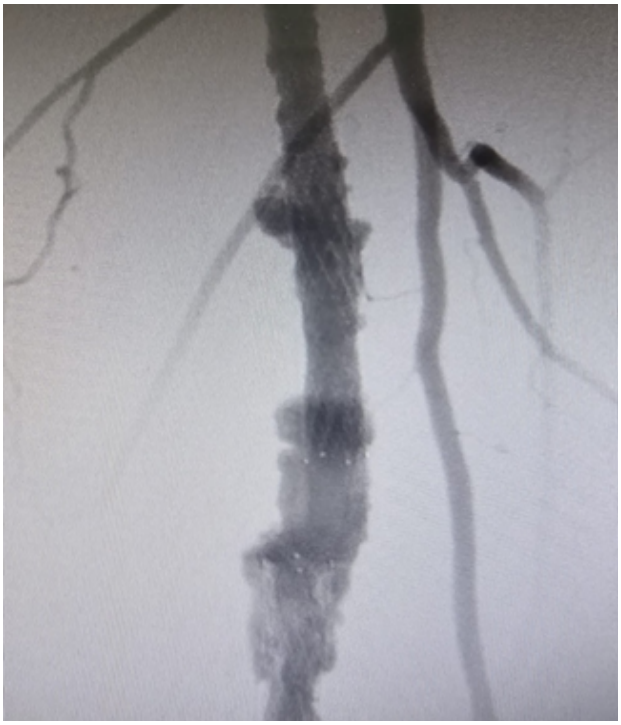


Figure 2. Pseudoaneurysms in proximal and distal SFA and thrombosed stent

The computed tomography scan showed us two SFA (Fig. 3). Images identified proximal and distal stents that had eroded into the tissue around SFA (Fig. 4). We decided these pseudoaneurysms could not be repaired invasively and needed surgical intervention. The patient underwent surgical removal of the extruded SFA stents due to the risk of infection from foreign matter and femoropopliteal bypass surgery with an 8 mm PTFE synthetic vascular graft. After the groin incision, the femoral artery's pseudoaneurysm was reached. The proximal and distal femoral artery was prepared for surgery. Proximal dissection was challenging due to significant inflammation. Fluid collection and stents were encountered within thigh muscle tissue. The pseudoaneurysm sac in the femoral region was opened. After the extruded stents were removed, the proximal common femoral artery was prepared for anastomosis at the bifurcation site, including the deep femoral artery. Thus, the flow of the deep femoral artery was preserved. Following the removal of the stent in the distal region, the vascular graft was used for the bypass to the traditional anastomosis site (Fig. 5A, B, and C). Multiple reactive lymph nodes were observed in the femoral region, and the area was enlarged after the pseudoaneurysm was removed. Based on our experience, we decided to close the enlarged femoral groin. The wound was irrigated with a chlorhexidine solution, and two 15F Blake drains were placed. After the surgery, the Doppler US was performed in the intensive care unit, and peripheral pulses were found to be triphasic. Postoperatively, Acinetobacter baumannii was identified in the wound culture, and antibiotic treatment was started based on sensitivity.

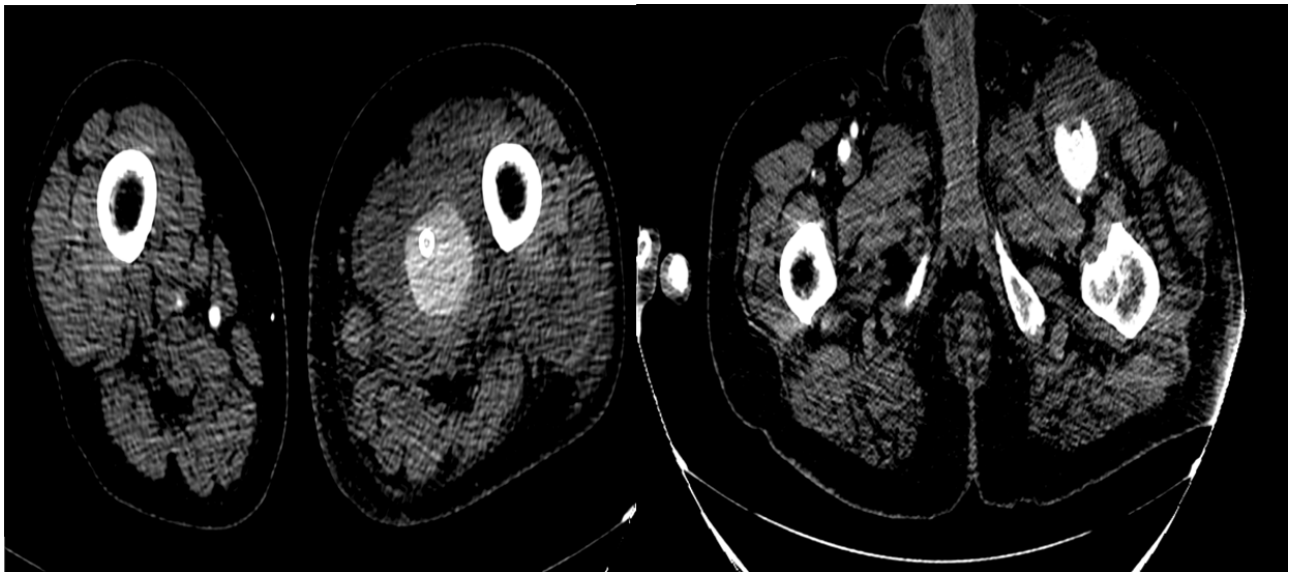


Figure 3. Pseudoaneurysms in proximal and distal SFA and thrombosed stent

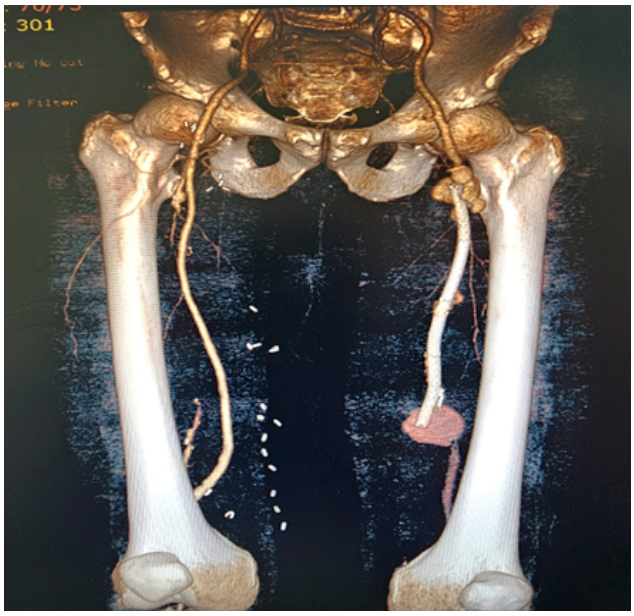


Figure 4. 3 D Computed tomography angiography images of pseudoaneurysm

Despite medical and compression treatments, 100-150 cc of serous lymph fluid was drained from the femoral area daily. After 10 days with no reduction in fluid flow, we decided to revise the femoral region following a plastic surgery consultation. Under general anesthesia, a partial sartorius flap was transferred to cover the vascular graft, reduce lymphorrhea, and prevent infection of the PTFE graft (Fig. 6A and B). The drains were replaced, and the femoral region was anatomically closed. On the 7th day after the second surgery, despite some reduction in lymphorrhea, the drains were not ready for removal. We decided to apply a 1% aethoxysklerol® injection and compression to further reduce the fluid. After three injections and compression over six days, the lymphorrhea decreased and eventually stopped. The patient was discharged in stable condition. A follow-up Doppler US at month 6 showed satisfactory graft patency, and the aneurysm was no longer palpable.

Discussion

In recent years, the increase in the use of arterial endovascular procedures has led to a rise in the frequency of their associated complications. Rarely, wire navigation or catheter manipulation results in vessel wall trauma that may be of sufficient force to cause fatal perforation. In general, prompt use of balloon tamponade is critical once a perforated vessel is identified, along with rapid reversal of anticoagulation and antiplatelet therapy. The SFA is a common site for the development of atherosclerotic plaques in people with symptomatic lower extremity arterial occlusive disease. Traditional treatment for this disease typically involved open arterial bypass surgery, with debate centered on the choice of bypass conduit: autogenous vein (often considered the "gold standard") versus synthetic graft. Several well-designed studies have evaluated this approach, and the results consistently demonstrate its efficacy in promoting long-term limb salvage and improving the quality of life for patients. However, in recent years, there has been a significant shift in the treatment paradigm, with many medical centers adopting an endovascular first approach for all patients. In numerous medical centers, catheter-based interventions are used as the primary treatment for

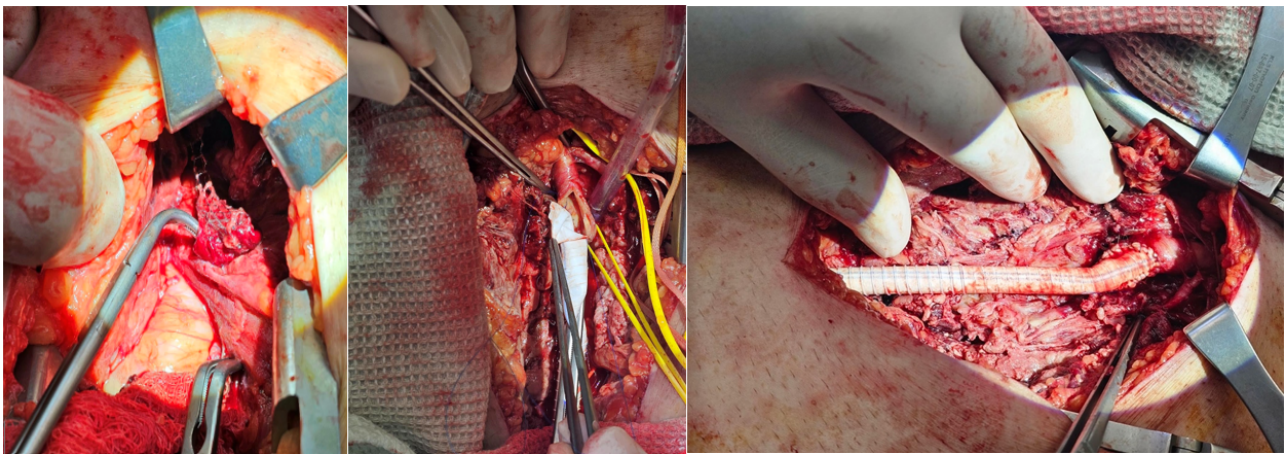


Figure 5. Removing the distal part of the stent material (A). Preserved deep femoral artery (B). Completed proximal anastomosis with 8mm PTFE vascular graft (C)

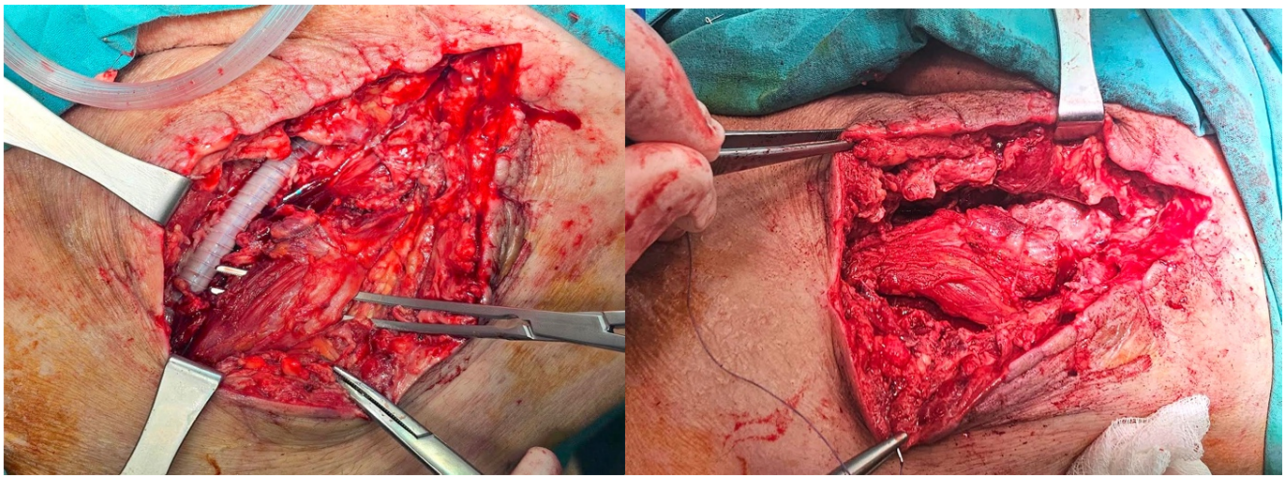


Figure 6. Preparing an incomplete musculus sartorius flap to cover a vascular graft. (A). Covered vascular graft as a result of the completed muscle flap procedure (B)

patients suffering from infrainguinal occlusive disease. Stent fracture is a specific complication of SFA stenting that can lead to restenosis, late clinical failure, and/or pseudoaneurysm development (3). Angioplasty, with or without stenting, is preferred because it has a low risk of complications, shorter recovery time, and is well-accepted by patients. However, the durability of the treatment and its cost-effectiveness are still matters of concern. In 2007, TASC II made the following recommendations for the treatment of femoropopliteal disease (4). Lesions classified as TASC A are most effectively treated by endovascular therapy, while those classified as TASC D are best treated by surgery. According to their recommendation, endovascular therapy is the preferred option for treating TASC B lesions, while surgery is preferable for TASC C lesions. Moreover, while treating B and C lesions, it is important to consider patient comorbidities, patient preference, and operator experience in the decision-making process. In addition, nowadays most patients are not stratified according to TASC classifications, and the results are rarely reported on a treatment basis. According to TASC II recommendations, the endovascular approach is preferred for shorter lesions while the bypass is suggested for longer lesions (4). Comparison of femoral artery stenting and bypass surgery is challenging due to varying study designs; however, the assessment of patency and overall results of different treatment modalities is not well-established (5). However, we suggest an endovascular approach be the primary recommendation for short lesions and elderly patients with severe comorbidities.

Conclusion

In the clinical case we mentioned after perforation of the artery, work was stopped and referred to us. As a result, the results of applying long-segment

stents during long-segment SFA CTOs remain a topic of debate today. Although we accept that endovascular treatments have successful results in appropriate cases, we believe that in such cases that we presented here, the surgical option will be more successful and less traumatic regarding long-term postoperative results.

Conflicts of interest

The authors declare no conflicts of interest.

References

1.Olin JW, White CJ, Armstrong EJ, Kadian-Dodov D, Hiatt WR. Peripheral artery disease: evolving role of exercise, medical therapy, and endovascular options. J Am Coll Cardiol. 2016;67(11):1338–57. https:// doi. org/ 10. 1016/j. jacc. 2015. 12. 049. ISSN 0735-1097.)

2.Wiseman JT, Fernandes-Taylor S, Saha S, Havlena J, Rathouz PJ, Smith MA, Kent KC. Endovascular versus open revascularization for peripheral arterial disease. Ann Surg. 2017;265(2):424–30. https:// doi. org/ 10. 1097/ SLA.00000 00000 001676

3.Schlager O, Dick P, Sabeti S, Amighi J, Mlekusch W, Minar E, Schillinger M. Long-segment SFA stenting—the dark sides: in-stent restenosis, clinical deterioration, and stent fractures. J Endovasc Ther. 2005;12(6):676–84. https:// doi. org/ 10. 1583/ 05- 1672.1

4.Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, et al. Inter-society consensus for the management of peripheral arterial disease (TASC II). J Vasc Surg 2007;45(Suppl S):S5-67

5.Dosluoglu HH, Cherr GS, Lall P, Harris LM, Dryjski ML. Stenting vs above knee polytetrafluoroethylene bypass for Trans Atlantic Inter-Society Consensus II C and D superficial femoral artery disease. J Vasc Surg 2008; 48: 1166–1174. Doi: 10.1016/j.jvs.2008.06.006

Received: 05 Dec 2024 | **Accepted:** 11 Mar 2025 **Genel Tıp Derg. Volume** 35/**Issue** 2 (April), 393-397
DOI: 10.54005/geneltip.1596435

CASE REPORT

Death Due to Artvin Viper Bite: A Case Report

Artvin Engereği Isırığına Bağlı Gelişen Ölüm: Olgu Sunumu

[1]Abdülkadir Sancı, [1]Burak Kaya

[1]Council of Forensic Medicine, Artvin Branch Office. Artvin, Türkiye

Correspondence

Abdulkadir SANCI
Council of Forensic Medicine, Artvin Branch Office. Artvin, Türkiye

E-Mail: akadirsanci@gmail.com

How to cite ?

Sancı A, Kaya B. Death Due to Artvin Viper Bite: A Case Report. Genel Tıp Derg. 2025;35 (2): 393-397

ABSTRACT

It is estimated that approximately 5.4 million people worldwide are heated each year, and 1.8 to 2.7 million of these suffer from poisoning. In Turkey, most snakes belong to the Viperidae family, and species such as the Artvin viper (Vipera kaznakovi) can pose serious health risks, especially in rural and forest areas. This can be found, the case of a 36-year-old foreign male who was bitten by a snake on his left lower extremity while picking tea and died the next day was examined and reported with autopsy ability. Laboratory test results of our case showed hemodynamic deterioration and changes in renal function. Autopsy findings confirmed that multiple organ damage and complications due to snakebite were the cause of death. In such cases, it is thought that simple preventive measures, as well as rapid access to health services, can be effective in reducing injury and mortality rates.

Keywords: Autopsy; snake bite; internal organ damage

ÖZ

Dünya genelinde her yıl yaklaşık 5,4 milyon insanın yılanlar tarafından ısırıldığı ve bunların 1,8 ila 2,7 milyonunun da zehirlenme vakası olduğu tahmin edilmektedir. Türkiye'de, zehirli yılanların çoğu Viperidae familyasına ait olup, Artvin engereği (Vipera kaznakovi) gibi türler, özellikle kırsal ve ormanlık alanlarda bulunarak ciddi sağlık riskleri oluşturabilmektedir. Bu çalışmada, çay toplarken sol alt ekstremitesinden yılan ısırığına maruz kalan ve ertesi gün hayatını kaybeden 36 yaşındaki yabancı uyruklu erkek olgu, otopsi bulgularıyla birlikte incelenerek sunulmuştur. Olgumuza ait laboratuvar test sonuçları, hemodinamik bozulma ve böbrek fonksiyonlarında değişiklikler olduğunu göstermektedir. Otopsi bulguları ise çoklu organ hasarı ile yılan ısırığına bağlı komplikasyonların ölüm sebebi olduğunu doğrulamaktadır. Bu tür vakalarda, sağlık hizmetl erine hızlı erişim kadar, koruyucu basit tedbirlerin de yaralanma ve ölüm oranlarının azaltılmasında etkili olabileceği düşünülmektedir.

Anahtar Kelimeler: Otopsi; yılan ısırığı; iç organ hasarı

Introduction

Snakebite is recognised as a major health problem worldwide. It is estimated that about 5.4 million people are bitten by snakes worldwide each year, and 1.8 to 2.7 million of these are poisoned by snakebites. Although snakebites affect people from almost every geographical region, the majority of deaths occur in rural areas, relatively far from health facilities (1). Approximately 50 snake species are known to live in Turkey. Among these, snakes belonging to the Viperidae (viper) and Elapidea families are the venomous ones (2). Almost all of the venomous snake bites in our country are from the Viperidae (viper) family and the subtypes vary regionally (3). Artvin viper, also known as Caucasian viper (Vipera kaznakovi), is a venomous snake species living in the Black Sea region of Turkey, especially in Artvin and its neighboring provinces (Figure 1). This snake is usually 60-90 cm in length, has a brown and yellow pattern, and has a high camouflage ability thanks to its ability to match the colour of its natural environment. Artvin's viper is usually seen in rural and forested areas and its bites can lead to serious health problems and death if left untreated (4).

Venomous snake bites can cause various toxic effects on the human body. These effects vary depending on the type of snake, venom content and the health status of the person. Snake bite causes various symptoms with local and systemic effects. Local effects include intense pain at the site of the bite, rapidly developing oedema, ecchymosis, hyperaemia and inflammation. Systemic effects include syncope, dyspnoea, nausea, vomiting and shock. Snake venom can affect the

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

nervous system and cause dizziness, while the venom of some species can affect the respiratory system and cause shortness of breath. Nausea and vomiting occur when the venom affects the digestive system. In snake bites with high venom toxicity and quantity, the body may go into a state of shock and this situation requires emergency intervention. Rapid recognition of symptoms after a snake bite is critical for treatment. Therefore, individuals exposed to snake bites should receive urgent medical treatment. Without timely medical intervention, the possibility of death is high. Death usually occurs within 6-48 hours (5).

Figure 1. Artvin (Caucasian) Viper (Vipera kaznakovi) (4)

In this study, it was aimed to discuss the findings obtained from toxicological and histopathological examination of the samples taken during the autopsy of a 36-year-old male case who was autopsied in Artvin Forensic Medicine Branch Directorate with the claim that he died as a result of snake bite while collecting tea, in the light of the findings obtained from toxicological and histopathological examination of the samples taken during the autopsy and to contribute to the forensic medicine practice and to contribute to the literature.

This study was approved by the Artvin Coruh University ethics committee (decision number: E-18457941-050.99-152219; decision date: November 21, 2024). The study was conducted in accordance with the Declaration of Helsinki and permission was obtained from the Council of Forensic Medicine, Education and Scientific Research Commission (decision number:21589509,72024/1448; decision date: December 03, 2024.

Case

According to the forensic and medical documents prepared for the 36-year-old case, who has dual citizenship of Afghanistan and Turkey; the patient was collecting tea as an agricultural worker in the district, after a while (One day later) he fell ill and fainted, then he was first taken to the district state hospital by 112 Emergency Health Services, the patient with tachycardia, hyperthermia, hypotension and Glasgow Coma Score 5 was intubated and transferred to a further health institution in the provincial centre, The diagnosis of 'Contact with Poisonous Snakes and Lizards (X20)' was made and the patient was admitted to the intensive care unit with the examination findings of 'poor general condition, intubated, unstable haemodynamics, bleeding oral structures, active bleeding in the nasogastric catheter': 11,5, Creatinine: 3,67 mg/dl, Amylase: 3046 u/L, snake antiserum (antivenom) and drug treatment was given, and despite all treatments, the patient was accepted as excitus during the day.

In the autopsy report; 'On external examination, there were two 0.3 cm diameter ecchymosis on the posterior aspect of the left knee with a distance of 1.5 cm between them, a total of 4 ecchymoses of similar size with a distance of 1.5 cm between them on the lateral side of this lesion and on the upper 1/3 of the left knee (Figure 2), bloody content in the form of plaster coming from the mouth, edema on the tongue, bleeding in the upper and lower gingiva, internal examination; 'On internal examination, it was reported that there were widespread haemorrhage areas on the heart surface, haemorrhage areas on the heart valve

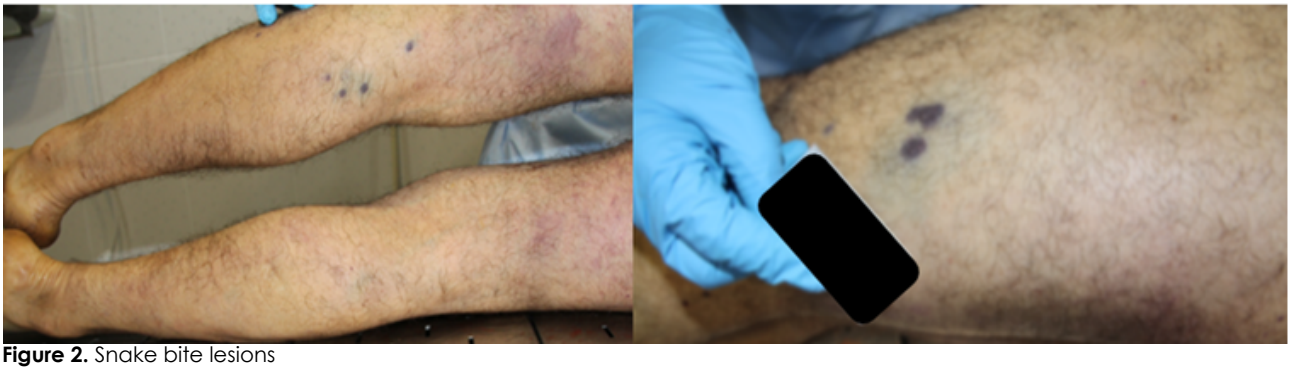


Figure 2. Snake bite lesions

structures, widespread intramuscular haemorrhage in the ventricular myocardium, haemorrhage in the clavicle attachment sites of the left neck muscles, haemorrhage areas in the thyroid and surrounding muscles, lung, trachea and oesophageal lumen, oedema and haemorrhage in the left epiglottis, multiple petechiae in the fundus of the stomach, haemorrhage foci in the corticomedullary areas of both kidneys' (Figure 3).

In the examination of the samples taken for toxicological analysis, it was stated that; 'drug active ingredients were found in the therapeutic dose used in allergy treatment and resuscitation procedures, there were widespread fresh bleeding areas in the heart, intraparenchymal bleeding in the lung, bleeding in the aortic adventitia in the samples taken for histopathological analysis, and bleeding findings were observed in the dermis and fatty tissue in three skin samples taken',

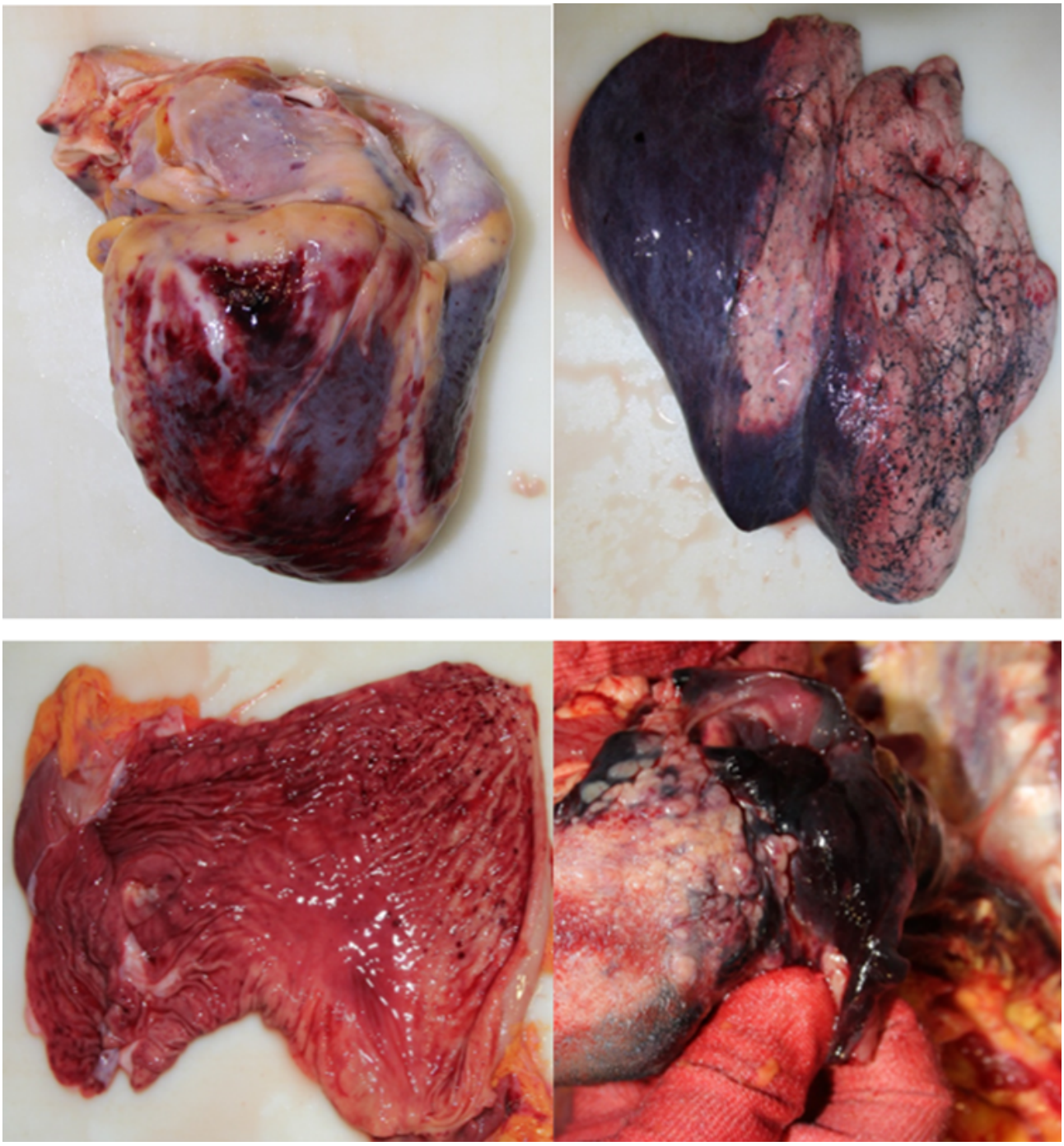


Figure 3. Haemorrhage areas and oedema around the heart, lung, stomach and epiglottis due to snake bite

As a result of the autopsy, it was stated that 'it was concluded that the death of the person occurred as a result of anaphylaxis and complications due to snake bite'.

Discussion

Snake bites are a major health problem affecting millions of people worldwide every year. The incidence of snakebites is particularly high in tropical and subtropical regions, where they are commonly encountered among agricultural workers and local people. The most common species causing bites is the viper (viperidae) snake. Snake venom has cardiotoxic, neurotoxic, myotoxic, nephrotoxic and haematotoxic properties (6,7).

Snake bites are medical emergencies that can have serious consequences with both local and systemic complications. Enzymes such as serine protease and arginine ester hydrolase in snake venom can activate the coagulation system and lead to the development of DIC. This may result in prolonged PT and aPTT, decreased fibrinogen levels, increased fibrin degradation products and decreased protein C levels. Although haematological disorders are usually mild, they may rarely lead to fatal complications such as intracranial, pulmonary and intra-abdominal haemorrhages. In a study conducted in India, 38 cases of death due to snake bite were investigated and it was reported that 65.8% of the cases had haemorrhage in the corticomedullary region of the kidney, 55.3% had acute tubular necrosis, 18.4% had haemorrhage in the adrenal gland and 52.6% had haemorrhage in the pituitary gland (8). In a study in which death cases due to various animal bites were evaluated, it was reported that toxicity developed in kidney and liver in cases of death due to snake bite and multiple organ damage developed in these cases (9). In studies conducted in our country, it has been reported that similar findings such as haemorrhage in subcutaneous fat and muscle tissue, haemorrhage in serous membranes, oedema and haemorrhage in internal organs were obtained in cases of death due to snake bite (8,9). The results obtained from the medical documents of our case showed that haemodynamics became unstable and renal function tests deteriorated. In our study, the findings on the left lower extremity at autopsy consisted of ecchymoses frequently seen in snake bites as reported in the literature. Multiple organ damage was found in the form of haemorrhage and oedema areas in the heart, myocardium, lung, stomach, kidney and neck. The findings obtained are similar to the studies in which snake bite injuries were analysed. The findings obtained in our study reinforce the severity of the clinical picture in snakebite-related deaths and the need for detailed examination of all organs by forensic medicine specialists.

The treatment of a snake bite varies depending on the type, toxicity and amount of venom. As first aid, it is recommended to immobilise the bitten area and seek emergency medical attention. The World Health Organisation (WHO) recommends that antivenom should be administered according to the symptoms of systemic and local envenomation in the treatment of snakebite cases, taking into account potential side effects and taking necessary precautions. Antivenom is used to prevent local swelling from increasing and to alleviate blood disorders and general intoxication (10). Antivenom is the most effective treatment for snake bites and should be administered as soon as possible. Studies have shown that there is a significant correlation between cases where antivenom treatment is delayed and deaths due to snake envenomation (11,12). In a similar study, it was reported that antivenom given early and in adequate dosage is life-saving in snakebite injuries. Considering the information that the first application to the health institution of our case was made one day after the snake bite, that he was taken to the district state hospital and then referred to the state hospital in the provincial centre, although the first medical intervention and antivenom treatment was performed, considering the elapsed time and literature information, it increases the possibility that the snake bite may result in death. In such cases, all procedures performed during the preparation of medical documents should be recorded in order to respond to future allegations. In addition, an autopsy is important for the evaluation of allegations in this parallel.

In conclusion, snake bites pose a serious risk, especially for those working in agricultural activities. In such cases, rapid transport of the patient to the health institution is of great importance for the effectiveness of the treatment process. It is of vital importance to have antivenoms used in treatment in the emergency departments of hospitals in the region where venomous snake bites are common. It is important to provide on-the-job training on snake bites to physicians working in hospital emergency departments and primary health care services in order to treat patients correctly and quickly. Raising awareness of individuals living or working in areas with venomous snakes about snake

bites, as well as wearing appropriate protective footwear such as boots or boots, is an effective prevention method. It should not be overlooked that suspicious deaths, especially in rural areas, may have developed due to snake bites. Histopathological and toxicological analyses of samples taken during autopsy reveal the damage caused by the venom in the body due to snake bite and help to understand the exact cause of death.

Author contributions

Conception: A.S., B.K., Design: A.S., B.K., Supervision: A.S., B.K., Resource: A.S., B.K., Materials: A.S., B.K., Data Collection and/or Processing: A.S., B.K., Analysis and/or Interpretation: A.S., B.K., Literature Review: A.S., B.K., Writer: A.S., B.K., Critical

Review

A.S., B.K.

Acknowledgments

We would like to thank the Council of Forensic Medicine for their work permit and contributions.

References

1.World Health Organization. Snakebite envenoming. Last Accessed Date: 03.12.2024. Available from: https://www.who.int/news-room/fact-sheets/detail/snakebite-envenoming. Snakebite envenoming.

2.Bıcılıoğlu Y. Snake Bite. In: Durgül Y, editor. Emergency Approach to Childhood Poisoning. 1st ed. Ankara: Türkiye Klinikleri; 2021. p. 100–5.

3.Bilir Ö, Ünlü A, Ersunan G, Ayaz T. Retrospective Evaluation of Snake Bites in Eastern Black Sea Region. Eurasian Journal of Toxicology. 2020;1(2):40–3.

4.Tok CV. Snake in Turkish Culture From Past to Present. Doğa ve Sürdürülebilirlik Derneği, Doğanın Sesi. 2023;6(12):48–61.

5.Çiftçi T, Akay A, Adıgön A, Güneş F. A snake bite case developing thrombocytopenia. Journal of Clinical and Experimental Investigations. 2012;3(2): 293-295.

6.Büyük Y, Koçak U, Yazıcı YA, Gürpınar S, Kır Z. Yılan Isırığına Bağlı Ölüm. Turkiye Klinikleri J Foren Med. 2007;4:127–30.

7.Vural T, Ketenci HÇ, Reyhan U. Çay Bitkisi Toplarken Yılan Isırığına Bağlı Gelişen Ölüm Olgusu. Turkish Journal of Forensic Medicine. 2024;29;38(1):76–9.

8.Sathish K, Shaha KK, Patra AP, Rekha JS. Histopathological profile of fatal snake bite autopsy cases in a tertiary care center in South India. Egypt J Forensic Sci. 2021;13;11(1):3.

9.Chen L, Huang G zhao. Poisoning by toxic animals in China--18 autopsy case studies and a comprehensive literature review. Forensic Sci Int. 2013;232(1–3):e12–23.

10.World Health Organization. Guidelines for the management of snakebites, 2nd edition. 2016. Last Accessed Date: 03.12.2024. Available from: https://www.who.int/publications/i/item/9789290225300.

11.Hanbeyoğlu O, Urfalıoğlu A, Hünerel T. Yoğun Bakım Ünitesinde Takip Edilen Yılan Isırması Olgularının Demografik ve Klinik Özelliklerinin Retrospektif Analizi. Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Dergisi. 2022;2;17(3):129–37.

12.Caiaffa WT, Vlahov D, Antunes CMF, de Oliveira HR, Diniz CR. Snake bite and antivenom complications in Belo Horizonte, Brazil. Trans R Soc Trop Med Hyg. 1994;88(1):81–5.