HMJ

# Hitit Medical Journal

Hitit Üniversitesi Tıp Fakültesi Dergisi

VOLUME: 5 ISSUE: 3

OCTOBER - 2023

E-ISSN: 2687-4717

# Hitit Medical Journal

Hitit Üniversitesi Tıp Fakültesi Dergisi

HMJ

**Hitit Üniversitesi Tıp Fakültesi adına Derginin Sahibi**
*(Owner on behalf of Hitit University Medical Faculty)*

**Prof. Dr. Nurcan BAYKAM**
Hitit Üniversitesi Tıp Fakültesi Dekan V.

**Editör** / *Editor*
Doç. Dr. Abdulkerim YILDIZ

**Editör Yardımcıları** / *Assistant Editors*
Doç. Dr. Özgür KOÇAK
Doç. Dr. Selçuk KAYIR

**Editöryal Kurul** / *Editorial Board*
Doç. Dr. Dilek EKER BÜYÜKŞİRECİ
Doç. Dr. Lütfü BEKAR
Doç. Dr. Murat DOĞAN
Doç. Dr. Ramazan TOPÇU
Dr. Öğr. Üyesi Musa YILMAZ

**İstatistik Editörü** / *Statistical Editor*
Doç. Dr. Emre DEMİR

**Teknik ve Dil Editörleri** / *Technical and Language Editors*
Doç. Dr. Tolga DÜZENLİ
Dr. Öğr. Üyesi Gülce GÖKGÖZ ÖZIŞIK
Dr. Öğr. Üyesi Güven AKÇAY
Dr. Öğr. Üyesi Sertan ÖZYALÇIN

**Tasarım** / *Design*
Doç. Dr. Özgür KOÇAK
Mahmut Eren GÜLTEKİN

**Basım Tarihi** / *Date of Issue*
10.10.2023

Hitit Üniversitesi Tıp Fakültesi Dergisi yılda üç sayı olarak (Şubat, Haziran ve Ekim) yayımlanan, çift-kör hakemlik değerlendirmesi yapan bir tıp dergisidir.
Hitit Medical Journal is a double blind peer-reviewed medical journal which is published thrice per year (February, June, October).

**İletişim Adresi** / *Contact info*
Hitit Üniversitesi Erol Olçok Eğitim ve Araştırma Hastanesi 2. Kat. Çepni Mah. İnönü Caddesi No:176 Merkez ÇORUM
hmj@hitit.edu.tr

# Editörden

*Kıymetli okuyucular;*
*Hitit Medical Journal dergimizin yeni sayısı ile karşınızdayız. Dergimiz TR DİZİN/ULAKBİM tarafından dizinlenmeye başlandıktan sonra dergimize akademik camiadan yoğun ilgi gösterilmiştir. Bu durum ekibimizi hem heyecanlandırmış hem de gelecekteki çalımalarımız için ciddi motivasyon artışına yol açmıştır. Ek olarak dergimizin uluslararası kabul gören birçok indekste dizinlenmesi için de çalışmalarımız devam etmektedir. En kısa sürede buradan olumlu haberleri paylaşacağımızı umuyorum. Akademik dünyaya katkıda bulunmak için hazırladıkları makaleleri dergimiz aracılığı ile bilim dünyasına sunmayı tercih eden tüm yazarlar ve bu makalelere ilgi gösteren tüm okuyucularımıza sonsuz teşekkürlerimizi iletiyoruz.*
*Bu sayıda 17 adet orjinal/araştırma olmak üzere farklı alanlarda toplam 19 makaleyi bilim dünyasına sunuyoruz. Tüm okuyucularımıza keyifli ve yararlı okumalar diliyoruz.*
*Saygılar...*

**Doç. Dr. Abdulkerim YILDIZ**
HMJ Editöryal Kurul adına

# From the Editor

*Dear readers;*

*We are here with the new issue of our Hitit Medical Journal. Since the journal started to be indexed by TR DIZIN/ULAKBIM, we received intense interest from the academic community. This situation both excited our team and led to a serious increase in motivation for our future work. In addition, we continue to work to have our journal indexed in many internationally accepted indexes. I hope we will share positive news here as soon as possible. We would like to express our endless gratitude to all authors who choose to present their articles to the scientific world through our journal, and to all our readers who show interest in these articles.*

*In the current issue, we present a total of 19 articles in different fields, 17 of which are original/research paper. We wish all our readers enjoyable and useful reading.*

*With our respects...*

**Ass. Prof. Dr. Abdulkerim YILDIZ**
On behalf of the HMJ Editorial Board

# İÇİNDEKİLER - INDEX

## ARAŞTIRMA MAKALESİ / ORIGINAL ARTICLES

# İÇİNDEKİLER - INDEX

# HMJ

HİTİT ÜNİVERSİTESİ TIP FAKÜLTESİ DERGİSİ

HAZIRAN - 2023
JUNE - 2023

ELEKTRONİK DERGİ
ELECTRONIC JOURNAL

# Evaluation of Anterior Segment Parameters of Clinically Unilateral Pseudoexfoliation Syndrome Using Scheimpflug Imaging Technique

**Mustafa Duran[1], Tayfun Sahin[1], Selim Cevher[1]**

[1]Department of Ophthalmology, Hitit University Faculty of Medicine, Çorum, Türkiye.

**Address for Correspondence:** Department of Ophthalmology, Hitit University Faculty of Medicine, Çorum, Türkiye
e-mail: drmduran19@hotmail.com

**Orcid ID:** MD: 0000-0002-3178-2880 SC: 0000-0002-7968-4876
TS: 0000-0003-2319-0807

**Cite As:** Duran M, Sahin T, Cevher S. Evaluation of Anterior Segment Parameters of Clinically Unilateral Pseudoexfoliation Syndrome Using Scheimpflug Imaging Technique. Hitit Med J 2023;5(3): 126-130. https://doi.org/10.52827/hititmedj.1276468

## Abstract

**Objective:** We aimed to compare the intraocular pressure (IOP), keratometry values (K), and anterior segment parameters of patients with clinically unilateral pseudoexfoliation syndrome (PEX) with the other eyes without PEX and the control group.

**Material and Method:** Fifty four patients with unilateral PEX findings and 40 participants without PEX findings in both eyes were included in the study as a control group. IOP was measured by Goldmann applanation tonometry. K values and anterior segment parameters [central corneal thickness (CCT), anterior chamber depth (ACD), iridocorneal angle (ICA), and anterior chamber volume (ACV)] were measured using Scheimpflug imaging technique.

**Results:** The mean age of PEX patients was 67.9±9.2 years, while the mean age of the control group was 58.9±5.7 years. The IOP values of the eyes with PEX were significantly higher than the other eyes ($p=0.02$), and there was no significant difference between them and the control group (p=0.59). In terms of K values and anterior segment parameters, the measurements of eyes with PEX and the other eyes, and eyes with PEX and control group were similar ($p>0.05$).

**Conclusion:** In our study, eyes with PEX had higher IOP values than the fellow eyes and control group. In addition, thinner CCT, narrower ACD, and ICA values were found in eyes with PEX than in the other eyes. However, these values were not statistically significant.

**Keywords:** Anterior segment parameters, Corneal topography, Intraocular pressure, Pseudoexfoliation syndrome

## Özet

**Amaç:** Klinik olarak tek taraflı psödoeksfoliasyon sendromu (PES) olan hastaların, göziçi basıncı (GİB), keratometri değerleri (K) ve ön segment parameterlerini, PES olmayan diğer gözleri ve kontrol grubu ile karşılaştırmayı amaçladık.

**Gereç ve Yöntem:** Tek taraflı PES bulguları olan 54 hasta ile iki gözünde de PES bulguları olmayan 40 kişi kontrol grubu olarak çalışmaya dahil edildi. GİB, Goldmann aplanasyon tonometrisi ile ölçüldü. K değerleri ve ön segment parametreleri (santral kornea kalınlığı, ön kamera derinliği, iridokorneal açı, ön kamera hacmi) Scheimpflug görüntüleme tekniği kullanılarak ölçüldü.

**Bulgular:** PES hastalarının yaş ortalaması 67,9±9,2 iken, kontrol grubunun yaş ortalaması 58,9±5,7 idi. PES'li gözlerin GİB değerleri diğer gözlerinden anlamlı olarak yüksek idi ($p=0,02$), kontrol grubuyla aralarında anlamlı fark yoktu ($p=0,59$). K değerleri ve ön segment parametreleri bakımından PES'li gözler ile diğer gözleri ve kontrol grubu ölçümleri benzer idi ($p>0,05$).

**Sonuç:** Çalışmamızda PES'li gözler, diğer gözlerinden ve kontrol grubundan daha yüksek GİB değerlerine sahipti. Ayrıca PES'li gözlerde diğer gözlerinden daha ince santral kornea kalınlığı, daha dar ön kamera derinliği ve iridokorneal açı değerleri bulundu ancak bu değerler istatistiksel olarak anlamlı değildi.

**Anahtar Sözcükler:** Göziçi basıncı, Korneal topografi, Ön segment parametreleri, Psödoeksfoliasyon sendromu

**Date of Submission:** 03.04.2023
**Date of Acceptance:** 20.08.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** Hitit University Ethics Committee approval was obtained for the study (No: 327, Date: 08.09.2020).
**Plagiarism Checks:** Yes - iThenticate
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: MD, TŞ, SC Design: MD, TŞ, SC Data Collection/Data Processing: MD, TŞ, SC Data Analysis: MD, TŞ, SC Article Preparation: MD, TŞ, SC
**Informed Consent:** The written consent form was obtained from the participants.
**Financial Disclosure:** No financial support has been received.

## Introduction

Pseudoexfoliation syndrome (PEX) is an age-related systemic microfibrillopathy, mostly seen in the structures of the anterior chamber of the eye, in which extracellular granular material accumulates (1). Depending on this material accumulation, it may cause ocular pathologies such as secondary open-angle glaucoma, angle-closure glaucoma, weakness in the zonules, phacodonesis, lens dislocation, and weak pupil dilation (2). While the prevalence of PEX is around 10-20% over the age of 60, this rate is around 40% over the age of 80. In addition, its prevalence is also affected by ethnicity and race (3,4).

Unlike primary open-angle glaucoma (POAG), PEX-induced glaucoma (PEXG) is characterized by higher intraocular pressure (IOP), higher diurnal variation, more severe optic nerve damage, and more rapid visual field loss. In addition, PEXG is more resistant to medical treatment and requires more surgery than POAG (5). Accordingly, PEXG is one of the common causes of blindness worldwide (6). While the PEXG development rate is 5% for 5 years, this rate rises to 60% over 15 years (7,8).

PEX accumulates in the lens capsule, zonules, anterior chamber, and cornea layers. It affects these structures (2). It causes intra/postoperative complications due to zonullar instability, phacodonesis, melanin dispersion, and posterior synechia (9). Scorolli et al. they found that there was a 5-fold higher risk of intraoperative complications in cataract surgery in patients with PEX (10).

Although PEX is usually diagnosed unilaterally, it is a bilateral disease with asymmetric initiation. Despite its unilateral onset, PEX has been shown to be bilateral in electron microscopy studies (11). PEX findings were also found in conjunctival biopsies taken from the other eyes of clinically unilateral patients (12).

Evaluation of IOP, CCT, and anterior segment structures [anterior chamber depth (ACD), iridocorneal angle (ICA), and anterior chamber volume (ACV)] is important for diagnosis and follow-up in patient with PEX. The Sirius scheimpflug imaging system can objectively evaluate cornea and anterior segment structures non-invasively and rapidly.

In this study, we aimed to compare the IOP, anterior segment parameters, and K values of patients with clinically unilateral PEX with other eyes without PEX and the control group.

## Material and Method

This prospective study was carried out in the ophthalmology department of Hitit University Çorum Erol Olçok Training and Research Hospital. 54 clinically unilateral PEX patients and 40 healthy control participants were included in the study. The study was carried out in accordance with the Declaration of Helsinki and with the approval of the ethics committee of Hitit University (2020-327). The written consent form was obtained from the participants.

Patients who had bilateral PEX findings, previous intra and/or extraocular surgery or a history of trauma, glaucoma, active blepharitis or conjunctivitis, using contact lenses, corneal pathologies, using topical or systemic drugs that affect the anterior segment, refractive errors greater than ±3 diopters (D), and with systemic disease (cardiovascular, pulmonary disease, diabetes mellitus except hypertension) were excluded from the study.

After dilating the pupil with topical 1% cyclopentolate and 1% tropicamide, patients with unilateral PEX findings in the anterior lens capsule and/or pupillary edge but without glaucomatous changes were included in the study. The fellow eyes of the same patients without PEX findings in the lens, pupillary margin and angle were considered clinically normal. In addition, participants who did not have PEX findings in both eyes in the post-dilatation examination constituted the control group. At least 2 days later, IOP and corneal topography measurements were made at the same room conditions (between 10-12 am) of the participants. Right eye measurements of the control group were used in the study.

The best corrected visual acuities of all participants were evaluated with snellen charts. Slit-lamp biomicroscopy was performed and IOP was measured with Goldmann applanation tonometry. Detailed fundus examination was performed with a 90 D lens. Trabecular angle was evaluated using the Goldmann tri-mirror for gonioscopy. Participants without glaucomatous cups and normal visual field analysis (Humphrey Automated Perimeter; Humphrey Instruments, San Leandro, CA, USA) were included in the study. All examinations and measurements were performed by the same ophthalmologist under dim light conditions and without pupil dilation (TS).

Anterior segment parameters were evaluated with Scheimpflug-based corneal topography (Sirius; Costruzione Strumenti Oftalmici, Florence, Italy). The Sirius system is a system that uses a scheimpflug camera and a placido disc to evaluate the anterior segment non-contactly. Participants were asked to blink 3 times in a comfortable sitting position after placing their chin and forehead on the device's extraction point. Corneal topography images were taken immediately after blinking. Images with at least 90% acquisition quality were recorded. In our study, IOP, CCT, ACD, ACV, ICA, and K flat (K1), K steep (K2), K mean (Km) values were used. The PEX and non-PEX eyes of the patients in the PEX group were compared and the right eye measurements of the control group without PEX findings in both eyes were compared.

*Statistical Analysis*

In this study, statistical analyzes were done using SPSS (Version 22.0, SPSS Inc., Chicago, IL, USA) package program. It was tested whether the data were normally distributed with the Kolmogorov-Smirnov test. Data were shown as mean±standard deviation (mean±sd). Normally distributed data were evaluated with the Independent Samples T test between groups, and those that did not show normal distribution were evaluated with the Mann Withney U test. Statistical significance level was accepted as $p<0.05$.

## Results

Of the 54 clinically unilateral PEX patients included in the study, 51.9% (n= 28) were female and 48.1% (n= 26) were male. In the 40 healthy control group, 48.3% (n= 19) were male and 51.7% (n= 21) were female. There was no significant difference between the groups in terms of gender. The distribution of the PEX eyes included 36 right eyes (66.6%), and 18 (33.3%) left eyes. Right eye measurements of the control group were included in the study. The mean age of PEX patients was 67.9 (range, 47-79) years, and the mean age of the control group was 58.9 (range, 52-74) yaers. There was a significant difference between the two groups in terms

of age values (*p<0.01*).

The comparison of the IOP, CCT, ACD, ICA, ACV, K1, K2, and Km values of the PEX eye of the patients with PEX and the other healthy eye is shown in Table 1. The mean IOP was 2.9 mmHg higher in eyes with PEX (*p<0.02*).

The comparison of IOP, CCT, ACD, ICA, ACV, K1, K2, and Km values of eyes with PEX and control group eyes is shown in Table 2. There was no significant difference between the measurements (*p>0.05*). The comparison of IOP, CCT, ACD, ICA, ACV, K1, K2, and Km values of the other eyes of the patients with PEX and the eyes of the control group is shown in Table 3. There was a statistically significant difference in ICA and ACV measurements between fellow eyes and control groups (*p=0.01, p=0.03*. respectively). The distribution of IOP values of these three groups is shown in Figure 1.

**Table I.** Comparison of clinically unilateral PEX patient with PEX and normal fellow eye

| | PEX (n= 54) | Fellow Eye (n= 54) | P |
|---|---|---|---|
| **AGE** | 67.9± 9.2 (47- 79) | | |
| **GENDER (M/F)** | 26/ 28 | | |
| IOP | 18.1±4.1 | 15.2±3.2 | ***0.02***[a] |
| CCT | 539.8±36.4 | 543.0±34.5 | *0.75*[b] |
| ACD | 2.56±0.4 | 2.59±0.4 | *0.70*[b] |
| ICA | 39.9±8.6 | 43.3±10.2 | *0.19*[b] |
| ACV | 118.2±29.3 | 107.3±26.2 | *0.16*[b] |
| K1 | 43.59±1.5 | 43.59±1.5 | *0.96*[b] |
| K2 | 45.23±1.6 | 45.31±1.8 | *0.87*[b] |
| Km | 44.40±1.5 | 44.45±1.5 | *0.91*[b] |

IOP: Intraocular pressure, CCT: Central corneal thickness, ACD: Anterior chamber depth, ICA: Iridocorneal angle, ACV: Anterior chamber volüme, K1: Flat keratometry, K2: Steep keratometry, Km: Mean keratometry, [a]: Wilcoxon test, [b]: Dependent Samples T-test, bold: *p<0.05*

## Discussion

**Table II.** Comparison of PEX eye and control group measurements

| | PEX (n= 54) | Control (n= 40) | *P* |
|---|---|---|---|
| **AGE** | 67.9±9.2 (47- 79) | 58.9±5.7 (52- 74) | ***<0.01*** |
| **GENDER (M/F)** | 26/ 28 | 19/ 21 | *1.00*[*] |
| **IOP** | 18.1±4.1 | 17.0±3.0 | *0.59*[a] |
| **CCT** | 539.8±36.4 | 528.5±30.4 | *0.21*[b] |
| **ACD** | 2.56±0.4 | 2.65±0.3 | *0.33*[b] |
| **ICA** | 39.9±8.6 | 36.9±5.4 | *0.14*[b] |
| **ACV** | 118.2±29.3 | 121.7±20.4 | *0.61*[b] |
| **K1** | 43.59±1.5 | 43.78±1.8 | *0.75*[b] |
| **K2** | 45.23±1.6 | 45.54±1.9 | *0.09*[b] |
| **Km** | 44.40±1.5 | 44.16±1.8 | *0.45*[b] |

IOP: Intraocular pressure, CCT: Central corneal thickness, ACD: Anterior chamber depth, ICA: Iridocorneal angle, ACV: Anterior chamber volüme, K1: Flat keratometry, K2: Steep keratometry, Km: Mean keratometry, a: Mann-Whitney U test, b: Independent Samples T-test, *: Fisher's exact test, bold: *p<0.05*.

**Figure I.** Comparison of IOP values of PEX eye, fellow eye and control group

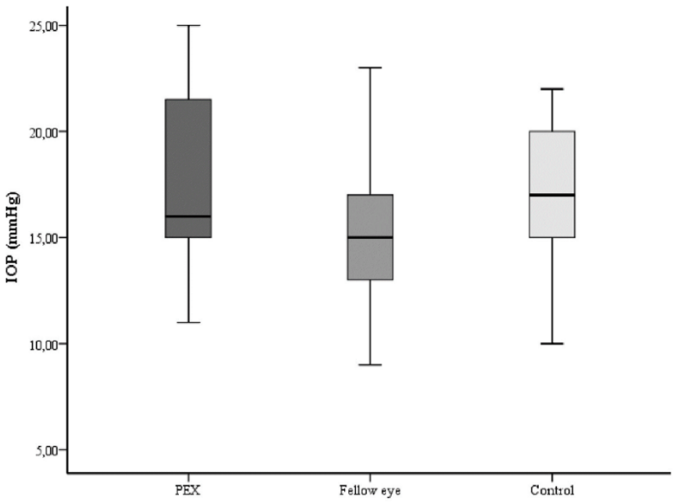



**Table III.** Comparison of fellow eye and control group measurements

| | Fellow Eye (n= 54) | Control (n= 40) | *P* |
|---|---|---|---|
| **AGE** | 67.9±9.2 (47- 79) | 58.9±5.7 (52- 74) | ***<0.01*** |
| **GENDER (M/F)** | 26/ 28 | 19/ 21 | *1.00*[*] |
| **IOP** | 15.2±3.2 | 17.0±3.0 | *0.43*[b] |
| **CCT** | 543.0±34.5 | 528.5±30.4 | *0.10*[b] |
| **ACD** | 2.59±0.4 | 2.65±0.3 | *0.59*[b] |
| **ICA** | 43.3±10.2 | 36.9±5.4 | *0.01b*[*] |
| **ACV** | 107.3±26.2 | 121.7±20.4 | *0.03b*[*] |
| **K1** | 43.59±1.5 | 43.78±1.8 | *0.79*[b] |
| **K2** | 45.31±1.8 | 45.54±1.9 | *0.08*[b] |
| **Km** | 44.45±1.5 | 44.16±1.8 | *0.39*[b] |

IOP: Intraocular pressure, CCT: Central corneal thickness, ACD: Anterior chamber depth, ICA: Iridocorneal angle, ACV: Anterior chamber volüme, K1: Flat keratometry, K2: Steep keratometry, Km: Mean keratometry, [b]: Independent Samples T-test, *: Fisher's exact test, *p<0.05*.

PEX is a systemic disease in which fibrillar material is deposited, especially in the ocular anterior segment structures. PEX is one of the common causes of unilateral glaucoma. Poor response to medical treatment and rapid progression of optic nerve damage are the features that distinguish PEX from other types of glaucoma (5). In our study, we compared the patients with clinically detectable PEX with the other eyes without PEX findings and the control group. The mean IOP was higher in eyes with PEX than in the fellow eyes and control group. In terms of other parameters, there was no significant difference between eyes with PEX, fellow eye, and control groups.

In the Vesti and kivela studies, they found IOP approximately 2 mmHg higher in the eye with PEX than in the other eye without PEX (13). In the "Reykjavik Eye Study", the IOP value was found to be significantly higher in the PEX group than in their normal eyes (14). Gaile et al. evaluated 29 patients with at least one-sided PEX and 42 patients with non-PEX cataract before surgery, and they found higher IOP in the PEX group (15). In our study, IOP was on average 2.9 mmHg higher in eyes with PEX than in fellow eyes. In addition, the IOP of eyes with PEX was on average 1.1 mmHg higher than the control

group.

Consideration of CCT is important for correct assessment of IOP. However, studies on CCT in patients with PEX are inconsistent in the literature. While there are studies showing that it is thinner in the PEX group (16-18), there are also studies showing that it is thicker (19-21). There are also studies showing that CCT does not change (20,22,23). They attributed the reason for these different results to the measurement method, ethnic differences, and the difference in the number of participants. In our study, although the CCT of the PEX group was thicker than the control group, there was no significant difference.

There are also different results in studies on anterior chamber parameters and K values. Ozcura et al. in their study with 48 (PEX and PEXG) and 48 control group patients, no difference was found between the groups in terms of anterior chamber parameters and keratometry values (18). Bartholomew et al., found no difference between PEX and normal groups in terms of ACD (24). The 'Reykjavik Eye Study' showed that PEX was unrelated to CCT, and aqueous depth (AD) (21).

In contrast to these studies, You et al. showed that PEX was associated with age and narrow AC (25). Doğanay et al., while they found that the ACD was narrower in the PEXG group, they did not find a significant difference between the PEX and control groups (17). Mohammedi et al. found a narrower ACD in the PEX group (26). They used anterior segment optical coherence tomography. Damji et al. in their study with A scan biometry, showed that those with PEX had narrower AC than those with POAG (27). Omura et al. found higher IOP, narrow ACV, and decreased endothelial number in the PEX group, but they did not find any difference between the groups in terms of CCT and AD (28). The narrower ACD in patients with PEX has been attributed to the anterior shift of the lens due to weakening of the lens zonules (27,29,30). In our study, when comparing ACD, ICA, ACV, and K values, there were no significant differences between eyes with PEX and fellow eyes or eyes with PEX and control groups.

There are also limitations of our study. First, there was a significant age difference between the PEX group and the control group. Secondly, the number of participants was relatively small. Third, the patient group with PEXG was not included in the study. In addition, since Turkish people were included in the study, different results may occur in other racial and ethnic groups.

## Conclusion

PEX is a disease that affects both eyes, although it starts unilaterally. The high IOP (compared to the fellow eye and control group) even before the development of glaucoma findings in the early-onset eye indicates that these patients should be followed closely. If PEX patients are diagnosed and followed early, glaucoma damage and blindness can be prevented. Especially in cataract surgery, it should be kept in mind that the anterior chamber of patients with PEX are narrower and their zonules may be weaker. Further studies with larger populations are needed to understand the effects of PEX on the anterior segment.

## References

1. Ritch R, Schlötzer-Schrehardt U, Konstas AG. Why is glaucoma associated with exfoliation syndrome? Progress in retinal and eye research 2003; 22(3):253-275.

2. Ringvold A. Epidemiology of the pseudo-exfoliation syndrome. Acta Ophthalmologica Scandinavica 1999; 77:371-375.

3. Jonasson F, Damji KF, Arnarsson A, et al. Prevalence of open-angle glaucoma in Iceland: Reykjavik Eye Study. Eye 2003; 17(6):747-753.

4. Thorleifsson G, Magnusson KP, Sulem P, et al. Common sequence variants in the LOXL1 gene confer susceptibility to exfoliation glaucoma. Science 2007; 317(5843):1397-1400.

5. Konstas AG, Stewart WC, Stroman GA, Sine CS. Clinical presentation and initial treatment patterns in patients with exfoliation glaucoma versus primary open-angle glaucoma. Ophthalmic Surgery, Lasers and Imaging Retina 1997; 28(2):111-117.

6. Musch DC, Shimizu T, Niziol LM, Gillespie BW, Cashwell LF, Lichter PR. Clinical characteristics of newly diagnosed primary, pigmentary and pseudoexfoliative open-angle glaucoma in the Collaborative Initial Glaucoma Treatment Study. The British journal of ophthalmology 2012; 96(9):1180–1184.

7. Henry JC, Krupin T, Schmitt M, et al. Long-term follow-up of pseudoexfoliation and the development of elevated intraocular pressure. Ophthalmology 1987; 94(5):545-552.

8. Jeng SM, Karger RA, Hodge DO, Burke JP, Johnson DH, Good MS. The risk of glaucoma in pseudoexfoliation syndrome. Journal of glaucoma 2007; 16(1):117-121.

9. Tekin K, Inanc M, Elgin U. Monitoring and management of the patient with pseudoexfoliation syndrome: current perspectives. Clinical Ophthalmology (Auckland, NZ) 2019; 13:453.

10. Scorolli L, Scorolli L, Campos EC, Bassein L, Meduri RA. Pseudoexfoliation syndrome: a cohort study on intraoperative complications in cataract surgery. Ophthalmologica 1998; 212(4):278-280.

11. Hammer T, Schlötzer-Schrehardt U, Naumann GO. Unilateral or asymmetric pseudoexfoliation syndrome? An ultrastructural study. Archives of ophthalmology 2001; 119(7):1023-1031.

12. Kivelä T, Hietanen J, Uusitalo M. Autopsy analysis of clinically unilateral exfoliation syndrome. Investigative ophthalmology & visual science 1997; 38(10):2008-2015.

13. Vesti E, Kivelä T. Exfoliation syndrome and exfoliation glaucoma. Progress in retinal and eye research 2000; 19(3):345-368.

14. Arnarsson AM, Damji KF, Sverrisson T, Sasaki H, Jonasson F. Prevalence of Pseudoexfoliation and Association With IOP, Corneal Thickness, and Structural Optic Disc Parameters in the Reykjavik Eye Study. Investigative Ophthalmology & Visual Science 2007; 48(13):1562.

15. Mažeikaitė G, Daveckaitė A, Šiaudvytytė L, Kuzmienė L, Janulevičienė I. Comparison of anterior segment parameters, intraocular pressure and cataract surgery complications in eyes with and without pseudoexfoliation syndrome. In The International Congress of Advanced Technologies and Treatments for Glaucoma (ICATTG): 29-31 October 2015, Milan, Italy: Program [poster presentations, abstracts, poster abstracts]/Glaucoma Research Foundation.[Milan]: Glaucoma Research Foundation, 2015.

16. Bozkurt B, Güzel H, Kamış Ü, Gedik Ş, Okudan S. Characteristics of the anterior segment biometry and corneal endothelium in eyes with pseudoexfoliation syndrome and senile cataract. Turkish Journal of Ophthalmology 2015; 45(5):188.

17. Doganay S, Tasar A, Cankaya C, Firat PG, Yologlu S. Evaluation of Pentacam-Scheimpflug imaging of anterior segment parameters in patients with pseudoexfoliation syndrome and pseudoexfoliative glaucoma. Clinical and Experimental Optometry 2012; 95(2):218-222.

18. Özcura F, Aydin S, Dayanir V. Central corneal thickness and corneal curvature in pseudoexfoliation syndrome with and without glaucoma. Journal of Glaucoma 2011; 20(7):410-413.

19. Krysik K, Dobrowolski D, Polanowska K, Lyssek-Boron A, Wylegala EA. Measurements of corneal thickness in eyes with pseudoexfoliation syndrome: comparative study of different image processing protocols. J Healthc Eng 2017;2017:4315238.

20. Tomaszewski BT, Zalewska R, Mariak Z. Evaluation of the endothelial cell density and the central corneal thickness in pseudoexfoliation syndrome and pseudoexfoliation glaucoma. Journal of ophthalmology 2014;2014:123683.

21. Arnarsson A, Damji KF, Sverrisson T, Sasaki H, Jonasson F. Pseudoexfoliation in the Reykjavik Eye Study: prevalence and related ophthalmological variables. Acta Ophthalmologica Scandinavica 2007; 85(8):822-827.

22. Demircan S, Atas M, Yurtsever Y. Effect of torsional mode phacoemulsification on cornea in eyes with/without pseudoexfoliation. International Journal of Ophthalmology 2015; 8(2):281.

23. Sarowa S, Manoher J, Jain K, Singhal Y, Devathia D. Qualitative and quantitative changes of corneal endothelial cells and central corneal thickness in pseudoexfoliation syndrome and pseudoexfoliation glaucoma. Int J Med Sci Public Heal 2016; 5(12):1.

24. Bartholomew RS. Anterior chamber depth in eyes with pseudoexfoliation. The British Journal of Ophthalmology 1980;64(5):322.

25. You QS, Xu L, Wang YX, et al. Pseudoexfoliation: normative data and associations: the Beijing eye study 2011. Ophthalmology 2013; 120(8):1551–1558.

26. Mohammadi M, Johari M, Eslami Y, et al. Evaluation of anterior segment parameters in pseudoexfoliation disease using anterior segment optical coherence tomography. American Journal of Ophthalmology 2022; 234:199-204.

27. Damji KF, Chialant D, Shah K, et al. Biometric characteristics of eyes with exfoliation syndrome and occludable as well as open angles and eyes with primary open-angle glaucoma. Canadian Journal of Ophthalmology 2009; 44(1):70-75.

28. Omura T, Tanito M, Doi R, et al. Correlations among various ocular parameters in clinically unilateral pseudoexfoliation syndrome. Acta Ophthalmologica 2014; 92(5):e412-413.

29. Ritch R, Vessani RM, Tran HV, Ishikawa H, Tello C, Liebmann JM. Ultrasound biomicroscopic assessment of zonular appearance in exfoliation syndrome. Acta Ophthalmologica Scandinavica 2007; 85(5):495-499.

30. Sbeity Z, Dorairaj SK, Reddy S, Tello C, Liebmann JM, Ritch R. Ultrasound biomicroscopy of zonular anatomy in clinically unilateral exfoliation syndrome. Acta Ophthalmologica 2008; 86(5):565-568.

# Konjenital Kataraktlı Olgularımızda Cerrahi Tedavi ve Takip Sonuçlarımız

**Metin Uçar[1], Orhan Baykal[2]**

[1]Sağlık Bilimleri Üniversitesi, Erzurum Bölge Sağlık Uygulama ve Araştırma Merkezi, Erzurum, Türkiye
[2]Atatürk Üniversitesi, Tıp Fakültesi, Göz Hastalıkları Anabilim Dalı, Erzurum, Türkiye

**Yazışma Adresi:** Sağlık Bilimleri Üniversitesi, Erzurum Şehir Hastanesi, Göz Hastalıkları Anabilim Dalı, Erzurum, Türkiye
e-posta: mucarmucar1976@gmail.com

**Orcid NO:** MU: 0000-0003-4989-4511
OB: 0000-0001-8321-1767

**Atıf:** Uçar M, Baykal O. Konjenital Kataraktlı Olgularımızda Cerrahi Tedavi ve Takip Sonuçlarımız. Hitit Med J 2023;5(3): 131-137. https://doi.org/10.52827/hititmedj.1212429

## Özet

**Amaç:** Konjenital katarakt tanısı almış ve klinik takibimizde olan hastaların cerrahi tedavi ve takip sonuçlarını incelemektir.

**Gereç ve Yöntem:** Bu çalışmada konjenital katarakt tanısı konularak, ön kesintisiz kürvilineer kapsüloreksis, fakoaspirasyon, arka kesintisiz kürvilineer kapsüloreksis, anterior vitrektomi operasyonu yapılmış, afakik takipte olan veya siliyer sulkusa göz içi lensi implantasyonu uygulanmış, ameliyat tarihinde yaşları 0-34 yıl arasında olan, 50 hastanın 84 gözü çalışma kapsamında değerlendirilmiştir.

**Bulgular:** Takip süreleri ortalama 30,9±23 ay olarak tespit edildi. 16 göz ortalama 33 ay takip edildikten sonra, ortalama 45. Ayda, 57 göze ise ilk operasyonda siliyer sulkusa göz içi lensi uygulaması yapıldı. Takip süresince yedi gözde sekonder glokom, dokuz gözde göz içi lensi dislokasyonu, 17 gözde pupilla düzensizliği ve irisde lokalize iris atrofileri, beş gözde ön vitreusta membran geliştiği görüldü. Hastaların preoperatif en iyi düzeltilmiş görme keskinliği 0,08±0,02 (P+P+ veya el hareketleri seviyesi - 5 metreden parmak sayma, postoperatif en iyi düzeltilmiş görme keskinliği 0,4±0,3 tespit edilmiş olup, istatiksel olarak anlamlıydı( *P<0,001*). Afakik takibi yapılıp sekonder göz içi lensi uygulanan 16 hastanın son kontrol muayenelerindeki görme düzeyleri ortalama 0,2 seviyesinde tespit edildi.

**Sonuç:** Konjenital kataraktın cerrahi tedavisinde, ön kesintisiz kürvilineer kapsüloreksis, fakoaspirasyon, arka kesintisiz kürvilineer kapsüloreksis, anterior vitrektomi ve/veya siliyer sulkusa göz içi lens implantasyonu, arka kapsül kesafetini önlemede ve cerrahiye ait komplikasyonların minimalize edilmesinde etkili, güvenilir, iyi görsel sonuçlar veren tekniktir.

**Anahtar Sözcükler:** Afakik tashih, Anterior vitrektomi, Arka kesintisiz kürvilineer kapsüloreksis, Göz içi lens implantasyonu, Konjenital katarakt

**Geliş Tarihi:** 30.11.2022
**Kabul Tarihi:** 30.07.2023
**Yayım Tarihi:** 10.10.2023

**Hakem Değerlendirmesi:** Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
**Etik Beyanı:** Çalışma Atatürk Üniversitesi Etik Komite Başkanlığından onay almıştır. (Onay Numarası: B.30.2.ATA.0.01.00/24)
**İntihal Kontrolleri:** Evet - intihal.net
**Çıkar Çatışması:** Yazarlar arasında çıkar çatışması belirtilmemiştir.
**Şikayetler:** hmj@hitit.edu.tr
**Katkı Beyanı:** Fikir/Hipotez:MU,OB. Tasarım: MU,OB. Veri toplama/Veri işleme: MU,OB. Veri analizi: MU,OB. Makalenin hazırlanması: MU,OB. Makalenin Kontrolü: MU,OB
**Hasta Onamı:** Çalışmada kullanılan tüm hastalardan onam alınmıştır.
**Finansal Destek:** Finansal destek alınmamıştır.

# Surgical Treatment And Follow-Up Results In Our Congenital Cataract Cases

**Metin Ucar[1], Orhan Baykal[2]**

[1]Health Sciences University, Erzurum City Hospital, Department of Ophthalmology, Erzurum, Türkiye
[2]Ataturk University, Department of Ophthalmology, Erzurum, Türkiye

**Adress for Correspondence:** Health Sciences University, Erzurum City Hospital, Department of Ophthalmology, Erzurum, Türkiye
e-mail: mucarmucar1976@gmail.com

**Orcid ID:** MU: 0000-0003-4989-4511
OB: 0000-0001-8321-1767

**Cite As:** Ucar M, Baykal O. Surgical Treatment And Follow-Up Results In Our Congenital Cataract Cases. Hitit Med J 2023;5(3): 131-137. https://doi.org/10.52827/hititmedj.1212429

## Abstract

**Objective:** Our aim to examine the results of surgical treatment and follow-up of patients diagnosed with congenital cataract and who are under our clinical follow-up.

**Material and Method:** In this study, a diagnosis of congenital cataract was made, anterior continuous curvilinear capsulorhexis, phacoaspiration,posterior continuous curvilinear capsulorhexis, anterior vitrectomy operation and/or intraocular lens implantation was performed in the ciliary sulcus, apakic follow-up was performed, and patients aged 0-34 years at the time of surgery. 84 eyes of 50 patients were evaluated

**Results:** The mean follow-up period was 30.9±23months.After an average of 33 months of follow-up in 16 eyes, intraocular lens was applied to the ciliary sulcus in 57 eyes at an average of 45 months. During the follow-up period, secondary glaucoma was observed in 7eyes, intraocular lens dislocation in 9 eyes, pupillary irregularity and localized iris atrophy in 17 eyes,and anterior vitreous membrane development in 5 eyes. The preoperative best corrected visual acuity of the patients was 0.08±0.02 (P+P+ or hand motion-5m counting finger), and the postoperative best corrected visual acuity was 0.4±0.3, which was statistically significant(*P<0.001*).Apakic follow-up and secondary intraocular lens were applied to 16 patients, with an average visual acuity of 0.2.

**Conclusion:** In the surgical treatment of congenital cataracts, anterior continuous curvilinear capsulorhexis, phacoaspiration, posterior continuous curvilinear capsulorhexis, anterior vitrectomyand/or intraocular lens implantation into the ciliary sulcus is an effective, reliable, and good visual technique in preventing posterior capsule occlusion and minimizing surgical complications.

**Keywords:** Apakic correction, Anterior vitrectomy, Congenital cataract, Intraocular lens implantation, Posterior continuous curvilinear capsulorhexis

**Date of Submission:** 30.11.2022
**Date of Acceptance:** 30.07.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** The study received approval from Atatürk University Ethics Committee. (Approval No: B.30.2.ATA.0.01.00/24)
**Plagiarism Checks:** Yes - intihal.net
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: MU,OB Design: MU,OB Data Collection/Data Processing: MU,OB Data Analysis: MU,OB Article Preparation: MU,OB
**Informed Consent:** Informed consent was obtained from the patient.
**Financial Disclosure:** No financial support has been received.

## Giriş

Konjenital kataraktlar çocukluk çağı körlük nedenleri arasında en sık görülen tedavi edilebilir hastalıktır. Konjenital kataraktın mümkün olan en erken zamanda tedavi edilmesi gerektiği bilinmektedir. Erken tanı ve tedavi, hastalığın seyrini etkilemektedir (1).

İnfantil ve çocukluk çağı kataraktlarının tedavisinden sonraki görme düzeyi kataraktın başlangıç yaşı, ameliyat zamanı, ameliyat yöntemi, kullanılan göz içi lensinin yapısı, ameliyat sonrası komplikasyonların özellikle de sekonder kataraktın önlenmesi ve tedavisi, katarakta eşlik eden oküler ve sistemik patolojilerin varlığı, ambliyopi tedavisinin uygulanabilmesi gibi faktörlere bağlıdır (2). Çocuk gözü, büyümekte olan bir gözdür. Doğumda gelişimini henüz tamamlamamıştır, merkezi sinir sistemi de gelişimini henüz tamamlamadığı için büyüme anormalliklerine ve gelişimsel geriliklere karşı oldukça hassastır (3). Cerrahiye inflamatuar yanıtı daha belirgindir. Pediatrik katarakt cerrahisinde başlıca iki teknik kullanılmaktadır: Pars plana yaklaşım ve limbal yaklaşım (3).

Konjenital kataraktın tek tedavisi lensektomidir (3). Lensektomi sonrası refraksiyon kusurunu gidermek ve ambliyopiyi önlemek için afakik gözlük, kontaklens, göz içi lensi (GİL) implantasyonu, epikeratofaki gibi değişik tedavi yöntemleri uygulanmaktadır. Güncel cerrahi yaklaşımlarla tekniğe ait komplikasyonların minimalize edildiği konjenital kataraktlı hastalarda iyi bir optik düzeltme; ambliyopi tedavisi ve uzun süreli yakın takip gerekmektedir (2).

Çalışmamızın amacı; kliniğimizde lens aspirasyonu, anterior vitrektomi, posterior kapsülotomi ve/veya siliyer sulkusa GİL implantasyon, operasyonu uygulanan konjenital kataraktlı çocukların cerrahi tedavi sonuçlarını irdelemektir.

## Gereç ve Yöntemler

*Çalışma dizaynı*

Bu çalışma retrospektif kesitsel çalışma olarak üçüncü basamak bir merkezde konjenital katarakt nedeniyle göz servisine başvuran hastalarda yürütülmüştür. Hastalardan bilgilendirilmiş olur formu ve lokal etik kurul (B.30.2.ATA.0.01.00/24) onayı alınmıştır.

*Çalışma popülasyonu*

Çalışmaya ameliyat tarihinde yaşları, 0- 34 yıl (1- 404 ay) arasında değişen 105 olgu alındı. Son kontrol muayenesine gelebilen, ön kesintisiz kürvilineer kapsüloreksis (ÖKKK) fakoaspirasyon, arka kesintisiz kürvilineer kapsüloreksis (AKKK), anterior vitrektomi operasyonu yapılmış, afak veya sulkus GİL implantasyonu uygulanan 50 hastanın 84 gözü çalışma kapsamında değerlendirildi. Son kontrol muayenelerine gelemeyen, arka kapsül müdahalesi ve ön vitrektomi uygulanmayan, GİL yerleştirilenlerden sulkusa implantasyon uygulanmayan, travma öyküsü bulunan, miroftalmi, mikrokornea, nanoftalmi, persistan hiperplastik primer hipervitreus, konjenital glokom birlikteliği olan ve üveit gibi diğer göz anomalilerinin/ hastalıklarının eşlik ettiği hastalar çalışma kapsamı dışında tutuldu.

Ameliyatlar alanında deneyimli tek cerrah tarafından yapıldı. Hastalara 13,5/6,5 mm rijid sulkus (polimetil metakrilat (PMMA) arka kamara) GİL kullanıldı. Hidrodisseksiyon yapıldıktan sonra lens materyali bütün olgularda fakoemülsifikasyon elçeği kullanılarak aspire edildi. Bazı olgularda kısa süreli ultrasonik enerji kullanılarak lens aspirasyonu kolaylaştırıldı. Daha sonra fako aspirasyon irrigasyon elçeği kullanılarak kalan kortikal materyal dikkatlice ve titizlikle temizlendi. Ön kamara viskoelastik madde ile doldurulduktan sonra lens aspirasyonu için oluşturulan açıklıktan kistotom veya insülin enjektörü yardımıyla arka kapsül açıklığı oluşturulup ÖKKK şeklinde tamamlanmaya çalışıldı. Vitrektomi probu yardımıyla arka kapsül genişliği yaklaşık 5,5-6 mm olacak şekilde ayarlandı. Oluşturulan arka kapsül açıklığından ön vitrektomi yapıldı ve ön kamaradaki vitreus tamamen temizlendi. Afak hastalara ön kamara viskoelastik madde ile doldurulduktan sonra limbal kesi genişletilerek siliyer sulkusa PMMA GİL implantasyonu uygulandı.

*Takip*

Konjenital katarakt nedeniyle kliniğimize başvuran hastalar etiyolojik araştırmalar yapılması eşlik eden patolojilerin araştırılması amacıyla pediatri kliniğine preoperatif veya postoperatif yönlendirildi. Hasta aileleri hastanın durumu, ameliyat sonrası kontrol muayenelerinin sıklığı, ambliyopinin anlamı, kapamanın önemi, kontak lensin kullanımı ve avantajları konusunda bilgilendirildi.

Hastalar son kontrol muayenelerindeki yaşlarına göre 36 aydan küçük (0-3yaş) grup 1, 36 ay- 60 ay arası (3 yaş-5 yaş) grup 2, 60 aydan büyük (5 yaş üzeri) grup 3 olmak üzere 3 gruba ayrıldı. Son kontrol muayenelerinde görme keskinliği grup 1'de ışık reaksiyonları ve obje takibiyle (Persepsiyon=ışığı görebilme, projeksiyon= ışığın yönünü tayin edebilme. P+P+), grup 2 ve grup 3'de ise değerlendirilebilen ve kooperasyonu iyi olan hastalarda Allen resimleri ve Snellen eşeli ile değerlendirildi. Kontrollerde yaşı 36 ay'ın altında olan hastalarda, bilateral katarakt operasyonu uygulanan gözlerde fiksasyonun santral ve sabit olmasına göre dominant göz tespit edildi. Otuz altı ayın üzerindeki hastalarda ise Allen resimleri ve Snellen eşeline göre görme düzeyi tespitleri yapıldı. İki göz arasında 2 sıra ve daha fazla fark olması ambliyopi olarak kabul edildi. İyi gören göze kapama tedavisi uygulandı. Yaşamının ilk 1 yılında opere edilen hastalarda kapatılan gözde ambliyopiye engel olmak için kapama tedavisi dikkatli olarak planlandı. Uyanık olduğu sürelerin önceleri %50'si 1 yaşından sonrada %80'i olarak dominant göze kapama tedavisi uygulandı. Hastalar son kontrol muayenelerinde glob duruş ve hareketleri, refraksiyon, en iyi düzeltilmiş görme keskinliği (EİDGK), biyomikroskopik ön segment muayenesi (kornea, iris, pupilla, GİL, ön- arka kapsül), tansiyon oküler (TO) ölçümü, fundus muayenesi dikkatli bir şekilde yapıldı. Grup 1'deki hastalarda ise indirek oftalmoskop ile fundus muyenesi yapıldı.

Hastalaların preoperatif ve postoperatif TO değerlendirilmesi pnomatik tonometre ve Shiötz tonometre ile ölçüldü. Ara kontrolllerde göz içi basıncı (GİB) değerlendirilebilen hastalarda TO değeri 22 mmHg üzeri çıkmışsa ve fotofobi, epitelyal ödem tabloya eşlik ediyorsa glokom olarak kabul edildi. Takip ve tedavisi yapıldı.

*İstatiksel analiz*

Veriler SPSS for Windows version 18.0 (SPSS Inc., Chicago, IL, USA) ile analiz edildi. Sonuçlar yüzde, ortalama, standart sapma (SS), ortanca, minimum ve maksimum şeklinde ifade edildi. Sayısal verilerin analizi normal dağılıyorsa simple t test ile, normal dağılmıyorsa Mann-Whithney U testi ile yapıldı. P değeri $<0,05$ istatiksel olarak anlamlı kabul edildi.

## Bulgular

Çalışmaya alınan 50 hastanın (25 kız, 25 erkek) 84 gözü

çalışma kapsamında değerlendirildi. Hastaların 34'ünde bilateral, 16'ında unilateral katarakt vardı. Ameliyat öncesi yapılan muayenede 6 tip katarakt tespit edilmişti. Bütün olgularda katarakt santral yerleşimli, yoğun ve 3 mm çapından daha geniş idi. Otuz beş göz total kesif (%41,7), 15 göz (%17,9) kortikal ve nükleer, 13 göz (%15,5) kortikal, 12 göz nükleer (%14,3), 5 göz (%6) arka kapsüler, 4 göz de (%4,8) ise polar katarakt tespit edilmişti. Opere edilen gözlerin ameliyat öncesi yaş ortancası 60 ay (1- 396), son kontrol tarihinde ortanca yaşı 88,6 aydı (17- 408). Takip süreleri 30,9 ay (4- 92) olarak tespit edildi.

Bütün hastalara standart ÖKKK, katarakt aspirasyonu, AKKK, anterior vitrektomi yapıldı. Opere edilen gözlerin 27'sine katarakt operasyonu sırasında GİL implantasyonu yapılmadı. Bu gözler opere edildiklerinde yaş ortancaları 7,3 ay (1-18 ) idi. On altı (%19) göz 33 ay (29 -84) afakik takip edildikten sonra, siliyer sulkusa sekonder GİL yerleştirildi. Elli yedi (%67) göze ise ilk operasyonda siliyer sulkusa GİL uygulaması yapıldı. Bu hastaların GİL ortanca yaşı 68 aydı (5- 396). On bir (%13) göz ise yaklaşık 19 aydır afak olarak takip edilmekteydi. On dört gözün afakik korreksiyonu slisoft kontakt lens ile, 2 gözün ise post op ilk 24 ay kontakt lens ile, kontakt lense uyum sağlayamadığı tespit edilince, 44 ay süreyle de afakik gözlük ile sağlandı. On bir gözün afakik korreksiyonu ise kontakt lens ile devam ettirilmektedir. Takip süreleri 19 ay (13- 29) idi.

Post operatif son kontrol muayenelerinde otomatik refraktometre (Topcan- ORM) ile 73 hastaya ait tekrarlayan ölçümler alınarak sferik eşdeğer ve silindirik eşdeğerler tespit edildi (Tablo I). Sferik eşdeğer-1,02±1,40 sph, silindirik eşdeğer -0,25± 2,70 cyl idi.

Hastaların ameliyat öncesi görme muayeneleri yapıldı. Otuz altı ayın altında olan ve kooperasyon kurulamayan hastalarda pupil ışık refleksi (PIR) değerlendirildi ve kooperasyon kurulabilen hastalarda da obje takibi yapıldı. Anneyi takip etme, çevreye ilgi gibi anamnez bilgileri sorgulandı. Otuz beş hastanın PIR +/+, 9 hasta el hareketleri seviyesinde (EHS), 4 hasta 1 metreden parmak sayma (mps), 4 hasta 3mps, 1 hasta 4 mps, 4 hasta 5 mps görme düzeyleri vardı. Diğer hastalarda da gözlükle EİDGK 0.1-1,0 arasında değişmekteydi. Görme düzeyleri Snellen değerine çevrildi. (P+P+= 0,0001, EHS:0,001, 10 mps:0,008, 1 mps: 0,016, 2 mps:0,03, 3 mps:0,05, 4 mps:0,06 5 mps: 0,08-0,1-0,2-0,3-0,4-0,5-0,6-0,7-0,8-0,9-1).

Opere edilen gözlerin son kontrol muayenelerinde de postoperatif gözlük tashihi ile EİDGK sonuçları tespit edilerek kaydedildi. Hastaların preoperatif EİDGK 0,08±0,02 (P+P+ veya EHS- 5mps), post operatif EİDGK 0,4±0,3 tespit edilmiş olup, preoperatif EİDGK'e göre, postoperatif EİDGK'nin anlamlı derecede artmış olduğu görüldü (p<0,001).

Afakik takibi yapılıp sekonder GİL uygulanan 16 hastanın son kontrol muayenelerindeki görme düzeyleri ortalama 0,2 (0,05-0,8) seviyesinde tespit edildi.

Tek taraflı kataraktı olanlarla çift taraflı kataraktı olan hastalar arasında da görme düzeyleri arasında, anlamlı derecede (*p <0,05*) fark vardı ve çift taraflı kataraktı olan olgularda daha iyi görme sonuçları elde edilmişti. Görme düzeyi değerlendirilebilen son kontrol tarihinde yaş ortalamaları 36 ay üzerinde olan 67 gözün verileri incelendiğinde, 16 (%23,8) gözün 0,8 ve üzerinde görme seviyesine sahip olduğu görüldü ve bu hastaların tamamı bilateral idi. Elli bir (%76) gözde ise 0,8'in altında görme seviyeleri vardı. Bu hastaların hepsi ambliyopi nedeniyle takip edilmekteydiler. Görme seviyesi 0,1'in altında olan 21 (%31) göz vardı. Bunların 9'u unilateral, 12'si bilateral cerrahi geçirmiş olgulardı (Tablo II).

Son kontrol muayenelerinde 36 ayın altındaki 17 hastanın postoperatif görme düzeyi tespitleri ışık reaksiyonları ve obje takibiyle yapıldı. Hastaların muayenelerinde hepsinin santral-sabit-sürekli fiksasyon yapması, obje takiplerinin ve anneye olan ilgilerinin iyi olması görme artışı lehine değerlendirildi.

Ameliyat öncesi belirlenen katarakt tipleriyle postoperatif EİDGK karşılaştırıldığında en iyi görme düzeylerinin polar ve kortikal katarakt tiplerinde ve en kötü görme düzeylerinin de total kesif kataraktlarda olduğunu tespit ettik.

Son kontrol muayenelerinde hastalar yaşlarına göre 3 gruba ayrıldılar: Grup1:(0-36 ay), Grup:2 (36-60 ay), Grup 3:(> 60 ay). Gruplara ait genel özellikler Tablo III' de gösterilmiştir. Grup 1'de 18, grup 2'de 16 ve grup 3'de 50 göz opere edilmişti. Opere edildikten sonra son kontrol muayenesine kadar ki ortalama 24,5 ± 23 ay süre sonunda hastalara ait gelişmiş olan bütün komplikasyonlar Tablo IV'de özetlendi.

**Tablo I.** Afakik Takibi Yapılan Ve Sekonder Gil Uygulanan Hastaların Son Kontrol Muayenesine Kadarki Takip Verileri

| No: | Son kontrol muayenesindeki yaş(ay) | Afakik takip süresi(ay) | Afakik korreksiyon | GİL takılma yaşı(ay) | Son kontrol EİDGK (Snellen değeri) |
|---|---|---|---|---|---|
| 1 | 35 | 26 | KL | 29 | - |
| 2 | 35 | 16 | KL | 29 | - |
| 3 | 40 | 14 | KL | 32 | - |
| 4 | 40 | 10 | KL | 32 | - |
| 5 | 78 | 44 | KL | 47 | 0,1 |
| 6 | 78 | 43 | KL | 47 | 0,2 |
| 7 | 80 | 2 | KL | 36 | 0,1 |
| 8 | 67 | 25 | KL | 33 | 5 mps |
| 9 | 96 | 68 | KL+Afakik gözlük | 84 | 0,4 |
| 10 | 96 | 68 | KL+Afakik gözlük | 84 | 0,8 |
| 11 | 90 | 46 | KL | 47 | 5 mps |
| 12 | 95 | 48 | KL | 60 | 0,1 |
| 13 | 95 | 48 | KL | 60 | 0,2 |
| 14 | 84 | 35 | KL | 41 | 3 mps |
| 15 | 51 | 24 | KL | 33 | 0,2 |
| 16 | 51 | 24 | KL | 33 | 0,1 |
| Ortalama değer ±SS | 66±30 | 33 (29-84) | - | 45±22 | 0,2±0,09 |

GIL; göz içi lensi, EİDGK; en iyi düzeltilmiş görme keskinliği, KL: Kontakt lens

**Tablo II.** Opere edilen unilateral ve bilateral gözlerde kaydedilebilen görme düzeyleri

| Snellen | Unilateral | Bileteral (n=göz sayısı) | Toplam (n=göz sayısı) |
|---|---|---|---|
| 0,1'in altı | 9 (%13,2) | 12 (%17,6) | 21 (%30,8) |
| 0,1.-0,2 | 3 (%4,4) | 10 (%11,7) | 13 (%19,1) |
| 0,3-0,4 | 1 (%1,4) | 8 (%9,5) | 9 (%13,2) |
| 0,5-0,6 | 1 (%1,4) | 7 (%10,2) | 8 (%9,5) |
| 0,7-0,8 | - | 9 (%13,2) | 9 (%13,2) |
| 0,9-1,00 | - | 7 (%10,2) | 7 (%10,2) |

(Yaş: 36 ay üzerindeki hastalar n=67 göz)

Takip süresince 8 (%9,5) göze GİL değiştirme operasyonu uygulanmıştı. Pupilla düzensizliği ve irisde lokalize iris atrofileri takip süresince 17 (%20,2) gözde tespit edilmiş olup, bu hastaların 1'i (%1,1) afak, 3'ü (%3,5) sekonder GİL implantasyonu yapılmış,13 (%15) göz ise ilk operasyonda sulkus GİL implantasyonu yapılmış olgulardı. 1 hasta da optik aksın kaymış olduğu tespit edilince pupilloplasti operasyonu uygulanmıştı. On altı göze ise herhangi bir müdahalede bulunulmamıştı.

**Tablo III.** Gruplara ait genel özellikler

| | Grup 1 (0-36 ay) | Grup 2 (36 -60 aylık) | Grup 3 (> 60 ay) | Toplam (n=50 hasta) |
|---|---|---|---|---|
| **Kız** | 7 | 4 | 14 | 25 (%50) |
| **Erkek** | 3 | 6 | 16 | 25 (%50) |
| **Ortalama Yaş (min-mak)** | 27(17-35 ) | 51 (40 - 59) | 107(64-408) | - |
| **Tek taraflı katarakt** | 2 | 4 | 10 | 16 (%32) |
| **Çift taraflı katarakt** | 8 | 6 | 20 | 34 (%68) |
| **Toplam göz sayısı** | 18 | 16 | 50 | 84 (%100) |
| **Nistagmus** | 2 | 1 | 6 | 9 ( %18 ) |
| **Şaşılık** | 3 | 3 | 6 | 12 (%24) |

Min: minimum, mak: maksimum

**Tablo IV.** Takipte Görülen Komplikasyonlar

| **Takipte görülen komplikasyonlar** | **Grup 1** (0-36 ay n=16) | **Grup 2** (36-60 ay n=18) | **Grup 3** (> 60 ay n=50) | **Toplam** (n=84) |
|---|---|---|---|---|
| Posterior kapsül kenarı fibrozisi | 10 | 17 | 51 | 78 (%92,8) |
| Pupiller alanda membran | 1 | - | 1 | 2 (%2,3) |
| Ön vitrede membran | - | - | 3 | 3 (%3,5) |
| Glokom | 2 | - | 5 | 7 (%8,3) |
| GİL dislokasyonu | - | - | 9 | 9 (%12,3) |
| Pupil çekintisi | 3 | 3 | 11 | 17 (%20,2) |

GİL: Göz içi lens

## Tartışma

Biz çalışmamızda konjenital kataraktlı gözlerde, limbal yaklaşımla ÖKKK, fakoaspirasyon, AKKK, anterior vitrektomi opereasyonu uygulanmış afakik takipte olan veya afakik takip sonrası siliyer sulkusa sekonder GİL uygulaması yapılmış hastaların özelliklerini ve takip sonuçlarını inceledik. Takip sonuçlarımız bize, konjenital katarakt tanısı alan hastaların cerrahi tedavisinde, ÖKKK, lens aspirasyonu, AKKK, anterior vitrektomi ve/veya siliyer sulkusa GİL implantasyonu arka kapsül kesafetini önlemede ve cerrahiye ait komplikasyonların minimalize edilmesinde etkili, güvenilir, iyi görsel sonuçlar veren güncel bir teknik olduğunu gösterdi. Ancak, afakik düzeltme şekli ve süresi, sekonder GİL uygulama zamanlaması, cerrahiye sekonder gelişen glokom, ambliyopi, GİL'e ait komplikasyonlar sonuç görmeyi etkileyen önemli faktörlerdir. Konjenital kataraktla birlikte görülen, şaşılık, nistagmus, mikroftalmi gibi ek oküler patolojilerde vizüel gelişimi olumsuz yönde etkilemektedir.

Pediyatrik kataraktları yetişkin kataraktlardan ayıran pek çok özellik vardır. Çocuklarda lens kapsül elastisitesinin fazla, skleral rijiditenin daha az, vitreusun daha yoğun bir jel yapısında olması ve lens epitel hücrelerinde mitotik aktivitenin bulunması, dolayısıyla da arka kapsül opaklaşma insidansının daha yüksek olması, konjenital kataraktlara olan yaklaşımın yetişkin kataraktlardan farklı olmasını gerektiren özelliklerdir (4). Konjenital kataraktlarda prognoz yalnızca uygulanan cerrahinin başarısı tarafından belirlenmemekte, yukarıda sayılanlar gibi çocuk gözüne özgü pek çok faktör tedavinin başarısını etkilemektedir. Arka kapsül kesafeti ve sekoder membran oluşumu tedavi başarısını düşürmektedir. Güncel pediyatrik katarakt cerrahisi ve GİL uygulaması anlayışı açık bir görme aksının sürdürülebilmesi için santral arka kapsülün ve ön vitreusun alınmasını işaret etmektedir (5-8). Konjenital kataraktlı olgular preoperatif cerrahi özellikleri açısından farklı oldukları gibi, sistemik hastalık olasılıkları, postoperatif izlemleri ve komplikasyonları açısından da ayrıcalıklıdır. Bu olgularda postoperatif afakinin düzeltilmesi en önemlisi ambliyopinin tedavisi dikkat edilmesi gereken başlıca özelliklerdendir (9).

Konjenital kataraktlı çocuklarda cerrahi sonrası dönemde erişkinden daha fazla enflamasyon görülmesiyle birlikte, arka kapsül kesifliği (AKK) başta olmak üzere, fibrinöz üveit, pupiller membran oluşumu, arka yapışıklıklar, GİL dislokasyonu gibi komplikasyonlar daha sık ve şiddetli olmaktadır (10). Takibimizde olan hastalara ait kayıtlı verilerin analizinde, post operatif birinci gün muayenelerinde 16 gözde (%19) fibrinöz üveit tablosu, 2 (%2,3) olguda da pupiller alanda ve GİL üzerinde membran şeklinde fibrinoid reaksiyon tespit edildi. Bu hastalar yoğun steroid tedavisi ile sorunsuz bir şekilde düzeldiler.

Arka kapsülü yerinde bırakmak ya da anterior vitrektomi yapmadan posterior kapsülotomi yapmak lens epitelyum hücrelerinin üzerinde çoğalması için geride bir kalıp bırakmaktır. Bu nokta da genel yaklaşım 6 yaşından küçük çocuklarda 3,5-4 mm boyutlarında arka kapsüloreksis ile ön vitrektominin birlikte yapılmasının gerektiğidir. Neodmiyum donedyiltriyum aliminyum garned (Nd-YAG) Lazer kapsülotomi için uyum sağlayabilecek çocuklarda ise (7 yaş ve üzeri) ön vitrektomi yapılmaksızın arka kapsüloreksis yapılmasının yeterli olacağı şeklindedir (4,6,11). Ancak ön vitrektomi yapılmadan AKK gelişiminin önlenemeyeceği sadece geciktirilebileceği belirtilmektedir (6,11). Yapılan çalışmalarda ön vitrektomi ve arka kapsüloreksis yapılan olgularda AKK oranı %11,8-15, ön vitrektomi ve arka kapsüloreksis yapılmayan olgularda AKK gelişme oranını %40-76,9 arasında gösterilmiştir (12-14). Er ve arkadaşları çocukluk çağı katarakt cerrahisinde arka kapsülün sağlam bırakıldığı grupla arka kapsüloreksis yapılmış grubu karşılaştırdıklarında, arka kapsüle dokunulmayan grupta %43 oranında AKK geliştiğini buna karşılık arka kapsüloreksis grubunda ise hiçbir olguda AKK gelişmediğini bildirmişlerdir (15). Arka kapsüloreksis limbal cerrahilerde sıklıkla GİL yerleştirilmeden önce yapılmaktadır (4). Pediatrik katarakt cerrahisinde arka kapsülotomiye rağmen ikincil membran oluşumu da sık (%10-63) karşılaşılan komplikasyonlardandır (5,16,17). Bizim çalışmamızda 5 hastada (%5,9) ön vitreusta veya pupiller alanda membran şeklinde AKK geliştiğini tespit ettik. Nd-YAG lazer ile membranektomi uygulayarak sorunsuz bir şekilde aks açıklığını sağladık. Olguların 79'da (%92,8) ise optik aks açık, posterior kapsül kenarında fibrozis (sommering) geliştiğini gördük.

GİL implantasyonu, yaşamın ilk 2 yılındaki aksiyel uzunluk artışı ve korneal kurvatür değişikliği nedeniyle çoğunlukla 2 yaşın üstündeki olgulara uygulanmaktadır (18). Yerleştirilecek olan GİL gücü pediatrik katarakt cerrahisinin uzun dönem sonuçlarını en fazla etkileyen faktörlerden biridir. GİL diyoptrisinin hesaplanmasında gözün aksiyel büyümesi göz önünde bulundurulmalıdır. Hastanın cerrahi geçirdiği yaş, cerrahi öncesi ve sonrası görme keskinliği, GİL konup konmaması, kataraktın tek veya çift taraflı olması gibi pek çok faktör gözün aksiyel büyümesini etkileyebilmektedir (19). Pediatrik olgularda keratometri, A-scan ultrasonografi (USG)

kullanılarak SRK-T, Holaday ya da Hofer Q formülü gibi teorik formüllerle oldukça doğru GİL gücü hesabi yapılabilir (20). Prost çocuklarda gözün aksiyel uzunluğunu ve korneanın refraktif gücünü de dikkate alarak afakide kullanılabilecek GİL gücü için bir formül geliştirmiştir (21). Buna göre 1-2 yaş arasındaki çocuklarda yerleştirilecek olan göz içi lensi, hesaplanana göre %20, 2-4 yaş arasında %15 azaltılarak seçilmelidir. Bölgemizde ekonomik koşullar ve eğitim düzeyinin düşük olması ve hastaların takiplerinde sıkıntılar yaşanması nedeniyle postoperatif ambliyopi gelişimini kontrol altında tutmak için ameliyat sırasındaki yaşı 36 ayın (3 yaş) üzerinde olan hastaların 1,00 D myopik bırakılmaları hedeflendi. Bu hastalarda uygulanan GİL gücü %10 daha fazla düzeltildi. 12-36 ay hastalarda refraksiyonun +1,00 D, 12 ay'ın altındaki hastalarda da +2,00 D hipermetropik bırakılmaları hedeflendi. 1 yaşın altındaki hastalarda USG ile tespit edilen AL değerine göre, 1 yaşın üzerinde ise keratometrik değerleri ölçülebilen ve uyum sağlayabilen hastalarda SRK-2 formülü kullanılarak GİL gücü hesabı yapıldı.1 yaşın altındaki hastalarda tespit edilen değerin %80'ı verildi. Hastaların yaş ortancalarının son kontrol tarihinde 88,6 ay (17-408) olduğu göz önüne alındığında istediğimiz sonuca ulaşabildiğimizi görmekteyiz.

Genellikle açık açılı tip olan sekonder glokom pediatrik katarakt cerrahisi sonrası ortaya çıkan en önemli komplikasyonlardan biridir. Vishwanath ve arkadaşlarının bildirdiği rapora göre hayatın ilk bir ayında bilateral lensektomi yapılmış çocukların %50'sinde 5 yıllık takipte bir veya her iki gözünde glokom gelişmiştir (22). Lundvall ve Kugelberg hayatlarının ilk 4 haftasında konjenital katarakt cerrahisi geçiren konjenital kataraktlı çocukların %80'inde glokom geliştiğini buldu (23). Arıtürk ve ark. 2 yaşından önce ameliyat yapılan olgularda glokom oranını %68, Asrani ve Wilensky ise %64 olarak bildirmişlerdir (24,25). Son yıllarda yapılmış olan iki büyük kohort çalışmasında, cerrahi sonrasında gelişebilecek afakik glokom için en önemli risk faktörünün küçük yaş olduğu belirtilmiş olup, riskli yaş sınırı iki çalışmada sırasıyla, 1 yaş ve 9 ay olarak belirtilmiştir (19,26). Güncel bir meta-analizde 2 yaş altı çocuklarda bilateral konjenital katarakt cerrahisinde primer GIL implantasyonunun sekonder glokom gelişme riskini %9,5 azalttığı belirtilmiştir (27). Bizim takiplerimizde 1 aylıkken bilateral katarakt cerrahisi geçiren bebekte afakik takibinin beşinci ayında afakik glokom tespit edilmiş olup sağ gözüne antimetabolitle kombine trabekülektomi uygulanmış, diğer gözde ise topikal antiglokomatözlerle glokom kontrol altına alınmıştır.

Pek çok çalışmada konjenital katarakt cerrahisinde erken cerrahinin görme gelişiminde olumlu etkilerinden bahsedilmektedir (6,16,28). Lorenz ve ark. iki taraflı kataraktı olan erken cerrahi ve optik düzeltmesi yapılmış olguların %50'sinde 20/50 ve daha iyi, %70'inde ise 20/100 veya daha iyi görme edildiğini ve bu gurubun %50'sinde bir miktar binoküler fonksiyon geliştiğini göstermişlerdir (29). Önal M ve ark 10 olgunun 16 gözünde yaptıkları bir çalışmada, 5 yıllık takip sonunda ortalama preoperatif görme keskinliği 15/200'den 20/30'a yükselmiştir (30). Bizim çalışmamızda hastaların preop EİDGK'e göre, postop EİDGK'nin anlamlı derecede artmış olduğu görüldü.

Sonuç olarak, konjenital katarakt tanısı alan hastaların cerrahi tedavisinde, ÖKKK, lens aspirasyonu, AKKK, anterior vitrektomi ve/veya siliyer sulkusa GİL implantasyonu arka kapsül kesafetini önlemede ve cerrahiye ait komplikasyonların minimalize edilmesinde etkili, güvenilir, iyi görsel sonuçlar veren güncel bir tekniktir. Ancak, afakik düzeltme şekli ve süresi, sekonder GİL uygulama zamanlaması, cerrahiye sekonder gelişen glokom, ambliyopi, GİL'e ait komplikasyonlar sonuç görmeyi etkileyen önemli faktörlerdir. Konjenital kataraktla birlikte görülen, şaşılık, nistagmus, mikroftalmi gibi ek oküler patolojilerde vizüel gelişimi olumsuz yönde etkilemektedir. Konjenital katarakt cerrahisi geçiren gözler ömür boyu sıkı takip altında tutulup, hastanın ve ailenin görme ile ilgili beklentilerinin bu uzun sürece göre ayarlanması yerinde olacaktır.

## References


1. Potter WS. Pediatric cataracts. Pediatr Clin North Am 1993;40(4):841-853.
2. Zhao QH, Zhao YE. Commentary review: challenges of intraocular lens implantation for congenital cataract infants. Int J Ophthalmol 2021;14(6):923-930.
3. Jody N, Santana M, Rudell J. Pediatric cataract surgery: considerations and updates in diagnosis and management. Curr Opin Ophthalmol 2023;34(1):58-63.
4. Vasavada AR,Nihalani BR. Pediatric cataract surgery. Current Opinion in Ophyalmology 2006;17(1): 54-61.
5. Buckley EG, Klombers LA, Seaber JH, Scalise-Gordy A, Minzter R.. Management of the posterior capsule during pediatric intraocular lens implantation: Am J Ophthalmol 1993;115(6):722-728.
6. Vasavada A, Desai J. Primary posterior capsulorhexis with and without anterior vitrectomy in congenital cataracts: J Cataract Refract Surg 1997;23(1):645-651.
7. Self JE, Taylor R, Solebo AL, et al. Cataract management in children: a review of the literature and current practice across five large UK centres. Eye (Lond) 2020;34(12):2197-2218.
8. Bremond-Gignac D, Daruich A, Robert MP, Valleix S. Recent developments in the management of congenital cataract. Ann Transl Med 2020 Nov;8(22):1545.
9. Mohammadpour M, Shaabani A, Sahraian A,et al. Updates on managements of pediatric cataract. J Curr Ophthalmol 2018;31(2):118-126.
10. Zhang JS, Wang JD, Yusufu M, et al. The effect of retaining intact posterior capsule in congenital cataract surgery in children aged 4-8 years. BMC Ophthalmol 2021;21(1):332.
11. Guo S, Wagner RS, Caputo A. Management of the anterior and posterior lens capsules and vitreus in pediatric cataract surgery. J Pediatr Ophthalmol Strabismus 2004;41(6):330-337.
12. Jensen AA, Basti S, Greenwald MJ, Mets MB. When may the posterior capsule be preserved in pediatric intraocular lens surgery? Ophthalmology 2002;109(2):324-327.
13. Luo Y, Lu Y, Lu G, Wang M. Primary posterior capsulorhexis with anterior vitrectomy in preventing posteriorcapsule opacification in pediatric cataract microsurgery. Microsurgery 2008;28(2):113-116.
14. Ram J, Brar GS, Kaushik S, Gupta A, Gupta A. Role of posterior capsulotomy with vitrectomy and intraocular lens design and material in reducing posterior capsule opacification after pediatric cataract surgery. J Cataract Refract Surg 2003;29(8):1579-1584.

15. Er H, Doganay S, Evereklioglu C, Erten A, Cumurcu T, Bayramlar H. Retrospective comparison of surgical techniques to prevent secondary opacification in pediatriccataracts. J Pediatr Ophthalmol Strabismus 2000;37(5):294-298.

16. Chen J, Chen Y, Zhong Y, Li J. Comparison of visual acuity and complications between primary IOL implantation and aphakia in patients with congenital cataract younger than 2 years: a meta-analysis . J Cataract Refract Surg 2020;46(3):465-473.

17. Zettestrom C, Kugelberg M. Pediatric cataract surgery. Acta ophthalmol Scand 2007;85(7):698- 710.

18. Simons BD, Siatkowski RM, Schiffman JC, Flynn JT, Capo H, Munoz M. Surgical technique, visual outcome, and complications of pediatric intraocular lens implantation. J Pediatr Ophthalmol Strabismus 1999;36(3):118-124.

19. Vasavada AR, Raj SM, Nihalani B. Rate of axial growh following congenital cataract surgery. Am J ophthalmol 2004;138(6):915-924.

20. Tromans C, Haigh PM, Biswas S, Lloyd IC. Accuracy of intraocular lens power calculation in paediatric cataract surgery. Br J Ophthalmol 2001;85(8):939-941.

21. Prost ME. İOL calculations in cataract operations in children. Klin Oczna 2004;106(4-5):691-694.

22. Vishwanath M, Cheong-Leen R, Taylor D, Russell-Eggitt I, Rahi J. Is early surgery for congenital cataract a risk factor for glaucoma? Br J Ophthalmol 2004;88(7):905-910.

23. Lundvall A, Kugelberg U. Outcame after treatment of congenital bilateral cataract. Acta Ophthalmol Scand 2002;80(6):593-597.

24. Arıtürk N, Öge Y, Erkan D, Süllü Y, Türkoğlu S. Konjenital katarakt cerrahisi sonrası sekonder glokom olguları. MN Oftalmoloji 1997;4(5):295-299.

25. Asrani GS, Wilensky JT. Glaucoma after congenital cataract surgery. Ophthalmology 1995;102(6): 863-867.

26. Vasavada AR, Trivedi RH, Sing R. Necessity of vitrectomy when optic captureis performed in children older than 5 years. J Cataract refract surg 2001;27(8):1185-1193.

27. Zhang S, Wang J, Li Y, Liu Y, He L, Xia X. The role of primary intraocular lens implantation in the risk of secondary glaucoma following congenital cataract surgery: A systematic review and meta-analysis. PLoS One 2019;14(4):e0214684.

28. Singh R, Barker L, Chen SI, Shah A, Long V, Dahlmann-Noor A. Surgical interventions for bilateral congenital cataract in children aged two years and under. Cochrane Database Syst Rev. 2022;9(9):CD003171.

29. Lorenz B, Wörle J, Friedl N, Boergen KP. Monocular and binocular fuctional result in case of contact lens corrected infant aphakia. İn Cotlier E, Lambert S, Taylor D eds. Congenital cataracts. Austin, Texas: RG Landes, 1994:151-163.

30. Onal M, Ozdek S, Koksal M, Hasanreisoğlu B. Pars plana lensectomy with dauble capsule supported intraoculer lens implantation in children. J Cataract Refract surg 2000;26(4):486-490.

# The Relationship Between Childhood Traumatic Experiences and Obsessive Beliefs in Alcohol Use Disorder

**Seda Kiraz[1], Fatma Gul Helvaci Celik[2]**

[1]Department of Psychiatry, Faculty of Medicine, Hitit University, Corum, Türkiye
[2]Department of Psychiatry, Faculty of Medicine, Giresun University, Giresun, Türkiye

**Address for Correspondence:** Hitit University, Faculty of Medicine, Department of Psychiatry, Corum, Türkiye
e-mail: drsedakiraz@gmail.com

**Orcid ID:** SK: 0000-0001-9393-6921
FGHC: 0000-0002-4802-9641

**Cite As**: Kiraz S, Celik Helvacı GF. The Relationship Between Childhood Traumatic Experiences and Obsessive Beliefs in Alcohol Use Disorder. Hitit Med J 2023;5(3): 138-143. https://doi.org/10.52827/hititmedj.1270671

## Abstract

**Objective:** Based on the pathophysiological similarities between alcohol use disorder (AUD) and obsessive compulsive spectrum disorders, as well as the close association between traumatic experiences and addiction, the goal of this study was to assess the relationship between obsessive beliefs and childhood traumas in patients with AUD by comparing them with the control group

**Material and Method:** The data of 60 AUD cases who applied to the Alcohol and Substance Treatment Center outpatient clinic consecutively and 56 healthy control groups were evaluated. Structured Clinical Interview for DSM-5, Obsessive Beliefs Questionnaire, Childhood Trauma Questionnaire, Hamilton Anxiety Inventory, and Hamilton Depression Inventory were applied to both groups. The Addiction Profile Index, which evaluates the severity of addiction, was applied to the patient group. Data were evaluated with SPPS 22.

**Results:** Obsessive beliefs, traumatic experiences, depression and anxiety scores were found to be significantly higher in AUD cases than in the control group. No significant relationship was found between traumatic experiences and obsessive beliefs. The most important predictors of obsessive beliefs were found to be anxiety and depression scores.

**Conclusion:** The current study is important since it is the first to assess how obsessive beliefs and childhood traumas relate to AUD patients. Further analysis in a larger sample in this area will be helpful in identifying risk factors and creating preventive interventions for AUD, a disorder that is difficult to treat and relapse.

**Keywords:** Alcohol use disorder, Childhood traumatic experiences, Obsessive beliefs

## Özet

**Amaç:** Bu çalışmada alkol kullanım bozukluğu (AKB) ve obsesif kompulsif spektrum bozuklukları arasında var olan benzerliklerden ve travmatik yaşantıların da bağımlılıkla olan yakın ilişkisinden yola çıkılarak, AKB tanılı hastalarda obsesif inanışlar ve çocukluk çağı travmalarının ilişkisinin, kontrol grubu ile karşılaştırılarak değerlendirilmesi amaçlanmıştır.

**Gereç ve Yöntem:** Alkol ve Madde Tedavi Merkezi polikliniğine ayaktan ardışık olarak başvuru yapan 60 AKB olgusu ile aynı özelliklere sahip ve aynı bölgeden rastgele seçilen 56 sağlıklı gönüllüden oluşan kontrol grubunun verileri değerlendirilmiştir. Her iki gruba da DSM-5 için yapılandırılmış Klinik Görüşme, Obsesif İnanışlar Ölçeği-44, Çocukluk Çağı Travmaları Ölçeği-28, Hamilton Anksiyete Ölçeği ve Hamilton Depresyon Ölçeği uygulanmış, hasta grubuna bağımlılık şiddetini değerlendiren Bağımlılık Profil İndeksi yapılmıştır. Veriler SPPS 22 ile değerlendirilmiştir.

**Bulgular:** AKB olgularında obsesif inanışlar, travmatik yaşantılar, depresyon ve anksiyete skorları anlamlı olarak kontrol grubundan yüksek saptanmıştır. Travmatik yaşantılar ile obsesif inanışlar arasında ise anlamlı bir ilişki tespit edilmemiştir. Obsesif inanışların en önemli öngörücüleri anksiyete ve depresyon belirtileri olduğu görülmüştür.

**Sonuç:** Bu çalışma AKB hastalarında obsesif inanışlar ile çocukluk çağı travmalarının ilişkisini değerlendiren ilk çalışma olması nedeniyle değerlidir. Bu alanda daha büyük örneklemde daha ileri analizler, tedavisi zor olan ve yinelemelerle giden bir bozukluk olan AKB için, risk faktörleri belirleme, önleyici müdaheleler oluşturma konusunda yararlı olacaktır.

**Anahtar Sözcükler:** Alkol kullanım bozukluğu, Çocukluk çağı travmatik yaşantıları, Obsesif inanışlar

**Date of Submission:** 24.03.2023
**Date of Acceptance:** 25.06.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** : The study was approved by the Hitit University Non-Interventional Research Ethics Committee (decision number 2022-01).
**Plagiarism Checks:** Yes - iThenticate
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: SK, FHC Design: SK, FHC Data Collection/Data Processing: SK, FHC Data Analysis: SK, FHC Article Preparation: SK, FHC
**Informed Consent:** Consent was obtained from the patients.
**Financial Disclosure:** No financial support has been received.

## Introduction

Alcohol use disorder (AUD) is a disease with a high incidence of significant disability and medical comorbidities in which biological, psychological, behavioral and social factors play a role (1). AUD includes compulsive heavy drinking and loss of control over alcohol intake, as well as other features of addiction (2). There is a high risk of relapse in AUD, as in all other addictions. Alcohol, like all addictive substances, reinforces its own use by affecting the brain reward circuits (3). Numerous studies have demonstrated that dopamine increases at synapses in the nucleus accumbens (NA), a crucial part of the ventral striatum, are a common mechanism through which both natural rewards and addictive chemicals influence behavior (4). The increase in NA dopamine induced by alcohol intake has been suggested as a necessary way to reinforce the repetitive urge to drink and the addictive process (5). Compulsive alcohol use is due to long-term changes in memory-related neural networks that receive input from midbrain dopaminergic neurons (6). When alcohol addiction occurs, a certain memory develops. For this reason, even a very small amount of alcohol use or reminder stimuli have a triggering effect. These triggers lead to alcohol seeking and compulsive use in addicted individuals (7).

Compulsive drinking, ritualistic behavior pattern, preoccupations; reflects the obsessive-compulsive spectrum-related side of AUD. In fact, many overlaps are known between impulse control disorders, addiction, and obsessive-compulsive spectrum disorders (8).

Addiction and traumatic experiences are also areas that have been frequently studied and shown to be related. Traumatic experiences seem to play a role, especially in addiction processes associated with avoiding negative emotions (9).

The development of obsessive-compulsive disorder (OCD) and the intrusive thoughts associated with OCD is believed to be influenced by maladaptive "obsessive beliefs" regarding threat, responsibility, uncertainty, perfectionism, importance, and control of thoughts, according to cognitive models of OCD (10). In the literature, obsessive beliefs have been studied in OCD (11), major depression (12) and anxiety disorders (13), but they have not been studied in AUD. The purpose of the current study was to assess the connection between traumatic experiences and obsessive beliefs in the AUD group, based on the relationship of addiction with trauma and obsessive-compulsive spectrum.

## Material and Method

Inclusion criteria for the study: being older than 18 and younger than 65, being literate, consenting to participate in the study and meeting the criteria for AUD for the patient group. Exclusion criteria: any psychotic disorder/mood disorder with psychotic features, mental retardation and substance use disorders were determined. The participants who signed the informed consent form after learning about the study and meeting the inclusion and exclusion criteria were included. Patients admitted to the study center eighty-two patients were evaluated for AUD by psychiatric interview. Eight patients were disqualified because the scales were improperly filled out. 3 patients were excluded from the study because of accompanying psychotic disorder, 2 patients due to mental retardation, and 9 patients did not volunteer to participate in the study. After exclusion 60 consecutive cases diagnosed with AUD who applied to the AMATEM outpatient clinic and 56 healthy volunteers, met the inclusion/exclusion criteria from the study. Then, psychiatric diseases were evaluated by the researcher of the study with Structured Clinical Interview for DSM-5 (SCID-5) in the patient and control groups. While the sociodemographic data form, Obsessive Beliefs Questionnaire (OBQ) and Childhood Traumatic Experiences Scale (CTQ) were applied to both groups, the Addiction Profile Index (API), which evaluates the severity of addiction, was applied only to the AUD group. The scale scores for the AUD and control groups were compared and the effect on obsessive beliefs was investigated by dividing the patient group into two according to whether they had childhood trauma or not.

The Hitit University Non-Interventional Research Ethics Committee approved the current cross-sectional, clinically based study (decision number 2022-01), and it was carried out in conformity with the Helsinki Declaration. Subjects who agreed to participate in the study after being informed of its existence and having completed the inclusion and exclusion criteria did so by signing consent forms.

Data Collection Tools

Sociodemographic information form

The researchers created a form that evaluated a wide range of sociodemographic and addiction-related factors, including educational attainment, substances used, and length of use. This form, which consists of 14 questions, includes age, gender, marital and employment status, age of onset of alcohol, duration, frequency, substance use, and the presence of concomitant mental and physical illness.

The Obsessive Beliefs Questionnaire (OBQ)

Due to the substantial association, the Obsessive Compulsive Cognitions Working Group first designed 87 items, and later a 44-item short form. It is a measure that evaluates perfectionism/intolerance of uncertainty, elevated sense of responsibility/exaggerated threat perception, and the value placed on one's thoughts/controlling thought. Boysan et al. conducted a validity-reliability assessment of the OBQ-44 in Turkey. The internal consistency rate for the entire scale was 0.95, and the 30-day test-retest correlation was 0.79 (14).

Childhood Trauma Questionnaire (CTQ-28)

The five sub-dimensions of this self-report scale, which Bernstein et al. established, are Emotional abuse, Physical abuse, Sexual abuse, Emotional neglect, and Physical neglect. It is rated from 1 to 5 on a Likert scale (15). The 28-question version of the scale was subjected to adaptation, validity, and reliability studies, and a cut-off score of > 35 points for the total score. Şar et al. determined the Turkish version's validity and reliability. The scale's Cronbach's alpha value was determined to be 0.93 (16).

Addiction Profile Index Scale (API)

It is a 37-item scale with 5 subscales that was created by Ögel et al. to examine various aspects of addiction and gauge the severity of addiction. Substance Use Characteristics Dimension, Addiction Diagnostic Criteria Dimension, Effect of Substance Use on One's Life Dimension, Severe Desire for Substance Use Dimension, Motivation to Stop Using Substances subscales. For the subscales, the Cronbach's

alpha coefficient ranged from 0.63 to 0.86, and for the total API, it was 0.89 (17).

Structured Clinical Diagnostic Interview (SCID-5)

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) diagnoses are covered by the SCID, a semi-structured clinical interview created by First (18). Elbir et al. carried out validity and reliability investigations in Turkey (19).

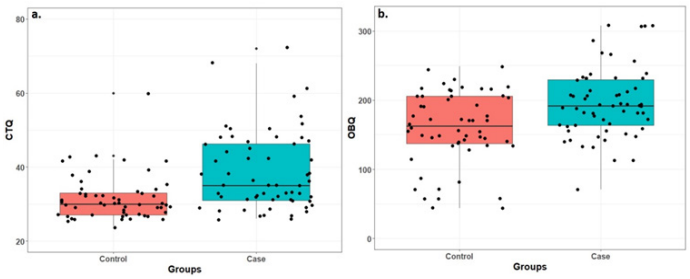
## Statistical Analysis

Statistical analyses of the data obtained from the questionnaires and scales were carried out using the SPSS (Version 22.0, SPSS Inc., Chicago, IL, USA) package program in the current study. To ascertain whether the data had a normal distribution, the Kolmogorov-Smirnov and Shapiro-Wilk tests were applied. When presenting descriptive statistics for numerical data, the mean and standard deviation (SD) were used if the data had a regularly distributed distribution; otherwise, the median (min-max) was used. Descriptive statistics of categorical variables obtained from socio-demographic questions and scales were reported as frequency and percentage (%). The Mann Whitney U test was employed for non-normally distributed data and the Student's t test for normally distributed data when comparing numerical data between two independent groups. Univariate linear regression analysis was used to determine the cause-effect relationship between the OBQ total score and socio-demographic characteristics and other scale scores. The accepted statistical significance level was $p<0.05$.

## Results

Sixty patients and 56 controls were analyzed in the study. All patients included in the study were male. The comparison of the socio-demographic characteristics, total and subscale scores of the OBQ and CTQ scales among the research groups is presented in Table I. Education and marital status distributions were statistically similar among the research groups (Respectively, $p=0.322$, $p=0.299$, Table I). The mean API of the patient group was 14.32±2.63 (7.20 – 20.75). The distribution of CTQ and OBQ scores between the AUD and control groups is shown in figure 1.

**Figure I.** Box plots showing the distribution of (a.) Childhood trauma questionnaire (CTQ) and (b.) Obsessive Beliefs Questionnaire (OBQ) scores between case and control groups




The AUD group's CTQ subscale scores for total, Emotional abuse, Physical abuse, and Emotional neglect were all substantially higher than those of the control group ($p0.001$, $p0.001$, $p=0.027$, and $p=0.006$, respectively) in comparison to the AUD group. There were no statistically significant differences in the rates of Sexual abuse and Physical neglect across the research groups ($p>0.05$).

The patient group's HAM-A and HAM-D scores were substantially higher than those of the control group ($p<0.001$). The patient group's OBQ total, Perfectionism, Conscientiousness, and Caring scores were significantly higher than the control group ($p=0.001$, $p=0.002$, $p<0.001$, $p=0.002$, respectively) Table I.

**Table I.** Comparison of socio-demographic characteristics and scale scores between research groups

| | | Control (n=56) | AUD group (n=60) | *p Values* |
|---|---|---|---|---|
| Education | Primary education<br>High school<br>University | 15 (26.8%)<br>25 (44.6%)<br>16 (28.6%) | 24 (40%)<br>22 (36.7%)<br>14 (23.3%) | *0.322*[a] |
| Marital status | Single<br>Married | 19 (33.9%)<br>37 (66.1%) | 26 (43.3%)<br>34 (56.7%) | *0. 299*[a] |
| Age | | 41.36±8.59 | 39.62±10.83 | *0.342*[b] |
| CTQ | No<br>Yes | 46 (82.1%)<br>10 (17.9%) | 29 (48.3%)<br>31 (51.7%) | ***<0.001***[a] |
| CTQ Emotional abuse | No<br>Yes | 49 (87.5%)<br>7 (12.5%) | 31 (51.7%)<br>29 (48.3%) | ***<0.001***[a] |
| CTQ Physical abuse | No<br>Yes | 52 (92.9%)<br>4 (7.1%) | 47 (78.3%)<br>13 (21.7%) | ***0.027***[a] |
| CTQ Sexual abuse | No<br>Yes | 49 (87.5%)<br>7 (12.5%) | 53 (88.3%)<br>7 (11.7%) | *0.890*[a] |
| CTQ Emotional neglect | No<br>Yes | 45 (80.4%)<br>11 (19.9%) | 34 (56.7%)<br>26 (43.3%) | *0.006*[a] |
| CTQ Physical neglect | No<br>Yes | 40 (71.4%)<br>16 (28.6%) | 43 (71.7%)<br>17 (28.3%) | *0.977*[a] |
| HAM-A | | 4 (1-11)<br>(4.75±2.65) | 20 (0-47)<br>(20.35±9.42) | *<0.001*[c] |
| HAM-D | | 7 (3-11)<br>(7.23±2.32) | 24 (12-53)<br>(26.88±10.23) | *<0.001*[c] |
| OBQ - Total | | 162.5 (44-249)<br>(159.5±53.3) | 192 (71-308)<br>(196.1±50.27) | *0.001*[c] |
| OBQ - P | | 61.77±22.46 | 73.93±18.91 | *0.002*[b] |
| OBQ - R | | 59.5 (16-94)<br>(58.59±19.50) | 74 (25-112)<br>(73.28±19.36) | *<0.001*[c] |
| OBQ - I | | 41 (10-70)<br>(38.04±15.61) | 48 (17-84)<br>(48.82±17.57) | *0.002*[c] |

[a]Chi-Square test
[b]Student's t test
[c]Mann Whitney U
CTQ: Childhood Trauma Questionnaire, OBQ: Obsessive Beliefs Questionnaire, OBQ – P: Perfectionism and Intolerance of Uncertainty, OBQ – R: Responsibility, OBQ – I: Importance and Control of Thoughts, HAM-A: Hamilton Anxiety Scale, HAM-D: Hamilton Depression Scale

Comparison of total and subscale scores of OBQ is presented in Table II, when the AUD group is divided into 2 according to the CTQ cutoff score. According to the existence of the CTQ, there was no statistically significant difference in the OBQ total and subscale scores. ($p>0.05$, Table II).

**Table II.** Comparison of the OBQ total and subscale scores of the groups formed according to the CTQ scale scores in the AUD group

| | CTQ (+) (n=31) | CTQ (-) (n=29) | *p values* |
|---|---|---|---|
| **OBQ – Total** | 206.2 ± 55.42 | 186.7±43.74 | *0.134*[b] |
| **OBQ – P** | 76.48 ±20.65 | 71.55±17.12 | *0.317*[b] |
| **OBQ – R** | 76.86±20.17<br>76 (25-112) | 69.94±18.26<br>68 (36-109) | *0.203*[c] |
| **OBQ – I** | 52.62±19.04 | 45.26±15.55 | *0.105*[b] |

[b]Student's t-test with mean±SD
[c]Mann-Whitney U test with median (min-max)
SD: Standard deviation, CTQ: Childhood Trauma Questionnaire, OBQ: Obsessive Beliefs Questionnaire, OBQ – P: Perfectionism and Intolerance of Uncertainty, OBQ – R: Responsibility, OBQ – I: Importance and Control of Thoughts.

In order to ascertain the cause-and-effect relationship between the total scores of the OBQ and sociodemographic characteristics, as well as the total and subscale scores of the CTQ scale, as well as the and 95% confidence intervals for each statistically significant parameter, a univarite regression analysis was conducted. The results are shown in Table III. According to the findings, for 1 unit increase in the HAM-A score, the OBQ total score increased by 1.61 (0.69-2.53) units and the 1 unit increase in the HAM-D score increased the OBQ total score by 1.43 (0.65-2.2) units (*p=0.001, p<0.001*, Table III). The OBQ scores of those who were alcohol addiction were increased by 36.7 (17.6-55.7) units (*p<0.001*). Age, education, marital status, CTQ total, Emotional Abuse, Physical Abuse, Sexual Abuse, Emotional Neglect, Physical Neglect subscale variables were not statistically insignificant in the univariate model (*p>0.05*, Table III).

**Table III.** Univariate regression analysis findings regarding the cause-effect relationship between OBQ total scores and socio-demographic characteristics and total and subscale scores of the CTQ in the entire group

| | Univariate | | |
|---|---|---|---|
| | ***p values*** | **Beta (CI 95%)** | **Standardized Beta Coefficients** |
| **Alcohol addiction (Case vs. control)** | ***<0.001*** | 36.7 (17.6-55.7) | 0.336 |
| **HAM-D** | ***<0.001*** | 1.43 (0.65-2.2) | 0.324 |
| **HAM-A** | ***0.001*** | 1.61 ( 0.69-2.53) | 0.310 |
| **Age** | *0.126* | - | |
| **Education** | *0.460* | - | |
| **Marital status** | *0.101* | - | |
| **CTQ** | *0.566* | - | |
| **CTQ emotional abuse** | *0.333* | - | |
| **CTQ physical abuse** | *0.395* | - | |
| **CTQ sexual abuse** | *0.142* | - | |
| **CTQ emotional neglect** | *0.697* | - | |
| **CTQ physical neglect** | *0.764* | - | |

CI: Confidence interval, CTQ: Childhood Trauma Questionnaire, OBQ: Obsessive Beliefs Questionnaire, OBQ – P: Perfectionism and Intolerance of Uncertainty, OBQ – R: Responsibility, OBQ – I: Importance and Control of Thoughts

Due to the very substantial connection between AUD, HAM-A, and HAM-D variables, all of which were significant in the univariate model, multiple regression analysis was not possible.

## Discussion

In this study, we demonstrated obsessive beliefs and negative childhood experiences in the AUD group by comparing them with the control group. The findings showed that obsessive beliefs and childhood traumatic experiences were significantly higher in the AUD group. However, it was found that obsessive beliefs were not associated with childhood trauma, however anxiety and depressive symptoms affected obsessive beliefs. As a result of our research, there is no study in the literature investigating obsessive beliefs in AUD and examining its relationship with childhood traumatic experiences.

Despite current effective treatments for AUD, high relapse rates and long-term dysfunction persist even in treated patients (20). This situation creates the need for a more comprehensive examination and a transdiagnostic approach in the pathophysiological mechanisms that play a role in AUD. Especially in recent years, studies have emphasized the relationship between OCD in the etiology of AUD (21, 22). Compulsiveness (persistent use despite negative results) in both these diseases is one of the most important common symptoms. Based on this, we confirmed in our study the hypothesis that obsessive beliefs, which almost match with OCD, will be high in AUD with compulsive side. However, the moderate effects of anxiety and depression on obsessive beliefs in OCD shown in studies (21, 23) were also seen in the AUD group in the present study.

As in many mental disorders, the effect of childhood trauma on symptoms in both addiction and OCD has been emphasized (24, 25). Based on this, we thought that obsessive beliefs would be significantly higher in the AUD group with childhood traumatic experience. In a study conducted in the general population, a relationship was found between negative childhood experience and obsessive beliefs. Moreover, this relationship was found to be independent of anxiety and depression. In the same study, it was stated that anxiety was associated with both negative childhood experience and obsessive beliefs (26). The fact that childhood traumatic experience was found to be significantly higher in the AUD group and our study was compatible with the literature in this respect. However, our findings showed that anxiety and depression symptoms rather than childhood traumas were effective on obsessive beliefs. According to our multivariate analysis, although they were close to each other, AUD, HAM-D and HAM-A effects were observed on OBQ, respectively. This situation hinders the comparison since there is no studied area in the literature. The reasons for this may be due to the small size of our sample, as well as the fact that AUD patients who applied to our institution participating in the study for treatment did not reflect the whole universe in terms of AUD. Therefore, it can be said that there is a need for research with a larger sample on the subject.

The role of obsessive beliefs in major depression and anxiety disorders was investigated. In patients with major depression, all subscale scores and total scores of obsessive beliefs were found to be significantly higher, and a significant

correlation was found between the HAM-D scale and the OBQ (12). Obsessive beliefs were shown to be substantially greater in those with general anxiety disorder than in healthy controls (27). Both depression and anxiety severity were found to be predictors of obsessive beliefs in the univariate model in our study. Considering that obsessive beliefs on subscales (especially Responsibility and Threat Satisfaction, Importance and Control of thoughts) may also cause anxiety in the person or there may be a predisposition to these cognitions due to anxiety, it is understandable that the severity of anxiety is high in individuals with high obsessive beliefs.

Limitations

The limitations of the study are that it consists of a cross-sectional and relatively small sample, and that all of the participants are male. Also, we want it to be known that the AUD cases included in our study do not reflect the entire AUD universe.

## Conclusion

All scale scores were discovered to be significantly higher than those of the control group, per the literature. Yet, there was no conclusive evidence linking childhood traumatic experience to obsessive beliefs. The current study is significant since it is the first to assess the connection between childhood trauma and obsessive beliefs in individuals with AUD. Knowing the neurobiological, behavioral and cognitive effects of addictive substances is very important in the treatment process of patients. Treatment approaches are modeled and applied based on this information. Transdiagnostic approaches that investigate the etiology, treatment and approaches in addiction from different perspectives will be important. In this context, it may be considerable to identify obsessive beliefs that affect the thought process of patients. The relationship between addiction and compulsive behaviors and how it affects the therapeutic process require more research.

## References

1. Obeid S, Akel M, Haddad C, et al. Factors associated with alcohol use disorder: the role of depression, anxiety, stress, alexithymia and work fatigue-a population study in Lebanon. BMC public health 2020;20(1):1-11.

2. Carvalho AF, Heilig M, Perez A, Probst C, Rehm J. Alcohol use disorders. Lancet 2019;394(10200);781-792.

3. Volkow ND, Wang GJ, Fowler JS, Tomasi D, Telang F, Baler R. Addiction: decreased reward sensitivity and increased expectation sensitivity conspire to overwhelm the brain's control circuit. Bioessays 2010;32(9):748-755.

4. Vannemreddy P, Slavin K. Nucleus accumbens as a novel target for deep brain stimulation in the treatment of addiction: a hypothesis on the neurochemical and morphological basis. Neurol India 2019;67(5): 1220.

5. Koob GF, Volkow ND. Neurocircuitry of addiction. Neuropsychopharmacology 2010;35(1); 217-238.

6. Domi E, Xu L, Toivainen S, et al. A neural substrate of compulsive alcohol use. Sci Adv 2021;7(34):1-12

7. Corbit LH & Janak PH. Habitual alcohol seeking: neural bases and possible relations to alcohol use disorders. Alcohol Clin Exp Res 2016;40(7):1380-1389.

8. Schmitz JM. The interface between impulse-control disorders and addictions: are pleasure pathway responses shared neurobiological substrates?. Sexual Addiction & Compulsivity 2005;12(2-3):149-168.

9. Guinle MIB, Sinha R. The role of stress, trauma, and negative affect in alcohol misuse and alcohol use disorder in women. Alcohol Res 2020;40(2):05.

10. Olatunji BO, Ebesutani C, Tolin DF. A bifactor model of obsessive beliefs: Specificity in the prediction of obsessive-compulsive disorder symptoms. Psychol Assess 2019;31(2):210–225.

11. Tolin DF, Woods CM, & Abramowitz JS. Relationship between obsessive beliefs and obsessive–compulsive symptoms. Cognit Ther Res 2003;27:657-669.

12. Bahceci B, Bagcioglu E, Çelik FH, et al. The role of obsessive beliefs in patients with major depressive disorder. Int J Psychiatry Clin Pract 2014;18(1):37-40.

13. Shams G, Milosevic I. A comparative study of obsessive beliefs in obsessive-compulsive disorder, anxiety disorder patients and a normal group. Acta Med Iran 2015;301-310.

14. Boysan M, Besiroglu L, Çetinkaya N, Atli A, Aydin A. The Validity and Reliability of the Turkish Version of the Obsessive Beliefs Questionnaire-44 (OBQ-44). Noro Psikiyatr Ars 2010;47(3):216.

15. Bernstein DP, Fink L, Handelsman L, et al. Initial reliability and validity of a new retrospective measure of child abuse and neglect. Am J Psychiatry 1994;151(8):1132-6

16. Şar V, Öztürk E, & İkikardeş E. Validity and reliability of the Turkish version of Childhood Trauma Questionnaire (CTQ). Turkiye Klinikleri Journal of Medical Sciences. 2012;32(4):1054–1063.

17. Ögel K, Evren C, Karadağ F, Gürol DT. The development, validity, and reliability of the Addiction Profile Index (API). Turk Psikiyatri Derg 2012; 23(4):263-75.

18. First MB. Structured Clinical Interview for the DSM (SCID). The Encyclopedia of Clinical Psychology 2014:1-6.

19. Elbir M, Alp Topbaş Ö, Bayad S, et al. Adaptation and Reliability of the Structured Clinical Interview for DSM-5-Disorders - Clinician Version (SCID-5/CV). Turk Psikiyatri Derg 2019;30(1):51-56.

20. Murthy P, Shadakshari D, Mahadevan J, Chand PK. Management of Alcohol Use Disorder in Patients With Alcoholic Liver Disease. J Clin Exp Hepatol 2022;12(6):1514-1526.

21. Randazza MP, McKay D, Bakhshaie J, Storch EA, Zvolensky MJ. Unhealthy Alcohol Use Associated with Obsessive-Compulsive Symptoms: The Moderating Effects of Anxiety and Depression. J Obsessive Compuls Relat Disord 2022;32: 100713.

22. Subramaniam M, Abdin E, Vaingankar J, et al. Obsessive-Compulsive Disorder in Singapore: Prevalence, Comorbidity, Quality of Life and Social Support. Ann Acad Med Singap 2020;49(1):15-25.

23. Tolin DF, Worhunsky P, Maltby N. Are "obsessive" beliefs specific to OCD? : a comparison across anxiety disorders. Behav Res Ther 2006;44(4):469-80.

24. Destrée L, Brierley ME, Albertella L, Jobson L, Fontenelle LF. The effect of childhood trauma on the severity of obsessive-compulsive symptoms: A systematic review. J Psychiatr Res 2021;142:345-360.

25. Moustafa AA, Parkes D, Fitzgerald L, et al. The relationship between childhood trauma, early-life stress, and alcohol and drug use, abuse, and addiction: An integrative review. Curr Psychol 2021;40:579-584.

26. Briggs ES, Price IR. The relationship between adverse childhood experience and obsessive-compulsive symptoms and beliefs: the role of anxiety, depression, and experiential avoidance. J Anxiety Disord 2009;23(8):1037-1046.

27. Viar MA, Bilsky SA, Armstrong T, Olatunji BO. Obsessive beliefs and dimensions of obsessive-compulsive disorder: An examination of specific associations. Cognit Ther Res 2011;35:108-117.

# A Preliminary Cross-Sectional Study: Does Music Listening Have a Negative Impact on Eating Behavior?

**Emine Fusun Akyuz Cim[1], Songul Gundogdu Kiran[2], Faruk Kurhan[3]**

[1]Department of Psychiatry, Florence Nightingale Hospital, Medical Faculty, Demiroglu Bilim University, Istanbul, Türkiye
[2]Department of Psychiatry, Medical Faculty, Yuzuncu Yil University, Van, Türkiye
[3]Department of Psychiatry, Medical Faculty, Yuzuncu Yil University, Van, Türkiye

**Adres for Correspodence:** Department of Psychiatry, Florence Nightingale Hospital, Medical Faculty, Demiroglu Bilim University, Abide-i Hurriyet Cd. No:166 — 34381, Sisli, Istanbul, Türkiye
e-mail: drfusunakyuz@hotmail.com

**Orcid ID:** EFAC: 0000-0001-9313-4056 FK: 0000-0003-3718-0458
SGK: 0000-0002-9614-9015

**Cite As:** Cim Akyuz EF, Gundogdu Kiran S, Kurhan F. A preliminary cross-sectional study: Does music listening have a negative impact on eating behavior? Hitit Med J 2023;5(3): 144-148. https://doi.org/10.52827/hititmedj.1340383

## Abstract

**Objective:** Cortical auditory and gustatory centers are considered to interact with each other. Studies have shown that music affects eating behavior. The present study aimed to investigate the effect of the time spent on engaging with music on eating behavior.

**Material and Method:** This is a randomized cross-sectional study. It included 40 volunteering undergraduates enrolled in the Department of Music, Fine Arts Faculty, Yuzuncu Yil University, Van, Turkey. All participants were administered a questionnaire to assess the time spent engaging with music, the Eating Attitudes Test (EAT-40), and the State-Trait Anxiety Inventory (STAI). The body mass index (BMI) was calculated for each participant.

**Results:** Eating behavior disorder (EBD) was detected in 11 (27.5%) participants. The EAT-40 scores established a positive correlation with the total time spent on music per week (Total-T) ($r=0.413$, $p<0.01$). The mean Total-T score was significantly higher in participants with EBD compared to those without EBD (16.45±15.896 vs. 6.24±6.418 h/week) ($p=0.006$). Furthermore, the mean score for the time spent playing a musical instrument per week (Inst-T) was significantly higher in participants with EBD compared to those without EBD (5.00±5.254 vs. 2.72±1.412 h/week) ($p=0.036$).

**Conclusion:** According to the data from this study, the time spent engaging with music increases eating behavior negatively.

**Keywords:** Eating behavior, Eating behavior disorder, Music, Musical instrument

## Özet

**Amaç:** Kortikal işitsel ve tatsal merkezlerin birbirleriyle etkileşim içinde olduğu düşünülmektedir. Yapılan çalışmalar müziğin yeme davranışı üzerinde etkili olduğunu göstermiştir. Bu çalışmanın amacı, müzikle geçirilen zamanın yeme davranışı üzerindeki etkisini araştırmaktır.

**Gereç ve Yöntem:** Çalışma, randomize kesitsel özelliklere sahiptir. Çalışmaya Van Yüzüncü Yıl Üniversitesi, Güzel Sanatlar Fakültesi, Müzik Bölümünde öğrenim gören 40 gönüllü lisans öğrencisi katılmıştır. Tüm katılımcılara bir anket (müzikle uğraşma süresini değerlendirmek için), Yeme Tutumları Testi (EAT-40) ve Durumluk-Sürekli Kaygı Envanteri (STAI) uygulanmıştır. Her katılımcı için beden kitle indeksi (BKİ) hesaplanmıştır.

**Bulgular:** Katılımcıların 11'inde (%27,5) yeme davranışı bozukluğu (YDB) tespit edilmiştir. EAT-40 puanları, haftalık müzik için harcanan toplam süre (Toplam-T) ile pozitif bir korelasyon göstermiştir ($r= 0,413$, $p<0,01$). Ortalama Toplam-T puanı, YDB olan katılımcılarda YDB olmayanlara kıyasla anlamlı derecede yüksek bulunmuştur (16,45±15,896'ya 6,24±6,418 saat/hafta) ($p=0,006$). Ayrıca, ortalama haftalık enstrüman çalma süresi (Inst-T) puanı YDB olan katılımcılarda YDB olmayanlara kıyasla anlamlı derecede yüksek bulunmuştur (5,00±5,254'e 2,72±1,412 saat/hafta) ($p=0,036$).

**Sonuç:** Bu çalışma verilerine göre, müzikle uğraşarak geçirilen zaman yemek yeme davranışını olumsuz yönde etkilemektedir.

**Anahtar Sözcükler:** Müzik, Müzikal enstrüman, Yeme davranışı, Yeme davranış bozukluğu

**Date of Submission:** 09.08.2023
**Date of Acceptance:** 02.09.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** The study was carried out with the permission of Van Yuzuncu Yil University Ethics Committee (Date: 27.12.2019; Decision No: 2019/18-03).
**Plagiarism Checks:** Yes - iThenticate
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: EFAC, Design: EFAC, Data collection/Data processing: EFAC, SGK, FK, Data Analysis: EFAC, Preparation of the article: EFAC
**Informed Consent:** Consents were obtained from the patients.
**Financial Disclosure:** No financial support has been received.

## Introduction

Eating behavior and music engagement are organized by cortical brain centers. Eating behavior is controlled by the gustatory center and music engagement is controlled by the auditory center. Cortical auditory and gustatory centers are considered to interact with each other. Additionally, the emotion arising from a sensorial perception (e.g., music) is likely to affect the process of another sensorial perception (e.g., gustatory) (1). Listening to liked music stimulates positive emotions, while listening to disliked music suppresses striatal pathways to reward. The gustatory sensation of an individual changes when listening to liked or disliked music. In addition, individuals experience a sweet taste and positive emotions when listening to music they like or neutral music, whereas they experience a bitter taste and negative emotions when listening to music they do not like (2).

In previous studies, the effect of music on eating behavior was evaluated with background music. Eating material and background music were the main elements of the studies. The specified times included a single eating period. In addition, the researchers determined the type and other characteristics of the music used in these studies, which focused on the effect of background music on eating behavior (3).

Eating behavior and gustatory processes are known to induce emotional changes. One of the negative emotions that affect eating behavior is anxiety. There are studies on the coexistence of anxiety disorders in patients with eating disorders. Patients with anorexia nervosa (AN) are more prone to anxiety disorders and have higher anxiety levels than the general population (4). Additionally, patients with AN have relatively higher premeal anxiety levels (5). The neurobiological effects of restricted eating modulate anxiety levels in patients with AN. Bulimia nervosa (BN) is another common eating disorder commonly accompanied by anxiety (6). Furthermore, numerous studies have suggested a relationship between BN and anxiety sensitivity (4).

The present study aimed to investigate the effect of weekly time spent on music on eating behavior. We also evaluated the effect of anxiety level on this bilateral relationship (eating behavior/engaging with music) due to the significant coexistence of eating disorders and anxiety disorders. The differences between our study and other studies include the evaluation of the level of anxiety and the effect of long-term engaging with music (not only listening to music but also playing instruments) on eating behavior.

In our study, music students were selected as the participant group because their music engagement continued in a stable order and long hours. In addition, we allowed the participants to choose the type of music, such as music therapy practices. In this way, cross-sectional data of individuals were obtained objectively without interference.

In this study, we aimed to investigate the effect of engaging with music on eating behavior. Our hypothesis is that listening to music increases abnormal eating behavior in the long term. In addition, we assumed that playing music before the study might have a similar effect on eating behavior as listening to music. It is important to prove the effect of engaging with music time on eating behavior. The time spent on music can be adjusted by individuals easily. Additionally, the person can change the time spent on music (increasing or decreasing as needed). Therefore, the results of our study can guide the methods in eating behavior disorders.

## Material and Method

Approval was obtained from the local ethics committee for this study on December 27, 2019 under the ethical decision number of 2019/18-03. The study was designed as a randomized cross-sectional study. It included 40 undergraduates aged 18-30 years who were enrolled in Yuzuncu Yil University Fine Arts Faculty Music Department. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

While determining exclusion and inclusion criteria, the participants' mental state, hearing problems, presence of illness, and/or drug use that indirectly affect appetite and eating behavior were taken into consideration. The inclusion criteria were as follows: being a student at Yuzunucu Yil University Fine Arts Faculty Music Department, volunteering to participate in the study and being over the age of 18. Exclusion criteria were: presence of active psychotic disorder, presence of disease related to the endocrine system (diabetes, Cushing syndrome, etc.), neurological disease (epilepsy, etc.) that could not be controlled by treatment, hearing loss, presence of psychotropic use, presence of any drug use affecting eating behavior (such as steroid hormone replacement).

Both verbal and written informed consent were obtained from all 40 participants who met the inclusion criteria. All participants were administered a questionnaire (formed by the reseachers), the Eating Attitudes Test (EAT), and the State-Trait Anxiety Inventory (STAI).

*Questionnaire*

The questionnaire collected information on the participants' sociodemographic features, body mass index (BMI), total time spent listening to music per week (List-T), total time spent playing a musical instrument per week (Inst-T) and the total time spent on music per week (Total-T).

*The Eating Attitudes Test (EAT-40)*

The Eating Attitudes Test (EAT-40), developed by Garner et al. (7), is a self-rated scale assessing disordered eating behaviors such as AN and BN. The reliability and validity study of the Turkish version of the EAT-40 was conducted by Savasır et al. (8). The test consists of 40 items consisting of a 6-point Likert rating scale (from "1=never" to "6=always"). In this test, the cutoff score was set as 30 points. Elal et al. (9) devised four factors for the EAT factor structure, including "dieting", "bulimia and food preoccupation", "oral control", and "ambivalence about food".

*State-Trait Anxiety Inventory (STAI)*

The State-Trait Anxiety Inventory (STAI), developed by Spielberger et al. (10), is a psychological inventory consisting of 40 items divided into two subscales with 20 items each. The State Anxiety (STAI-S) subscale is used to assess the severity of situational anxiety at a particular moment in time or under certain conditions. The trait anxiety (STAI-T) subscale is used to determine the severity of constant trait anxiety. The reliability and validity study of the Turkish version of the STAI was conducted by Oner et al. (11).

*Procedure*

After obtaining ethics approval from Yuzuncu Yil University of Ethics Committee, a proclamation of the study was first

made to draw in potential participants in Yuzuncu Yil University Fine Arts Faculty Music Department. Then, the aim of the research was presented to the voluntary participants. Informed approval was obtained from all participants included in the study. They were asked to complete the questionnaire set prepared. Filling out the questionnaires took almost 20 minutes.

Statistical Analysis

Statistical analysis was performed using SPSS 22.0 (Statistical Package for Social Sciences, IBM Inc., Chicago, IL, USA). The consistency of continuous variables to a normal distribution was checked with the Shapiro-Wilks test. Descriptive statistics of continuous variables are expressed as mean±SD (standard deviation). The presence of a correlation between the groups was determined by the Pearson correlation test, chi-square test for parametric variables and Spearman correlation test for nonparametric variables. Additionally, in the comparison of binary groups, we used the t test. The level of significance was set at p<0.05 for all tests.

## Results

The 40 undergraduates consisted of 21 males and 19 females. The BMI values of all participants were within normal ranges (range: 21.3-23.8 kg/m$^2$). There was no significant difference between the sexes with regard to EAT-40 (*r=0.148*), STAI-T (*r=0.646*) and total STAI scores (*r=0.079*) (*p>0.05* for all). However, the STAI-S scores were significantly higher in females than in males (*r=0.014, p<0.05*) (Table I).

The STAI-S scores increased as the total time spent listening to music (List-T) increased (*r=0.366, p<0.05*). The EAT-40 scores showed a positive correlation with the total time spent on music per week (Total-T) (*r=0.413, p<0.01*) and the time spent playing a musical instrument per week (Inst-T) (*r=0.35, p<0.05*). However, neither STAI-T nor STAI-S were affected by Inst-T and Total-T.

**Table I.** Evaluation of the change in state anxiety, trait anxiety, Total STAI, and eating attitudes test scores by sex

| | | n | Mean±SD | Min. | Max. | *p value |
|---|---|---|---|---|---|---|
| STAI-S | M | 21 | 37.81±10.38 | 26 | 73 | *0.014* |
| | F | 19 | 47.56±13.20 | 23 | 72 | |
| | Total | 40 | 42.31±12.61 | 23 | 73 | |
| STAI-T | M | 21 | 43.05±6.80 | 33 | 55 | *0.646* |
| | F | 19 | 44.56±12.99 | 13 | 68 | |
| | Total | 40 | 43.74±10.02 | 13 | 68 | |
| Tot-STAI | M | 21 | 81.33±14.41 | 64 | 127 | *0.079* |
| | F | 19 | 92.11±22.54 | 60 | 140 | |
| | Total | 40 | 86.31±19.14 | 60 | 140 | |
| EAT-40 | M | 21 | 21.14±10.37 | 7 | 43 | *0.148* |
| | F | 19 | 26.37±12.01 | 8 | 54 | |
| | Total | 40 | 23.63±11.34 | 7 | 54 | |

* t test; Values are given as mean and standard deviation; M=male; F=female; STAI-S=state anxiety; STAI-T=trait anxiety; Tot-STAI=Total STAI; EAT-40=eating attitudes Test; SD=standard deviation.

The EAT-40 scores indicated no significant correlation between age and List-T scores. Similarly, there was no significant correlation between the EAT-40 scores and the situational and constant anxiety scores (STAI-S, STAI-T and Tot-STAI) (Table II).

Participants with EAT-40 scores of 30 or greater were accepted as having an eating behavior disorder (EBD). EBD was present in 11 (27.5%) participants. There was no significant relationship between eating behavior and age (*p=0.76*) or sex among these participants (chi-square: 1.584, *p=0.208*) (Table III).

**Table II.** Evaluation of the relationship between age, time spent listening to music, total time spent on music, time spent playing a musical instrument, state anxiety, trait anxiety, total STAI and eating attitudes test score

| | | Age | List-T | Total-T | Inst-T | STAI-S | STAI-T | Tot-STAI | EAT-40 |
|---|---|---|---|---|---|---|---|---|---|
| Age | r | 1 | | | | | | | |
| List-T | r | 0.123 | 1 | | | | | | |
| Total-T | r | 0.287 | 0.954** | 1 | | | | | |
| Inst-T | r | 0.412* | 0.212 | 0.495** | 1 | | | | |
| STAI-S | r | 0.082 | 0.366* | 0.159 | -0.232 | 1 | | | |
| STAI-T | r | 0.202 | 0.210 | 0.237 | 0.073 | 0.461** | 1 | | |
| Tot-STAI | r | 0.160 | 0.326 | 0.225 | -0.112 | 0.884** | 0.815** | 1 | |
| EAT-40 | r | - 0.034 | 0.297 | 0.413** | 0.359* | -0.111 | 0.089 | -0.040 | 1 |

*; *p<0.05*, **; *p<0.01*, List-T=time spent listening to music (hours/week); Total-T=total time spent on music (hours/week); Inst-T=time spent playing a musical instrument (hours/week); STAI-S=state anxiety; STAI-T=trait anxiety; Tot-STAI=total STAI, EAT-40=eating attitudes test.

The mean Total-T score was significantly higher in participants with EBD compared to those without EBD (16.45±15.896 vs. 6.24±6.418 h/week) (*p=0.006*). Furthermore, the mean Inst-T score was significantly higher in participants with EBD compared to those without EBD (5.00±5.254 vs. 2.72±1.412 h/week) (*p=0.036*) (Table IV).

There was no significant difference between participants with and without EBD with regard to situational and constant anxiety scores (STAI-S, STAI-T and Tot-STAI).

**Table III.** Distribution of individuals with eating disorders by sex

| | | | Sex | | Total |
|---|---|---|---|---|---|
| | | | M | F | |
| EBD | No | n | 17 | 12 | 29 |
| | | % | 81.0 | 63.2 | 72.5 |
| | Yes | n | 4 | 7 | 11 |
| | | % | 19.0 | 36.8 | 27.5 |
| Total | | n | 21 | 19 | 40 |
| | | % | 100.0 | 100.0 | 100.0 |
| | | Chi-square: 1.584 | | | *P=0.208* |

EBD=eating behavior disorder; M=male; F=female

**Table IV.** Comparison of age, time spent listening to music, total time spent on music, time spent playing a musical instrument, state anxiety, trait anxiety, total STAI and eating attitudes test scores of individuals with and without eating disorders

| | | n | Mean±SD | Min. | Max. | *p value* |
|---|---|---|---|---|---|---|
| Age | Non-EBD | 26 | 22.69±2.36 | 18 | 27 | *0.760* |
| | EBD | 10 | 22.40±3.02 | 19 | 30 | |
| | Total | 36 | 22.61±2.52 | 18 | 30 | |
| Total-T | Non-EBD | 29 | 6.24±6.41 | 1 | 33 | *0.006* |
| | EBD | 11 | 16.45±15.89 | 2 | 44 | |
| | Total | 40 | 9.05±10.75 | 1 | 44 | |
| List-T | Non-EBD | 22 | 4.91±6.48 | 1 | 30 | *0.076* |
| | EBD | 10 | 11.90±15.27 | 1 | 40 | |
| | Total | 32 | 7.09±10.34 | 1 | 40 | |
| Inst-T | Non-EBD | 29 | 2.72±1.41 | 1 | 7 | *0.036* |
| | EBD | 11 | 5.00±5.2 | 1 | 20 | |
| | Total | 40 | 3.35±3.09 | 1 | 20 | |
| STAI-S | Non-EBD | 28 | 43.11±13.98 | 23 | 73 | *0.503* |
| | EBD | 10 | 39.90±8.69 | 28 | 57 | |
| | Total | 38 | 42.26±12.77 | 23 | 73 | |
| STAI-T | Non-EBD | 28 | 43.61±11.01 | 13 | 68 | *0.918* |
| | EBD | 10 | 44.00±7.76 | 33 | 58 | |
| | Total | 38 | 43.71±10.15 | 13 | 68 | |
| Tot-STAI | Non-EBD | 28 | 87.07±21.50 | 60 | 140 | *0.663* |
| | EBD | 10 | 83.90±12.26 | 69 | 108 | |
| | Total | 38 | 86.24±19.39 | 60 | 140 | |

* t test; Values are given as the mean and standard deviation; EBD=eating behavior disorder; List-T=time spent listening to music (hours/week); Total-T=total time spent on music (hours/week); Inst-T=time spent playing a musical instrument (hours/week); STAI-S=State Anxiety; STAI-T=trait anxiety; Tot-STAI=Total STAI; SD=standard deviation.

## Discussion

Our hypothesis was that engaging with music affects abnormal eating behavior in a way leading to an increase it. In our study, the total time spent on music (i.e., time spent listening to music and playing a musical instrument) and the total time spent playing a musical instrument were significantly higher in participants with EBD compared to participants without EBD (*p=0.006, p=0.036*, respectively). Furthermore, the EAT-40 scores (regardless of the presence of EBD) correlated with the total-T (*r=0.413, p<0.01*) and Inst-T scores (*r=0.359, p<0.05*).

Music can modulate basic taste perception features of food, such as sweetness and/or bitterness (12). Studies evaluating the impact of sound on eating behavior have shown that this can add significant value to people's experience of food and drink (13). Sounds that are unrelated to the food itself can affect flavor perception. Sound that changes the perception of flavor can be in the form of background music. It is believed that the positive emotions we associate with music can be transferred to the pleasure of food and beverages (14). Examples of this can be experienced in eating places such as restaurants, where sound can affect our perception of flavor (15).

Recent studies have identified a number of specific sonic and musical parameters that can be used to modify tasting experiences, thus adding notable pleasure to the consumer's overall eating experience (16,17). The assessment pleasantness of smells can rise in the presence of harmonic sounds (18). In particular, it is possible to compose soundscapes that systematically affect the perception of food flavor (19). Additionally, the more a person likes a sound, the more likely he/she is to perceive afterward-offer smell (20). This can be effective in eating behavior.

The data we obtained in our study suggest that the main parameter affecting eating behavior is not the time of listening to music but the duration of instrument playing. In music therapy, playing the musical instrument (such as discussing song lyrics or responding to music through art and song writing) is one of the parts of the therapy process. Music therapy is not a commonly used therapy for eating disorders (21). Studies evaluating the relationship between eating disorders and music therapy are generally case-level and limited in number (22). In addition, in the literature review, there was no study showing the effect of playing a musical instrument on eating behavior. Our study is unique exploring the effect of playing an instrument in isolation on eating behavior.

Studies have reported that music therapy has positive effects on anxiety. Music therapy was used as a treatment for anxiety in cancer patients, coronary artery disease (CAD) patients and patients requiring pain management (23-25). Another study indicated that listening to relaxing music reduced the physiological symptoms caused by stress and enhanced the participants' stress management skills (26).

In our study, we also evaluated the anxiety levels due to the common association between anxiety disorders and eating disorders. However, there was no significant correlation between the EAT-40 scores and the STAI-S or STAI-T. There was no significant difference between participants with and without EBD with regard to state and trait anxiety scores (*p=0.503; p=0.918*).

In our study, we evaluated the effect of eating behavior, engaging with music and anxiety levels on each other. The relationship between eating behavior/anxiety and music therapy/anxiety has also been evaluated in numerous studies. While anxiety is expected to increase in eating behavior disorders, the anxiety level of the individual is expected to decrease in therapeutic music applications. Our study found that the effect of anxiety on eating behavior was insignificant. We believe that this result may stem from the effect of engaging with music. To explain the effect of music on eating behavior, we believe that there is a need for additional long-term studies with a larger number of participants categorized by music genres.

## Conclusion

The data obtained in our study indicate that the time spent playing an instrument, one of the music engagements, increases negative eating behavior. The effect of anxiety on eating behavior in the participant group was found to be insignificant. Future research should examine the relationship between engaging with music and other eating disorders (such as binge eating disorder, food addiction) with larger populations.

## References

1. Woods AT, Poliakoff E, Lloyd DM, et al. Effect of background noise on food perception. Food Qualit Prefer 2011;22(1):42-47.

2. Carvalho FR, Wang QJ, de Causmaecker B, Steenhaut K, van Ee R, Spence C. Tune that beer! Listening for the pitch of beer. Beverages 2016;2(4):31.

3. Kantono K, Hamid N, Shepherd D, Yoo MJY, Carr BT, Grazioli G. The effect of background music on food pleasantness ratings. Psychol Music 2016;44(5):1111-1125.

4. Kaye WH, Bulik CM, Thornton L, Barbarich N, Masters K, Price Foundation Collaborative Group. Comorbidity of anxiety disorders with anorexia and bulimia nervosa. Am J Psychiatr 2004;161(12):2215-2221.

5. Haynos AF, Crosby RD, Engel SG, et al. Initial test of an emotional avoidance model of restriction in anorexia nervosa using ecological momentary assessment. J Psychiatr Res 2015;68:134-139.

6. Lloyd EC, Frampton I, Verplanken B, Haase AM. How extreme dieting becomes compulsive: a novel hypothesis for the role of anxiety in the development and maintenance of anorexia nervosa. Med Hypotheses 2017;108:144-150.

7. Garner DM, Garfinkel PE. The eating attitudes test: an index of the symptoms of anorexia nervosa. Psychological medicine 1979;9(2):273-279.

8. Savaşır I, Erol N. Eating attitude test: anorexia nervosa symptom index. Psikoloji Dergisi 1989;7(23):19-25. Available from: http://www.turklojizilari.com/PDF/TPD/23/02.pdf. Accessed in 2023 (April 27).

9. Elal G, Altug A, Slade P, Tekcan A. Factor structure of the Eating Attitudes Test (EAT) in a Turkish university sample. Eat Weight Disord 2000;5(1):46-50.

10. Spielberger CD, Gorsuch RL, Lushene RE, Vagg PR, Jacobs GA. Manual for the State-Trait Anxiety Inventory. Palo Alto: Consulting Psychologists Press; 1970.

11. Öner N, Le Compte A. Süreksiz Durumluk/Sürekli Kaygı Envanteri El Kitabı. 2. Basım. İstanbul: Boğaziçi Üniversitesi Yayınları, 1985;1-26.

12. Knoeferle KM, Woods A, Käppler F, Spence C. That sounds sweet: using crossmodal correspondences to communicate gustatory attributes. Psychology and Marketing 2015;32(1):107-120.

13. Salgado-Montejo A, Alvarado JA, Velasco C, Salgado CJ, Hasse K, Spence C. The sweetest thing: the influence of angularity, symmetry, and the number of elements on shape-valence and shape-taste matches. Front Psychol 2015;6:1382.

14. Carvalho FR, Wang QJ, van Ee R, Persoone D, Spence C. "Smooth operator": Music modulates the perceived creaminess, sweetness, and bitterness of chocolate. Appetite 2017;108:383-390.

15. Spence C, Michel C, Smith B. Airplane noise and the taste of umami. Flavor 2014;3(1):1-4.

16. Spence C. Sound bites and digital seasoning. ICMA Array 2016;571(SI15):9-15.

17. Reinoso Carvalho F, van Ee R, Touhafi A. TASTE- Testing Auditory Solutions toward the improvement of the Tasting Experience. In: 10th International Symposium on Computer Music Multidisciplinary Research (CMMR). Marseille: Publications du L.M.A., 2013;1(1);795-805. Available from: https://lirias.kuleuven.be/1786042?limo=0. Accessed in 2023 (May 8).

18. Seo HS, Lohse F, Luckett CR, Hummel T. Congruent sound can modulate odor pleasantness. Chem Senses 2014;39(3):215-228.

19. Reinoso Carvalho F, Wang QJ, van Ee R, Spence C. The influence of soundscapes on the perception and evaluation of beers. Food Qualit Prefer 2016;52:32-41.

20. Seo HS, Hummel T. Auditory-olfactory integration: Congruent or pleasant sounds amplify odor pleasantness. Chem Senses 2011;36(3):301-309.

21. Gold C, Solli HP, Krüger V, Lie SA. Dose-response relationship in music therapy for people with serious mental disorders: systematic review and meta-analysis. Clin Psychol Rev 2009;29(3):193-207.

22. Trondalen G. "Self-listening" in music therapy with a young woman suffering from anorexia nervosa. Nord J Music Ther 2003;12(1):3-17.

23. Bradt J, Dileo C, Magill L, Teague A. Music interventions for improving psychological and physical outcomes in cancer patients. Cochrane Database Syst Rev 2016;(8):CD006911.

24. Bradt J, Dileo C, Potvin N. Music for stress and anxiety reduction in coronary heart disease patients. Cochrane Database Syst Rev 2013;(12):CD006577.

25. Bradt J. The effects of music entrainment on postoperative pain perception in pediatric patients. Music and Medicine 2010:2(3):150-157. Available from: https://mmd.iammonline.com/index.php/ musmed/article/view/MMD-2010-2-3-4. Accessed in 2023 (April 27)

26. Burns J, Labbé E, Williams K, McCall J. Perceived and physiological indicators of relaxation: as different as Mozart and Alice in chains. App Psychophysiol Biofeedback 1999;24(3):197-202.

# Effect of Barley Grass Juice on Antioxidant Capacity and DNA Damage in Diabetic Rats

**Arzu Comba[1], Leyla Mis[2], Devrim Saripinar Aksu[2], Yildiray Basbugan[2], Bahat Comba[1]**

[1]Hitit University, Technical Sciences Vocational School, Corum, Türkiye
[2]Yuzuncu Yil University, Faculty of Veterinary Medicine, Van, Türkiye

**Adres for Correspodence:** Hitit University, Technical Sciences Vocational School, Corum, Türkiye
e-mail: bahatcomba@gmail.com

**Orcid ID:** AC: 0000-0001-9462-8998 DSA: 0000-0003-2524-6026 BC: 0000-0002-3419-4144
LM: 0000-0002-5110-2862 YB: 0000-0001-5124-7853

**Cite As:** Comba A, Mis L, Aksu DS, et al. Effect of Barley Grass Juice on Antioxidant Capacity and DNA Damage in Diabetic Rats. Hitit Med J 2023;5(3): 149-155. https://doi.org/10.52827/hititmedj.1281145

## Abstract

**Objective:** Worldwide, phytotherapy methods acquire great importance, and studies in this field are increasing their importance each day. This study, it was aimed to examine total antioxidant, oxidant status, oxidative DNA damage, glucose and hemoglobin A1c levels and the effects of barley grass juice on these parameters in rats with diabetes mellitus.

**Material and Method:** Four groups were formed for the study and 6 male rats weighing 250-350 g were used in each group. Control Group; physiological saline was injected via intraperitoneal., Diabetic Group; created using streptozotocin, Barley Grass Group; Barley grass juice (3 ml/rat/day) was given orally for 4 weeks, Diabetic and Barley Grass Group; was injected streptozotocin and barley grass juice was given by oral for 4 weeks.

**Results:** It was determined that barley grass juice decreased blood sugar, glucose, hemoglobin A1c, total oxidative status and oxidative stress index values, increased total anti-oxidative status value, and body weights in streptozotocin-induced diabetes. In addition, it was determined that the addition of barley grass juice provided a significant protective effect and improvement in these parameters.

**Conclusion:** Based on these findings, we can say that barley grass juice has an antidiabetic-antioxidant effect and weight gain in diabetes mellitus

**Keywords:** Antioxidant, Barley grass juice, Diabetes mellitus, DNA damage, Glucose, HbA1c, Oxidan

## Özet

**Amaç:** Dünya çapında fitoterapi yöntemleri büyük önem kazanmakta ve bu alandaki çalışmalar her geçen gün önemini artırmaktadır. Bu çalışmada deneysel olarak diyabet oluşturulan ratlarda toplam antioksidan, oksidan durum, oksidatif DNA hasarı, glikoz ve hemoglobin A1c düzeyleri ve arpa çimi suyunun bu parametreler üzerine etkisinin incelenmesi amaçlandı.

**Gereç ve yöntem:** Çalışma için 4 grup oluşturuldu ve her grupta 250-350 gr ağırlığında 6 erkek rat kullanıldı. Kontrol grubu; serum fizyolojik periton içi yol ile enjekte edildi, Diyabet grubu; diyabet, streptozotosin kullanılarak oluşturuldu, Arpa çimi grubu; 4 hafta oral olarak arpa çimi suyu (3 ml/sıçan/gün) verildi, Diyabet+Arpa çimi grubu; streptozotosin ile diyabet oluşturuldu ve 4 hafta boyunca arpa çimi suyu oral olarak verildi.

**Bulgular:** Arpa çimi suyu, streptozotosin kaynaklı diyabette kan şekeri, glikoz, HemoglobinA1c, toplam oksidatif durum ve oksidatif stres gösterge değerlerini düşürdüğü, toplam antioksidan değerini ve canlı ağırlıkları arttırdığı belirlendi. Ayrıca arpa çimi suyu ilavesinin bu parametreler üzerinde belirgin koruyucu etki ve iyileşme sağladığı tespit edildi.

**Sonuç:** Bu bulgulardan yola çıkarak arpa çimi suyunun şeker hastalığında anti-diyabetik, anti-oksidan etki gösterdiği ve kilo kaybını önlediğini söyleyebiliriz.

**Anahtar Sözcükler:** Antioksidan, Arpa çimi suyu, Diyabet, DNA hasarı, Glikoz, HbA1c, Oksidan

**Date of Submission:** 11.04.2023
**Date of Acceptance:** 25.08.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** Ethical approval for the study was granted by the Research Ethics Committee of Van Yuzuncu Yil University (Approval No: 2015/14).
**Plagiarism Checks:** Yes - iThenticate
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: AC, LM, DSA, YB, BC Design: AC, LM, DSA, YB, BC Data Collection/Data Processing: LM, YB, BC Data Analysis: AC, LM, YB Article Preparation: AC, BC
**Financial Disclosure:** No financial support has been received.

## Introduction

Barley and extracts contain 30 rich ingredients. Six components of barley grass (flavonoids, Gamma-aminobutyric acid, potassium-calcium, superoxide dismutase, tryptophan, and vitamins) are very important. These components can fight more than 20 chronic diseases (1).

Barley grass has been reported to be a very powerful plant used in the prevention of hypertension with its high calcium, potassium, magnesium, and low sodium values. However, one of the factors affecting the formation of cancer is that the pH of the environment shifts towards acidity, and the content of barley grass is an alkaline pH, so it can be used in cancer treatment (1).

Barley grass (BG) contains a wide variety of nutrients and plant hormones, antioxidants (superoxide dismutase, catalase, vitamin E, vitamin C, and carotenoids), and up to 3000 enzymes used by the body. BG has alkaline content, so it can reduce intense acidity, which has an important effect on cancer development (2).

Vitamin E is one of the fat-soluble antioxidant vitamins. There are 4 types of vitamin E in barley, α-tocopherol, α-tocotrienol, β-tocopherol and β-tocotrienol (3). Vitamin E in barley is 0.850-3.15 mg/100 g, and its antioxidant capacity is between 57.2 and 158.1 mg/100 g (4).

The balance between antioxidant defense and free radical production in the organism is very important for health. If there are too few free radicals or oxidants, this can lead to chronic permanent damage. The oxidant or antioxidant components can be measured separately, but this process is time-consuming and costly. Thus, total oxidative status (TOS), antioxidant status (TAS) and oxidative stress index (OSI) measurements reflect this situation and they are more economical and practical (5,6).

It is known that reactive oxygen species (ROS) are generally effective in various physiopathological conditions. ROS production can cause DNA damage that leads to chronic health problems. This can be observed in diseases such as cancer, aging, and chronic inflammation (7). Recently, 8-hydroxydeoxyguanosine (8-OHdG) has been used in laboratory analysis as a parameter of oxidative DNA damage.

Diabetes Mellitus (DM), is a chronic disease, it causes disorders of carbohydrate, fat and protein metabolism. Complications that may develop with the disease are microvascular, macrovascular, and neuropathic.

The organism has an antioxidant defense system. However, due to the increase in oxidative stress in some metabolic diseases such as diabetes, an increase in free radicals also occurs. This may cause loss of membrane integrity and genetic mutations; these effects of oxidants can be overcome by the application of antioxidants (8).

Streptozotocin (STZ) (9,10) and alloxan (11,12) are used in in vivo studies to induce DM in experimental animals. STZ is preferred in vivo studies because it causes beta cell cytotoxicity (13).

In recent years, although studies are examining the effect of BG on nephrotoxicity (14), wheatgrass on renal failure (15) and diabetes (10); the antioxidant effect of borax (16), boric acid (17), resveratrol (18,19) there is no study about the effect of barley grass on TOS, TAS, and DNA damage glucose and hemoglobin A1c (HbA1c) in diabetic rats. Therefore, we investigated the effects of barley grass on these parameters.

## Material and Method

Chemicals: physiological water with saline (% 0,09) was provided from Polifarma (Istanbul, Türkiye). STZ was obtained from Sigma-Aldrich Chemical Company. Anesthetic agents were purchased from Pfizer (Ketalar), and Bayer (Rompun). Barley grass was obtained from barley seed at 7 days under suitable conditions in a hasılmatik machine. The barley grass was crushed in the juice machine and the juice was obtained. Barley grass juice was given to rats, fresh.

Animals: In this study, a total of 24 Wistar albino male rats were used and their weights were between 250 and 350 g. Animals were obtained from Yuzuncu Yil University Experimental Animal Center. The animals were kept in an animal care center with climate control, where they were kept in rooms with 12 hours of light/dark, a temperature of 24± °C, and a relative humidity of 45±5 % and in non-condensed plastic cages. To ensure the animals' adaptation standard rat chow and water were given ad libitum 7 days before and throughout the study. Ethical approval for this study was approved by the local ethics committee of Van Yuzuncu Yil University in Turkey (2015/14). In addition, research and publication ethics were complied.

Experimental protocols: The experimental groups were formed as follows.

The control (C) group; was injected with isotonic saline intraperitoneal (i.p.).

Barley Grass (BG) group; was given BG juice (3 ml/rat/day) orally for 4 weeks.

Diabetes Mellitus (DM) group; Freshly prepared STZ solution (pH 4.5, 0.1 M cold citrate buffer) 45 mg/kg was administered as a single dose i.p. After 72 hours, blood glucose levels were measured. Animals with blood glucose values of more than 250 mg/dl were considered diabetic and included in this group.

Diabetes Mellitus + Barley Grass (DM+BG) group, a single dose of STZ solution (pH 4.5, 0.1 M cold citrate buffer) 45 mg/kg was injected i.p. After 72 hours, blood glucose levels were measured. Animals with blood glucose values of more than 250 mg/dl were considered diabetic and included in this group. Diabetic animals in this group were additionally given BG water (3 ml/rat/day) was given as gavage for 4 weeks.

Sample collection: At the end of the four-week experiment, the body weights of the animals were recorded and blood samples were taken from their hearts with a sterile syringe of all animals under anesthesia. Animals for anesthesia were given xylazine HCl (10 mg/kg), and ketamine HCl (70 mg/kg) as i.p.

Blood samples were quickly placed in tubes with anticoagulants. They were separated into serum by centrifugation at 1800xg (3000 RPM) for 10 minutes (+4 °C). The serums were stored in the freezer (-20 °C) until analysis.

Determination of glucose and HbA1c levels: These parameter levels were measured by the immuno-turbid metric method by the auto-analyzer (Modular P800i, Roche, Germany).

Determination of oxidative DNA damage: To determine DNA damage, the 8-hydroxy-2'-deoxyguanosine (8OHdG) value was measured. DNA damage was analyzed by ELISA kit (Enzo Life Sciences, USA).

This kit was worked on the Elisa reader and washer (Stat Fax, USA) according to the manufacturer's instructions. Other

technical data about the kit are as follows.

Measurement method: The Absorbance 96 is designed to carry out sensitive absorbance measurements. It measures the optical density (OD) of samples at defined wavelengths.

Measuring technique: Endpoint and Kinetic

Wavelength: 450 nm

Linearity: ≤ 1.5 % (0–2 OD), ≤ 3.0 % (2–3 OD)

Accuracy: ≤ 1.5 % + 0.010 OD (0–2 OD), ≤ 3.0 % + 0.010 OD (2–3 OD)

Reproducibility : ≤ 0.5 % + 0.005 OD (0.0–2.0 OD), ≤ 1 % + 0.005 OD (2.0–3.0 OD)

Measurement range 0–4.0 OD

Sensitivity: 0.59 ng/ml (range 0.94 - 60 ng/ml)

Determination of TOS, TAS and OSI levels: TOS and TAS values were determined by colorimetric kits (Rel Assay, Turkey) in blood serum. The oxidative stress index (OSI) was calculated with the ratio of TOS to TAS.

The TAS and TOS kits were studied in the spectrophotometer device (Shimadzu, Japan) according to the manufacturer's instructions. Other technical data about the kit are as follows.

Principle of TAS Assay: Antioxidants in the sample reduce dark bluegreen colored ABTS radical to colorless reduced ABTS form. The change of absorbance at 660 nm is related with total antioxidant level of the sample. The assay is calibrated with a stable antioxidant standard solution which is traditionally named as Trolox Equivalent that is a vitamin E analog .

Precision: Inter-assay coefficent of variation 2.8%, Intra-assay coefficent of variation 3.3%

Assay Range: 0.1 – 3.5 mmol Trolox Equiv. /L.

Wavelength: 660nm

Principle of TOS Assay: Oxidants present in the sample oxidize the ferrous ion– chelator complex to ferric ion. The oxidation reaction is prolonged by enhancer molecules, which are abundantly present in the reaction medium. The ferric ion makes a colored complex with chromogen in an acidic medium. The color intensity, which can be measured spectrophotometrically, is related to the total amount of oxidant molecules present in the sample. The assay is calibrated with hydrogen peroxide and the results are expressed in terms of micromolar hydrogen peroxide equivalent per liter (μmol H2O2 Equiv./L)

Precision: Inter-assay coefficent of variation 3.2%, Intra-assay coefficent of variation 3.9%

Assay Range: 0.2 – 80 μmol H2O2 Equiv. /L.

Wavelength 530nm

Determination of live weight: The live weights of the rats in the whole group were measured with a precision balance at the end of 4 weeks.

Statistical analysis: SPSS version 16.0 was used for statistical calculations. Statistical Data were given as mean±standard deviation (M±SD). The calculator was taken at a 5% significance level for analyses. The Kruskal-Wallis test was used to analyze all data and the Dunn test was used to identify different groups.

## Results

Effect of barley grass on 8-OHdG level: Administration of barley grass to rats injected with STZ did not change oxidative DNA damage. Therefore, there was no difference in mean serum 8-OHdG levels between all groups (*p=0.059*) (Table I).

Effect of barley grass on TOS and OSI activities: Streptozotocin- intoxicated elevated serum TOS and OSI in the Diabetic animals compared to animals in the control and BG groups. TOS (*p=0.035*) and OSI (*p=0.004*) values of rats in the DM+BG Group statistically decreased compared to the DM group (Table I)

Effect of barley grass on TAS activities: barley grass-treated increased serum total antioxidant status in animal's BG and DM+BG groups compared to other groups (*p=0.005*) (Table I).

Effect of barley grass on glucose and HbA1c values: these levels were significantly elevated in the DM animals compared to the other groups. BG treatment in Diabetic rats significantly decreased glucose (*p=0.006*) and HbA1c (*p=0.005*) values. These values of rats in the DM+BG Group were statistically decreased compared to the DM group and these value in the BG Group were close to the control group. (Table I).

Effects of barley grass on live weight: Streptozotocin- intoxicated decreased live weight in the diabetic animals. Barley grass treatment in diabetic animals significantly increased these parameters. The live weight of rats in the DM+BG Group was statistically increased (p=0.041) compared to the DM group. These values in the BG group were close to the control group. (Table I).

## Discussion

Free radical formation is seen in the occurrence of some

**Table I.** The values of serum 8-OHdG, TAS, TOS, OSI glucose, HbA1c and live weight values in all groups

| Parameters | Control (C) Mean±SD | Barley grass (BG) Mean±SD | Diabetes (DM) Mean±SD | Diabetes and Barley grass (DM+BG) Mean±SD | *p* |
|---|---|---|---|---|---|
| 8OHdG (ng/mL) | 13.35±6.25 | 15.55±8.18 | 18.98±8.23 | 17.38±6.57 | *0.059* |
| TAS (mmol Trolox Equiv/L) | 0.57±0.24$^{b}$ | 1.02±0.25$^{a}$ | 0.68±0.19b | 0.97 ±0.38$^{a}$ | *0.005* |
| TOS (μmol $H_2O_2$ Equiv/L) | 4.15±1.13$^{b}$ | 5.27±1.63$^{b}$ | 8.12±1.72a | 6.29±1.87$^{ab}$ | *0.035* |
| OSI (Arbitrary Unit) | 0.73±0.31$^{b}$ | 0.53±0.15$^{b}$ | 1.19±0.78a | 0.65±0.65$^{b}$ | *0.004* |
| Glucose (mg/dL) | 78.25±5.57$^{c}$ | 91.53±8.45$^{c}$ | 482.00±69.58$^{a}$ | 349.00±52.76$^{b}$ | *0.006* |
| HbA1c (%) | 2.58±0.35$^{c}$ | 2.98±0.5$^{c}$ | 6.74±1.15$^{a}$ | 4.45±0.95$^{b}$ | *0.005* |
| Live Weight (g) | 270.60±20.10$^{a}$ | 284.35±18.30$^{a}$ | 202.75±15.70c | 237,35±16.45$^{b}$ | *0.041* |

$^{a,b,c:}$ in the same line values with different letters show statistically significant differences.

$^{c}$: Control, BG: Barley Grass, DM: Diabetes Mellitus, 8-OHdG (8- hydroxy-2'-deoxyguanosine), TAS - Total antioxidant status; TOS - total oxidant status; OSI -oxidative stress index; HbA1c: Hemoglobin A1c

chronic diseases. Antioxidants that work against free radicals become increasingly important. Cytotoxic aldehydes are products of lipid peroxidation. It causes damage by attaching to DNA and proteins (20). In such cases, DNA integrity may be compromised and DNA damage may develop. 8-OHdG is a frequently used parameter in the determination of DNA damage (21).

In previous experimental studies, it was reported that oxidative stress due to diabetes causes DNA damage. As a result, it was emphasized that the level of 8-OHdG increased in the tissues and body fluids of these patients (22). In another study, it was revealed that an antioxidant-effective of lycopene (23) and wheatgrass (24) used reduced the level of 8OHdG and had a DNA protective effect. On the other hand, in some studies such as diabetes (10), and kidney failure (14,15) it was reported that DNA damage was not observed.

In this study, when all groups were examined, serum 8OHdG level was highest in the diabetic group, but this increase was not statistically significant. According to our results, we can say that short-term diabetes does not exactly cause DNA damage. Already, the 8OHdG level is compatible with the literature (10,14). In some cases, oxidative damage that occurs at low levels can be effectively repaired by metabolism, some enzymes involved in circadian control mechanisms (25). H2O2 does not directly damage DNA like O2, but OH is more effective on DNA (26). In addition, for OH radicals to have an effect on DNA, they must be formed either in DNA or very close to it.

Free radicals can damage tissues and some related diseases may occur. At the same time, free radicals can affect the nucleic acids of cells, resulting in cell death and premature aging. In addition, cells change to form cell lines that cause cancer and similar diseases (27).

Free radicals elevated in blood serum may cause membrane integrity loss and genetic mutations (8). Reactive oxygen species such as hydroxyl, superoxide anion, and oxygen radicals are believed to cause carcinogenesis, mutagenesis, aging, and arteriosclerosis. Endogenous antioxidants have been found to protect the body against reactive oxygen, but there is an exciting increase in the protective functions of natural antioxidants found in plants (28).

In other metabolic diseases such as diabetes mellitus, the main factor causing oxidative stress in cells is decrease in the amount of antioxidants and an increase in reactive oxygen species (ROS) is associated with hyperglycemia. Thus, hyperglycemia; in organs such as heart, kidney, eye, liver; It causes oxidative damage in the gastrointestinal tract, small and large vessels and nerve tissue (29). Studies have shown that free radical production increases in diabetes, resulting in delayed healing of wounds (10, 11).

Recently, serum TOS and OSI levels have been reported to be high in diabetes (10), kidney failure (14, 15), in methotrexate administration (19), cancer (16). This study, blood serum TOS and OSI values were found highest in the rats in the diabetes group. It was determined that these values decreased with the effect of barley grass and approached the values in the control group. In this case, we can say that barley grass has a healing effect on oxidative stress in diabetic rats and Barley Grass used in diabetes can reduce this increased oxidative stress state.

Antioxidants play a dual role by removing free radicals from cells, slowing and even preventing diseases (30). The reactive oxygen species activity may increase and the activity of the antioxidant enzymes may decrease (31). Some antioxidants have a protective effect on this toxicity, suggesting that these damages may be related to radical metabolism (32). Studies have shown that antioxidants prevent cell damage by neutralizing free radicals (27). Antioxidants in the body can partially protect the person against reactive oxygen species. It is necessary to take extra antioxidant supplements from outside. Antioxidants may be needed externally to prevent the damage of free radicals that increase diabetes (8).

In diabetes, glutathione reductase, catalase and glutathione peroxidase activities decrease (33). On the other hand, vitamins C and E reduce lipid peroxidation in diabetes (34). At the same time, vitamin E reduces fasting plasma glucose, fructosamine, thiobarbituric acid reactive substances (TBARS) and increases superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activities, insulin and C peptide levels, in Type 2 diabetes (35).

Some plants, such as barley grass, contain large amounts of antioxidant enzymes. There are high phenolic compounds with antioxidant properties in barley grass. These compounds are in the form of phenolic acids, proanthocyanidins, tannins, flavonols, chalcones, flavones and amino phenolic compounds, tocopherols, polysaccharide, dietary fiber, and phytic acid. The antioxidant activity of polyphenols in barley, in order from most to least, are flavanols, flavonols and hydroxycinnamic acids (36).

Barley grass reduces oxidants such as malondialdehyde (MDA) and glutathione (GSH), GSH-Px, SOD, catalase (CAT), etc. provides an increase in antioxidants (7). In previous studies, it has been reported that as a result of oral administration of barley grass extracts to 36 patients with type 2 diabetes for 4 weeks, 15 g per day, it reduces free oxygen radicals, preserves low density lipoprotein (LDL), Vitamin-E level, and reduces LDL oxidation (37). Another study determined that barley grass used in similar doses increased TAS levels (14).

Mis et al., (10) reported that TAS values in the wheatgrass group were higher than the diabetes group in their study. In this study, TAS level in rats with diabetes was found to be close to the values of the control group. In addition, TAS levels of the barley grass and diabetes barley grass group were found to be statistically higher than the control and diabetic group. These findings support the antioxidant content of barley grass.

Oxidative stress induced by diabetes leads to dysfunction of pancreatic B cells, glucose intolerance and insulin resistance. Phytochemicals such as phenolic acids, phytosterols, tocopherols and flavonoids in barley may be beneficial in treating of these diabetes disorders (38).

The treatment of diabetes aims to balance glucose homeostasis. For this reason, glucose production is reduced or insulin production is increased. In both cases, it is desired to reduce insulin resistance in the receptors of the relevant cells. For this purpose, many drugs and methods have been developed in the treatment of diabetes.

Barley contains important antidiabetic elements. These include β-glucans, phytosterols, phenolic compounds, tocopherols, resistant starches and arabinoxylans. β-glucan in barley can reduce serum lipids, arterial sclerosis, serum glucose and insulin resistance in obese mice (39). Furthermore, due

to β-glucan, long-term use of foods such as barley can improve insulin resistance and prolong the feeling of satiety (40). Slow-digesting starch and High phenolic content in barley cakes can improve the glycemic pathway (41).

In previous studies (42) the alcohol extract of barley was administered to diabetic rats at different doses for 11 days, and their blood glucose was monitored daily. A significant decrease in blood glucose in diabetics was determined with barley applications at doses of 250 and 500 mg/kg. In addition, it has been stated that if barley is applied for 4 weeks, it can eliminate these negative effects in diabetics by showing hypoglycemic and antioxidant effects (43).

In this study, it was determined that the glucose level, which was high in the diabetes group, decreased with barley grass application and this change was quite significant. This shows that barley grass is hypoglycemic and can be used therapeutically in diabetes patients.

Hemoglobin A1c (HbA1c), known as glycated hemoglobin, is a compound formed by hemoglobin with glucose and its amount varies depending on glucose concentration. HbA1c is a parameter that shows the glucose level for 8-12 weeks. It is used as a biomarker for complications that may develop in diabetes because it shows long-term glucose levels. HbA1c is required for long-term glucose control retrospectively in patients with diabetes. Therefore, it is widely used. In diabetes, the HbA1c level increases as a result of the reaction of high blood sugar and hemoglobin (44). In this study, the level of HbA1c was significantly higher in diabetic rats. A decrease in HbA1c level was observed with barley grass application. The results obtained were consistent with the literature (9).

Diabetes can cause bodyweight loss, increased fat and protein catabolism, and destruction of muscles . With the decrease in insulin secretion in the body, the peptide bonds of proteins are hydrolyzed, and broken down into peptides and amino acids. As a result, muscle tissue weakens (45). In another study, approximately a 35% increase in body weight in diabetic animals compared to the healthy group (9, 46).

In this study, the live weights of the animals in the diabetic group were found to be quite low. On the other hand, there was a gain in the live weight of the animals in the DM and BG Groups. It can be said that the blood sugar levels of rats may decrease due to barley grass extract given to the diabetic group. As a result, it should be considered that weight loss is less due to the decrease in lipolysis and proteolysis.

There are also studies showing the curative effect on obesity of barley. β-glucan found in barley plays a role in obesity treatment by increasing flow-mediated expansion by reducing serum p-cresyl sulfate, total cholesterol and low-density lipoprotein levels (47). β-glucan in barley, which improves food digestibility and adds antiobesity, can prevent obesity of visceral fat and increase stool score (48). Insulin resistance and obesity are associated with bile acid changes with low dietary fiber in the barley diet (49). Barley malt has an antiobesity effect thanks to the β-glucan and phenolic acids it contains (47).

Diabetes Mellitus disease, which is becoming more common day by day, has an increasing prevalence. Many mechanisms play a role in the pathogenesis and complications of the disease. The most accepted one is related to free radicals. By increasing the antioxidant capacity, oxidative stress caused by diabetes can be dealt with. Studies on the effects of antioxidants on diabetes are increasing.

Some studies have found that barley grass extract reduces oxidants such as MDA and increases antioxidants such as CAT, SOD, GSH and GSH -Px. However, according to our literature review, there is no published report on the effect of barley grass on TOS, TAS, OSI, DNA damage and serum oxidative stress parameters such as glucose and HbA1c in diabetic rats. Therefore, this study is important.

With this study, we revealed that the antioxidant defense system is strengthened by barley grass. In addition, it caused a decrease in glucose levels and body weight in diabetic rats. In other words, barley grass may contribute to diabetes management by reducing and preventing diabetic complications. For this reason, we recommend barley grass to beat oxidative stress in diabetic patients. We think that barley grass will also be beneficial due to its anti-oxidative, anti-hyperglycemic, and weight effects.

## References


1. Zeng Y, Pu X, Du J et al. Molecular mechanism of functional ingredients in barley to combat human chronic diseases. oxidative medicine and cellular longevity. Oxid Med Cell Long (3836172) 2020. Available from: URL: https://www.hindawi.com/journals/omcl/2020/3836172/. Date of Access: 19.01.2023.
2. Acar O, Türkan I, Özdemir F. Superoxide dismutase and peroxidase activities in drought sensitive and resistant barley (Hordeum vulgare L.) varieties. Acta Physiologiae Plantarum 2001; 23:351-356.
3. Lachman J, Hejtmánková A, Orsák M, Popov M, Martinek P. Tocotrienols and tocopherols in colored-grain wheat, tritordeum and barley. Food chemistry 2018; 240:725-735.
4. Do TDT, Cozzolino D, Muhlhausler B, Box A, Able AJ. Antioxidant capacity and vitamin E in barley: Effect of genotype and storage. Food chemistry 2015; 187:65-74.
5. Erel O. A novel automated method to measure total antioxidant response against potent free radical reactions. Clinical biochemistry 2004; 37:112-119.
6. Erel O. A new automated colorimetric method for measuring total oxidant status. Clinical biochemistry 2005; 38:1103-1111.
7. Yang JL, Weissman L, Bohr VA, Mattson MP. Mitochondrial DNA damage and repair in neurodegenerative disorders. DNA repair 2008;7: 1110-1120.
8. Vincent AM, Russell JW, Low P, Feldman EL. Oxidative stress in the pathogenesis of diabetic neuropathy. Endocrine reviews 2004; 25:612-628.
9. Çelik R, Mert M, Comba B, Mert N. Effects of cinnamaldehyde on glucose-6-phosphate dehydrogenase activity, some biochemical and hematological parameters in diabetic rats. Biomarkers 2022; 27:270–277
10. Mis L, Comba B, Uslu S, Yeltekin A. Effect of Wheatgrass on DNA damage, oxidative stress ındex and histological findings in Diabetic Rats. International Journal of Morphology 2018; 36:1235-1240.
11. Comba B, Taş A, Comba A, Yurdakul İ, Yörük İH. Effect of sildenafil citrate on MDA, GSH, retinol, vitamin D3 and α-tocoferole levels in wound healing: diabetic rat model. Journal

of Applied Biological Sciences 2015; 9: 82-85.

12. Taş A, Karasu A, Comba B, Aksu D, Düz E. Effects of sildenafil citrate on the hematological parameters in the early phase of wound healing in diabetic rats. Asian Journal of Animal and Veterinary Advances, 2011; 6: 290-296.

13. Gorogawa S, Kajimoto Y, Umayahara Y et al. Probucol preserves pancreatic β-cell function through reduction of oxidative stress in type 2 diabetes. Diabetes research and clinical practice, 2002; 57: 1-10.

14.Comba B, Mis L, Uslu S, Comba A The effect of barley grass on antioxidant capacity and DNA damage in rat with renal failure. Fresenius Environmental Bulletin 2017; 26: 6135-6140.

15. Mis L, Comba B, Basbugan Y, Yasar S, Comba A. Assessment of the wheatgrass effects on antıoxıdant capacıty and dna damage ın rats wıth experımental renal faılure. Fresenius Environmental Bulletin 2019; 28: 2876-2879.

16. Comba B, Oto G, Mis L, Özdemir H, Comba A. Effects of borax on inflammation, haematological parameters and total oxidant-antioxidant status in rats applied 3–methylcholanthrene - Kafkas Univ Vet Fak Derg 2016;22:539-544

17. Comba A, Oto G, Comba B, Ozdemir H, Keskin S. Effects of boric acid on proinflammation cytokines, total oxidativeantioxidative status and hematological parameters in rats applied benzo(a)pyrene, Fresenıus Envıronmental Bulletın 2020;29:3599-3605.

18. Yildirim S, Oto G, Comba B, Ekin S, Cinar DA. An investigation of the protective effects of resveratrol on some biochemical parameters and histopathological findings in experimentally-induced chronic flurosis in rats. Fluoride 2017; 50:365-373

19. Vadi M, Comba B. Effect of Resveratrol on Total Oxidative-Antioxidative Status and DNA Damage in Rats Induced Methotrexate. Cumhuriyet University Journal of Health Sciences Institute, 2022; 7: 84-91.

20. Pham-Huy LA, He H, Pham-Huy C. Free radicals, antioxidants in disease and health. Int J Biomed Sci. 2008;4: 89-96.

21.Piconi L, Quagliaro L, Ceriello A. Oxidative stress in diabetes. Clinical Chemistry and Laboratory Medicine, 2003;41:1144-1149.

22. Park KS, Kim JH, Kim MS et al. Effects of insulin and antioxidant on plasma 8-hydroxyguanine and tissue 8-hydroxydeoxyguanosine in streptozotocin-induced diabetic rats. Diabetes 2001;50:2837-2841.

23. Huang CS, Hu ML. Lycopene inhibits DNA damage and reduces hMTH1 mRNA expression in the liver of Mongolian gerbils treated with ferric nitrilotriacetate. Food and chemical toxicology 2011; 49:1381-1386.

24. Falcioni G, Fedeli D, Tiano L et al. Antioxidant activity of wheat sprouts extract in vitro: inhibition of DNA oxidative damage. Journal of food science 2002; 67: 2918-2922.

25. Sancar A, Lindsey-Boltz LA, Kang TH, Reardon JT, Lee JH, Ozturk N Circadian clock control of the cellular response to DNA damage. FEBS Letters 2010; 584:2618–2625.

26. Cooke MS, Evans MD, Dizdaroglu M, Lunec J. Oxidative DNA damage: mechanisms, mutation, and disease. The FASEB Journal 2003;17:1195-1214.

27. Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. Pharmacogn Rev. 2010; 4:118-126.

28 Ristow M, Schmeisser K. Mitohormesis. Promoting health and lifespan by increased levels of reactive oxygen species (ROS). Dose Response 2014; 12: 288–341.

29. Tunali S, Yanardag R. Effect of vanadyl sulfate on the status of lipid parameters and on stomach and spleen tissues of streptozotocin-induced diabetic rats. Pharmacological research 2006; 53:271-277.

30.Salehi B, Martorell M, Arbiser JL. et al, Antioxidants: positive or negative actors? Biomolecules, 2018;8:124.

31. Maldonado PD, Barrera D, Medina-Campos ON, Hernández-Pando R, Ibarra-Rubio ME, Pedraza-Chaverrı- J. Aged garlic extract attenuates gentamicin induced renal damage and oxidative stress in rats. Life Sciences 2003; 73:2543-2556.

32. Kavutcu M, Canbolat O, Ozturk S. et al. Reduced enzymatic antioxidant defense mechanism in kidney tissues from gentamicin-treated guinea pigs: effects of vitamins E and C. Nephron 1996;72:269-274.

33. Komosińska-Vassev K, Olczyk K, Olczyk P, Winsz-Szczotka K. Effects of metabolic control and vascular complications on indices of oxidative stress in type 2 diabetic patients. Diabetes research and clinical practice 2005; 68: 207-216.

34. Kutlu M, Naziroglu M, Simsek H, Yilmaz T, Kükner AS. Moderate exercise combined with dietary vitamins C and E counteracts oxidative stress in the kidney and lens of streptozotocin-induced diabetic rat. International journal for vitamin and nutrition research 2005; 75: 71-80.

35. Gokkusu C, Palanduz S, Ademoğlu E, Tamer S. Oxidant and antioxidant systems in NIDDM patients: influence of vitamin E supplementation. Endocrine research 2001; 27: 377-386.

36. Gangopadhyay N, Rai DK, Brunton NP, Gallagher E, Hossain MB. Antioxidant-guided isolation and mass spectrometric identification of the major polyphenols in barley (Hordeum vulgare) grain. Food chemistry 2016; 210, 212-220.

37. Yu YM, Chang WC, Chang CT, Hsieh CL, Tsai CE. Effects of young barley leaf extract and antioxidative vitamins on LDL oxidation and free radical scavenging activities in type 2 diabetes Diabetes Metab. 2002; 28:107-114.

38. Idehen E, Tang Y, Sang S. Bioactive phytochemicals in barley. journal of food and drug analysis 2017; 25: 148-161.

39. Tian MJ, Song JN, Liu PP, Su LH, Sun CH, Li Y. Effects of beta glucan in highland barley on blood glucose and serum lipid in high fat-induced C57 mouse. Zhonghua yu fang yi xue za zhi 2013; 47:55-58.

40. Ames N, Blewett H, Storsley J, Thandapilly SJ, Zahradka P, Taylor CA. Double-blind randomised controlled trial testing the effect of a barley product containing varying amounts and types of fibre on the postprandial glucose response of healthy volunteers. British Journal of Nutrition 2015; 113: 1373-1383.

41. Soong YY, Tan SP, Leong LP, Henry JK. Total antioxidant capacity and starch digestibility of muffins baked with rice, wheat, oat, corn and barley flour. Food chemistry 2014; 164:462-469.

42. Minaiyan M, Ghannadi A, Movahedian A, Hakim-Elahi I. Effect of Hordeum vulgare L.(Barley) on blood glucose levels of normal and STZ-induced diabetic rats. Research in pharmaceutical sciences 2014;9:173-176.

43.Khalaf G, Mohamed AG. Effect of barley (Hordeum vulgare) on the liver of diabetic rats: Histological and biochemical study. Egypt J Histol 2008; 31: 245-255.

44. Babu PS, Prabuseenivasan S, Ignacimuthu S. Cinnamaldehyde—a potential antidiabetic agent. Phytomedicine 2007;14:15-22.

45. Dilworth L, Facey A, Omoruyi F. Diabetes mellitus and its metabolic complications: the role of adipose tissues. Int J Mol Sci. 2021; 22:7644.

46. Anand, P, Murali K, Tandon V, Murthy P, Chandra R. Insulinotropic effect of cinnamaldehyde on transcriptional regulation of pyruvate kinase, phosphoenolpyruvate carboxykinase, and GLUT4 translocation in experimental diabetic rats. Chemico-biological interactions 2010; 186: 72-81.

47. Zhang J, Xiao X, Dong Y, Shi L, Xu T, Wu F. The anti-obesity effect of fermented barley extracts with Lactobacillus plantarum dy-1 and Saccharomyces cerevisiae in diet-induced obese rats. Food & Function 2017; 8: 1132-1143.

48. Clarke L, Sweeney T, Curley E, Duffy S, Rajauria, G, O'doherty J. The variation in chemical composition of barley feed with or without enzyme supplementation influences nutrient digestibility and subsequently affects performance in piglets. Journal of animal physiology and animal nutrition 2018; 102: 799-809.

49. Ghaffarzadegan T, Zhong Y, Hållenius FF, Nyman M. Effects of barley variety, dietary fiber and β-glucan content on bile acid composition in cecum of rats fed low-and high-fat diets. The Journal of Nutritional Biochemistry 2018;53:104-110.

# COVID-19 Hastalarında Olası İkincil Bakteriyel Pnömoni İçin Antibiyotik Kullanmanın Yoğun Bakıma Nakil Gerekliliğine Etkisi: Bir Retrospektif Kohort Çalışma

**Ahmet Sertçelik[1], Ümran Özden Sertçelik[2], Bircan Kayaaslan[3], Hatice Kılıç[2], Hatice Rahmet Güner[3]**

[1] Hacettepe Üniversitesi Tıp Fakültesi Halk Sağlığı Anabilim Dalı Epidemiyoloji Bilim Dalı, Ankara, Türkiye.
[2] Ankara Yıldırım Beyazıt Üniversitesi Tıp Fakültesi Göğüs Hastalıkları Anabilim Dalı, Ankara, Türkiye.
[3] Ankara Yıldırım Beyazıt Üniversitesi Tıp Fakültesi Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Ankara, Türkiye

**Yazışma Adresi:** Hacettepe Üniversitesi Tıp Fakültesi Halk Sağlığı Anabilim Dalı 2. Kat, Altındağ/ANKARA.
e-posta: ahmetsertcelik@gmail.com

**Orcid No:** AS: 0000-0003-4301-0586 BK: 0000-0002-2502-3810 HRG: 0000-0002-1029-1185
ÜÖS: 0000-0001-8394-6544 HK: 0000-0003-0568-3309

**Atıf:** Serçelik A, Sertçelik ÜÖ, Kayaaslan B, ve ark. COVID-19 Hastalarında Olası İkincil Bakteriyel Pnömoni İçin Antibiyotik Kullanmanın Yoğun Bakıma Nakil Gerekliliğine Etkisi: Bir Retrospektif Kohort Çalışma. Hitit Med J 2023;5(3): 162-169. https://doi.org/10.52827/hititmedj.1294868

## Özet

**Amaç:** COVID-19 nedeniyle serviste izlenen ikincil bakteriyel pnömoni olasılığı olan erişkin hastalarda antibiyotik kullanma sıklığı ve bunun yoğun bakıma nakil durumu ile ilişkisinin belirlenmesi amaçlandı.

**Gereç ve Yöntem:** Üçüncü basamak bir hastanede 10.03.2020-31.12.2020 tarihleri arasında COVID-19 hastalığı nedeniyle serviste takip edilen 18 yaş üzeri hastalardan olası ikincil bakteriyel pnömonisi olan hastalar retrospektif olarak incelendi. Pnömoni dışı bakteriyel infeksiyonu olanlar dışlandı. Bu hasta kohortu yoğun bakıma gidiş açısından yatış süreleri boyunca izlendi. Olası bakteriyel pnömoni tanısı için hastanın görüntülemede bakteriyel pnömoni ile uyumlu bulgu olması yanı sıra öksürük, balgam, 37°C üzeri vücut sıcaklığı, 10000/µl üzeri lökosit ve/veya, 0,16µg/l üzeri prokalsitonin düzeyinden en az birisinin varlığı arandı.

**Bulgular:** Dahil etme kriterlerine uyan 724 hastadan pnömoni dışında bir bakteriyel infeksiyon odağı olan 9 hasta dışlanmış ve analizler 715 hasta üzerinden tamamlanmıştır. Hastalar ortanca 7 (ÇADA=6) gün izlenmiş ve hastaların 462'si (%64,6) antibiyotik alırken, 253'ü (%35,4) almamıştır. Antibiyotik alan hastaların 33'ü (%7,1), almayan hastaların ise 26'sı (%10,3) izlem süresinde yoğun bakıma nakledilmiş olup, antibiyotik alanlarda almayanlara göre yoğun bakıma gitme rölatif riski 0,70 (%95 GA = 0,43 – 1,14)'tir. Lojistik regresyon analizinde yaş, cinsiyet, komorbidite bulunma durumu, ciddi COVID-19 varlığı, favipiravir, azitromisin ve hidroksiklorokin kullanma durumları eş zamanlı kontrol edildiğinde, antibiyotik kullanan hastalarda, kullanmayanlara göre yoğun bakıma nakil düzeltilmiş risk odds oranı koruyucu olsa da istatistiksel olarak anlamlı bulunmamıştır (0,56; %95GA=0,30-1,30). En çok tercih edilen antibiyotikler sefalosporinler (%42,5), makrolidler (%19,2) ve piperasilin-tazobaktam (%8,5)'dır.

**Sonuç:** Antibiyotik kullanmanın yoğun bakıma gidişi önleme konusunda istatistiksel olarak anlamlı bir etkisi bulunmamıştır. Olası tip 2 hata, antimikrobiyal direnç nedeniyle ampirik tedavinin yetersizliği yanı sıra tanı kriterlerinin geçerliliği, uygun antibiyotik seçimi benzeri konuların netleştirilmesi için prospektif kohortlara ihtiyaç vardır.

**Anahtar Sözcükler:** Antibakteriyel ajanlar, Bakteriyel pnömoni, İzlem, Koenfeksiyon, SARS-CoV-2

**Geliş Tarihi:** 09.05.2023
**Kabul Tarihi:** 15.08.2023
**Yayım Tarihi:** 10.10.2023

**Hakem Değerlendirmesi:** Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilir.
**Etik Beyanı:** Çalışma Ankara 1 Nolu Klinik Araştırmalar Etik Kurulu tarafından 23.03.2022 tarihinde E. Kurul-E1-22-2504 protokol numarası ile etik açıdan onaylanmıştır.
**İntihal Kontrolleri:** Evet - intihal.net
**Çıkar Çatışması:** Yazarlar tarafından herhangi bir çıkar çatışması beyan edilmemiştir.
**Şikayetler:** hmj@hitit.edu.tr
**Katkı Beyanı:** Fikir/Hipotez: AS, ÜÖS, BK Tasarım: AS, ÜÖS, BK Veri Toplama/Veri İşleme: AS, ÜÖS, BK, HK, HRG Veri Analizi: AS, ÜÖS, BK, HK, HRG Makalenin Hazırlanması: AS, ÜÖS, BK, HK, HRG
**Hasta Onamı:** Onama gerek yoktur.
**Finansal Destek:** Finansal destek alınmamıştır.

# The Effect of Antibiotic Use on Transfer to Intensive Care Unit in COVID-19 Patients with Possible Secondary Bacterial Pneumonia: A Retrospective Cohort Study

**Ahmet Sertcelik[1], Umran Ozden Sertcelik[2], Bircan Kayaaslan[3], Hatice Kilic[2], Hatice Rahmet Guner[3]**

[1]Hacettepe University Faculty of Medicine Department of Public Health Division of Epidemiology, Ankara, Türkiye
[2]Ankara Yildirim Beyazit University Faculty of Medicine Department of Chest Diseases, Ankara, Türkiye.
[3]Ankara Yildirim Beyazit University Faculty of Medicine Department of Infectious Diseases and Clinical Microbiology, Ankara, Türkiye

**Address for Correspondence:** Hacettepe University Faculty of Medicine Department of Public Health Division of Epidemiology, Ankara, Türkiye
Email: ahmetsertcelik@gmail.com

**Orcid ID:** AS: 0000-0003-4301-0586 BK: 0000-0002-2502-3810 HRG: 0000-0002-1029-1185
UOS: 0000-0001-8394-6544 HK: 0000-0003-0568-3309

**Cite As:** Sercelik A, Sertcelik UO, Kayaaslan B, et al. The Effect of Antibiotic Use on Transfer to Intensive Care Unit in COVID-19 Patients with Possible Secondary Bacterial Pneumonia: A Retrospective Cohort Study. Hitit Med J 2023;5(3): 162-169. https://doi.org/10.52827/hititmedj.1294868

## Abstract

**Objective:** We aimed to determine the frequency of antibiotics use for possible secondary bacterial pneumonia among hospitalized COVID-19 adults and its association with transfer to intensive care unit (ICU).

**Material and Method:** Hospitalized COVID-19 adults of a tertiary hospital followed retrospectively from 10 March through 31 December 2020, for possible secondary bacterial pneumonia and their transfer to ICU (if any). Patients with bacterial infections other than pneumonia were excluded. Possible bacterial pneumonia was defined as imaging compatible with bacterial pneumonia, together with (at least one of) cough sputum, body temperature above 37 °C, leukocyte count over 10000/μL and/or procalcitonin level over 0.16μg/L.

**Results:** Of the 724 eligibles, nine patients with a bacterial infection other than pneumonia were excluded, leaving 715 for analyses. Over a median of 7 (IQR=6) days of follow-up, 462 (64.6%) of the patients received antibiotics, while 253(35.4%) did not. Thirty-three (7.1%) of the patients receiving antibiotics were transferred to ICU, compared to 26 (10.3%) out of those who did not receive antibiotics: the risk of ICU was 0.70 (95%CI=0.43–1.14). In logistic regression analysis, transfer to ICU was lower, yet not statistically significant, among antibiotic receivers (0.56; 95%CI=0.30–1.03), adjusting for age, gender, comorbidity, COVID-19 severity, use of favipiravir, azithromycin, and hydroxychloroquine.

**Conclusion:** Antbiotic use did not statistically significantly affect transfer to ICU. Prospective cohorts are warranted for conclusive evidence to discard the potential for type 2 errors or ineffectiveness of ampiric treatment due to amtimicrobial resistance, and to further validate diagnostic criteria and appropriateness of ampiric regimens.

**Keywords:** 2019-nCoV Disease, Anti-Bacterial agents, Bacterial pneumonia, Coinfection, Follow-up study

**Date of Submission:** 09.05.2023
**Date of Acceptance:** 15.08.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** The study was ethically approved by Ankara No. 1 Clinical Research Ethics Committee on 23.03.2022 with protocol number E. Board-E1-22-2504
**Plagiarism Checks:** Yes - intihal.net
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: AS, UOS, BK Design: AS, UOS, BK Data Collection/Data Processing: AS, UOS, BK, HK, HRG Data Analysis: AS, UOS, BK, HK, HRG Article Preparation: AS, UOS, BK, HK, HRG
**Informed Consent:** Not applicable.
**Financial Disclosure:** No financial support has been received.

## Giriş

Ciddi akut respiratuar sendrom Koronavirüs 2 (SARS-CoV-2)nin neden olduğu COVID-19 pandemisi dünya genelinde önemli bir sağlık tehdidi olmaya devam etmektedir (1). COVID-19'a bağlı gelişen pnömoni ve hiperinflamatuar durum klinik açıdan kötüleşmeye ve ölüme neden olabilmektedir (2). Diğer yandan viral etkenler ile gelişen alt solunum yolu enfeksiyonlarında bakteriyel ko-infeksiyon ve süperinfeksiyon gelişimi artmakta ve bu durum klinik sonucu olumsuz etkilemektedir. SARS-CoV-2 öncesinde 2009 H1N1 pandemik influenza salgını da dahil viral alt solunum yolu infeksiyonlarında ikincil bakteriyel pnömonilerin ölümü ve yoğun bakıma gidişi artırdığı görülmüştür (3).

COVID-19 hastalarında yoğun bakıma ihtiyacın gelişmesinde etkili olan hiperinflamatuar durum ve ikincil bakteriyel pnömonileri ayırt etmek zor olabilmektedir. Hiperinflamatuvar durumda antibiyotik tedavinin etkili olması beklenmezken ikincil bakteriyel pnömonisi olan hastaların tedavisinde uygun antibiyotik tedavisinin verilmesi önerilmektedir (4, 5).

Literatürde önerilen bir olası bakteriyel pnömoni tanımı (6) üzerinden referans merkezi olan bir hastanede COVID-19 hastalığı nedeniyle serviste takip edilen erişkin hastalardan olası ikincil bakteriyel pnömonisi olan hastalarda kullanılan antibiyotiklerin saptanması ve antibiyotik kullanmanın yoğun bakım gerekliliğine olan etkisinin araştırılması amaçlanmaktadır.

## Gereç ve Yöntemler

Retrospektif kohort tipindeki bu araştırma, yaklaşık 3100 servis ve 700 yoğun bakım yatak kapasitesine sahip olan referans hastanede yürütüldü. Bu çalışmaya 10.03.2020 – 31.12.2020 tarihleri arasında SARS-CoV-2 polimeraz zincir reaksiyonu (PCR) pozitif COVID-19 hastalığı nedeniyle serviste takip edilen 18 yaş üzeri olası ikincil bakteriyel pnömonisi olan hastalar dahil edildi. İkincil bakteriyel pnömoni dışında bakteriyel bir infeksiyonu olan hastalar dışlandı. Herhangi bir örnek seçilmedi ve seçime uygun olan tüm hastalar çalışma grubunu oluşturdu. Hastalar hastanede bulundukları sürece yoğun bakıma nakil açısından kayıt sistemi üzerinden geriye dönük izlendi. Nisan 2022 sonrası veri temizliği, veri analizi, çalışma bulgularının yorumlaması ve raporlaması yapıldı. Araştırma Ocak 2023 itibarıyla tamamlandı.

COVID-19 hastalığı tanısı ile serviste izlenen hastaların demografik bilgileri, ek hastalıkları, başvuru sırasında steroid ve antineoplastik ilaç gibi bağışıklık baskılayıcı ilaç kullanma öyküleri, başvuru sırasındaki belirti ve fizik muayene bulguları, laboratuvar bulguları, radyolojik tetkik bulguları, antiviral etkinlik için kullanılan tedaviler, antibiyotik kullanma durumları kaydedildi. Hastalar taburcu olana veya yoğun bakıma nakil olana kadar, hangisi daha önce geldiyse, serviste izlendi. Yoğun bakıma nakledilen hastaların klinik sonuçları (ölüm veya hastaneden taburculuk) hastanenin elektronik kayıtlarından elde edildi. Hastalık seyrini belirlemede birincil sonlanım yoğun bakım ünitesine nakil olarak belirlendi.

Bu çalışmada değerlendirilen ana etken antibiyotik kullanma, sonuç yoğun bakıma nakledilme durumu olarak belirlendi. Hastanın yaşı, cinsiyeti, sigara içme durumu, ek hastalığının olması, başvuru öncesi steroid ve antineoplastik kullanma öyküsü, COVID-19 hastalığının şiddeti, antiviral amaçlı kullanılan tedaviler olası karıştırıcılar olarak düşünüldü. Ancak sigara içme durumu ve başvuru öncesi bağışıklık baskılayıcı ilaç kullanma ile ilgili kayıp verilerin fazlalığı nedeniyle çok değişkenli analize dahil edilmedi.

Hastaların seçiminde kullanılan olası ikincil bakteriyel pnömoni 1) öksürük ve balgam çıkarma, 2) lökosit > 10000/µl, 3) serum prokalsitonin > 0,16 µg/l, 4) Vücut sıcaklığı >37°C kriterlerinden en az birinin olmasıyla beraber 5) görüntülemede (akciğer grafisi veya toraks bilgisayarlı tomografi (BT)) bakteriyel pnömoni ile uyumlu bulgu olması olarak tanımlandı(6). Akciğer grafisinde opasite, infiltrasyon, toraks BT'de konsolidasyon, infiltrasyon, kaldırım taşı, hava bronkogramı ve tomurcuklanmış ağaç bulguları pnömoniyle uyumlu olarak değerlendirildi.

Solunum sayısının 30/dk üzerinde olması ya da oda havasında oksijen saturasyon değerinin %90 altında olması ciddi COVID-19 olarak kabul edildi (7) .

Çalışma Ankara Şehir Hastanesi Etik Kurulu tarafından 23.03.2022 tarihinde E. Kurul-E1-22-2504 protokol numarası ile etik açıdan onaylanmıştır. Bu araştırma Helsinki Bildirgesine uygun şekilde yürütülmüştür. Araştırma geriye dönük kayıtlar üzerinden elde edilen kimlik bilgilerinin olmadığı veri üzerinden yapıldığı için aydınlatılmış onam alınmamıştır.

## İstatistik Yöntemler

Kategorik değişkenler sayı ve yüzde olarak sunuldu ve gruplar Ki-Kare ya da Fischer'in kesin testi ile karşılaştırıldı. İlişkinin büyüklüğü açısından odds oranı ve ilişkili %95 güven aralıkları verildi. Sürekli veriler normal dağılıma uygunluk açısından değerlendirildi, normal dağılıma uymaması nedeniyle veriler ortanca (çeyrekler arası dağılım aralığı = ÇADA) olarak sunuldu ve gruplar arası karşılaştırma Mann-Whitney U testi ile yapıldı. İkili lojistik regresyon analizi ile antibiyotik kullanmanın yoğun bakıma nakille ilişkisi incelenirken olası karıştırıcılar "Enter" metodu ile modele dahil edilerek kontrol edildi. Model uyumu Hosmer-Lemeshow testi ile değerlendirildi. $p<0,05$ (çift yönlü) olması istatistiksel anlamlılık olarak değerlendirildi. Elde edilen verilerin analizinde Statistical Package for the Social Sciences (IBM SPSS, Armonk, New York, Amerika Birleşik Devletleri) sürüm 23 paket programı kullanıldı.

Bu çalışmayla benzer çalışma grubuna sahip bir araştırma olmadığı için örnek büyüklüğü hesabı yapılamadı ve geriye dönük olarak güç hesabı yapıldı. Çalışmanın gücü Open Source Epidemiologic Statistics for Public Health (OpenEpi) sürüm 3.01 ile hesaplandı ve %32,4 olarak bulundu (8).

## Bulgular

Araştırmanın yapıldığı 10.03.2020 – 31.12.2020 tarihleri arasında COVID-19 nedeniyle serviste yatarak izlenen ve dahil etme kriterlerine uyan 724 hasta bulundu. Pnömoni dışında ikincil bakteriyel bir infeksiyonu olan dokuz hasta çalışmadan çıkarıldı ve analizler 715 hasta üzerinden tamamlandı.

İleri yaşta, halen sigara kullanan ya da kullanıp bırakmış, herhangi bir eşlik eden hastalığı olan, hipertansiyon, astım veya aktif malignitesi bulunan ve ateş, öksürük, balgam ve dispne belirtileri olan hastalarda antibiyotiğin daha çok kullanıldığı görüldü. Kas-eklem ağrısı, halsizliği, tat ve koku alma bozukluğu olan grupta ise antibiyotiğin daha az tercih edildiği belirlendi (Tablo I).

Fizik muayenede ral tespit edilen, ciddi COVID-19 hastalığı bulunan, antiviral tedavi olarak hidroksiklorokin ve azitro-

**Tablo I.** Hastaların özellikleri ve başvuru sırasındaki belirtilerinin dağılımı

| | Toplam (N=715) n (%) | Yoğun bakıma gidenler (N=59) n (%) | Yoğun bakıma gitmeyenler (N=656) n (%) | OR (%95 GA) | *p-değeri* |
|---|---|---|---|---|---|
| Erkek cinsiyet | 436 (61,0) | 33 (55,9) | 403 (61,4) | 1,26 (0,73 – 2,15) | *0,41* |
| Ortanca yaş (ÇADA) yıl | 715 | 56,0 (18,0) | 56,0 (28,0) | - | *0,29* |
| Sağlık çalışanı | 32 (4,6) | 2 (3,4) | 30 (4,7) | 0,72 (0,17 – 3,08) | *>0,99** |
| Sigara içme durumu | | | | | *0,36* |
| Aktif içici | 89 (18,2) | 8 (20,5) | 81 (18,0) | 1,06 (0,44 – 2,35) | |
| Bırakmış | 60 (12,2) | 2 (5,1) | 58 (12,9) | 0,37 (0,09 – 1,60) | |
| İçmemiş (ref.) | 341 (69,6) | 29 (74,4) | 312 (69,2) | 1,00 | |
| Komorbidite | 416 (58,2) | 38 (64,4) | 378 (57,6) | 1,33 (0,76 – 2,32) | *0,31* |
| Ortanca Toplam komorbidite sayısı (ÇADA) | 715 | 1,0 (2,0) | 1,0 (2,0) | - | *0,32* |
| Hipertansiyon | 244 (34,1) | 21 (35,6) | 223 (34,0) | 1,07 (0,62 – 1,87) | *0,80* |
| Diyabet mellitus | 125 (17,5) | 15 (25,4) | 110 (16,8) | 1,69 (0,91 – 3,15) | *0,094* |
| Koroner arter hastalığı | 106 (14,8) | 8 (13,6) | 98 (14,9) | 0,89 (0,41 – 1,94) | *0,78* |
| Kronik böbrek yetersizliği | 31 (4,3) | 5 (8,5) | 26 (4,0) | 2,24 (0,83 – 6,08) | *0,17** |
| Kronik obstrüktif akciğer hastalığı | 31 (4,3) | 3 (5,1) | 28 (4,3) | 1,20 (0,35 – 4,08) | *0,74** |
| Astım | 41 (5,7) | 3 (5,1) | 38 (5,8) | 0,87 (0,26 – 2,91) | *>0,99* |
| Aktif malignensi | 27 (3,8) | 5 (8,5) | 22 (3,4) | 2,67 (0,97 – 7,33) | *0,063** |
| Başvurudaki belirtiler | 715 (100,0) | 59 (100,0) | 656 (100,0) | - | - |
| Ateş | 352 (49,2) | 28 (47,5) | 324 (49,4) | 0,93 (0,54 – 1,58) | *0,78* |
| Öksürük | 582 (81,4) | 43 (72,9) | 539 (82,2) | 0,58 (0,32 – 1,07) | *0,079* |
| Balgam | 67 (9,4) | 2 (3,4) | 65 (9,9) | 0,32 (0,08 – 1,34) | *0,10* |
| Baş ağrısı | 52 (7,3) | 7 (11,9) | 45 (6,9) | 1,83 (0,79 – 4,26) | *0,18** |
| Kas / eklem ağrısı | 126 (17,6) | 12 (20,3) | 114 (17,4) | 1,21 (0,62 – 2,36) | *0,57* |
| Boğaz ağrısı | 73 (10,2) | 6 (10,2) | 67 (10,2) | 1,00 (0,41 – 2,40 | *0,99* |
| Halsizlik | 184 (25,7) | 9 (15,3) | 175 (26,7) | 0,50 (0,24 – 1,03) | *0,055* |
| Burun akıntısı | 12 (1,7) | 2 (3,4) | 10 (1,5) | 2,27 (0,49 – 10,60) | *0,26** |
| Bulantı-kusma | 35 (4,9) | 5 (8,5) | 30 (4,6) | 1,93 (0,72 – 5,20) | *0,20** |
| İshal | 35 (4,9) | 5 (8,5) | 30 (4,6) | 1,93 (0,72 – 5,20) | *0,20** |
| Nefes darlığı | 306 (42,8) | 25 (42,4) | 281 (42,8) | 0,98 (0,57 – 1,68) | *0,95* |
| Tat alma bozukluğu | 33 (4,6) | 4 (6,8) | 29 (4,4) | 1,57 (0,53 – 4,64) | *0,34** |
| Koku alamama | 28 (3,9) | 5 (8,5) | 23 (3,5) | 2,55 (0,93 – 6,97) | *0,072** |
| İştahsızlık | 30 (4,2) | 2 (3,4) | 28 (4,3) | 0,79 (0,18 – 3,39) | *>0,99** |
| **Başvuru sırasında aldığı bağışıklık baskılayıcı ilaçlar** | | | | | |
| Sistemik steroid | 6 (0,9) | - | 6 (0,9) | - | *>0,99** |
| Antineoplastikler | 7 (1,0) | 2 (3,5) | 5 (0,8) | 4.70 (0,89 – 24,78) | *0,10** |

OR: Odds oranı, GA: Güven aralığı, ÇADA: Çeyrekler arası dağılım aralığı, ref.: referans
*Fischer'in kesin testi

misin alan hastaların istatistiksel anlamlı şekilde antibiyotiği daha çok ve antiviral tedavi olarak favipiravir alanların daha az aldığı görüldü (Tablo II ve III). Olası ikincil bakteriyel pnömonisi olan ve serviste takip edilen erişkin COVID-19 hastalarından 462'si (%64,6) antibiyotik alırken, 253'ü (%35,4) antibiyotik almamıştı. Antibiyotik alan grupta ortanca izlem süresi 6 (ÇADA=6), almayan grupta 7 (ÇADA=6), çalışma grubunun tamamında 7 (ÇADA=6) gündü.

Antibiyotik alan hastaların 33'ü (%7,1), almayan hastaların ise 26'sı (%10,3) yoğun bakıma nakledilmiş olup antibiyotik alanlarda almayanlara göre yoğun bakıma nakil rölatif riski 0,70'ti (%95 güven aralığı (GA) = 0,43 – 1,14) (Tablo III).

Olası ikincil bakteriyel pnömonisi olan ve serviste izlenen erişkin COVID-19 hastalarında antibiyotik kullanımının yoğun bakıma nakille ilişkisinin incelendiği ikili lojistik regresyon analizine dahil edilecek değişkenlerdeki kayıp veriler için herhangi bir veri türetilmedi ve kayıp veriler nedeniyle analiz 601 hasta üzerinden tamamlandı. Hosmer-Lemeshow testi p-değeri 0,44'tü. Antibiyotik kullanan hastalarda, kullanmayanlara göre yoğun bakıma nakil düzeltilmiş risk odds oranı 0,55 (% 95 GA = 0,29 – 1,01, *p=0,055*) olarak saptanmış olup gruplar arasındaki fark istatistiksel olarak anlamlı bu-

**Tablo II.** Hastaların başvuru sırasındaki muayene, laboratuvar ve radyolojik bulguları

| | Toplam (N=715) | Yoğun bakıma giden (N=59) n (%) | Yoğun bakıma gitmeyen (N=656) n (%) | OR (%95 GA) | *p-değeri* |
|---|---|---|---|---|---|
| **Başvurudaki vital bulgular** | | | | | |
| Vücut sıcaklığı (>37,8°C) | 237 (33,1) | 20 (33,9) | 217 (33,1) | 1,04 (0,59 – 1,82) | *0,90* |
| Nabız (>100/dk) | 27 (3,8) | 3 (5,1) | 24 (3,7) | 1,41 (0,41 – 4,83) | *0,58* |
| Yüksek kan basıncı (>140/90 mmHg) | 66 (10,5) | 5 (9,4) | 61 (10,6) | 0,88 (0,34 – 2,30) | *0,80* |
| Solunum sayısı (>30/dk) | 5 (0,8) | 2 (4,2) | 3 (0,5) | 8,03 (1,31 – 49,27) | *0,053** |
| Oksijen saturasyonu (<%90,0) | 145 (23,2) | 17 (32,1) | 128 (22,4) | 1,63 (0,89 – 3,01) | *0,11* |
| Ral | 94 (13,1) | 12 (20,5) | 82 (12,5) | 1,79 (0,91 – 3,51) | *0,088* |
| **Başvurudaki laboratuvar bulguları; Ortanca (ÇADA)** | | | | | |
| Lökosit (x1000/µL) | 715 | 7,65 (5,93) | 5,93 (3,54) | - | *<0,001* |
| Lenfosit lökosit (x1000/µL) | 715 | 0,88 (0,81) | 1,33 (0,90) | - | *<0,001* |
| Nötrofil lenfosit oranı | 715 | 6,18 (7,28) | 2,71 (2,53) | - | *<0,001* |
| C-reaktif protein (mg/dl) | 709 | 100,0 (97,0) | 14,0 (42,3) | - | *<0,001* |
| Prokalsitonin (ng/ml) | 715 | 0,11 (0,25) | 0,03 (0,04) | - | *<0,001* |
| Laktat dehidrogenaz (IU/ml) | 696 | 376,0 (95,0) | 227,0 (95,0) | - | *<0,001* |
| Fibrinojen (g/l) | 570 | 5,65 (2,35) | 3,80 (1,70) | - | *<0,001* |
| Ferritin (µg/l) | 661 | 448,0 (896,5) | 143,5 (246,5) | - | *<0,001* |
| d-dimer (mg/l) | 644 | 1,06 (1,31) | 0,50 (0,60) | - | *<0,001* |
| İnterlökin-6 (pg/ml) | 321 | 31,6 (44,6) | 13,5 (24,8) | - | *0,003* |
| Kan üre nitrojeni (mg/dl) | 643 | 46,0 (29,5) | 30,0 (12,0) | - | *<0,001* |
| Kreatinin (mg/dl) | 707 | 0,90 (0,42) | 0,80 (0,23) | - | *0,001* |
| Alanin transaminaz (IU/l) | 702 | 22,0 (30,0) | 29,0 (26,0) | - | *0,47* |
| Aspartat transaminaz (IU/l) | 705 | 35,0 (38,0) | 25,0 (21,0) | - | *<0,001* |
| Albumin (g/dl) | 686 | 38,0 (5,0) | 43,5 (6,0) | - | *<0,001* |
| Vitamin D2 (ng/ml) | 345 | 12,0 (7,0) | 14,0 (12,8) | - | *0,092* |
| **Radyolojik bulgular** | | | | | |
| Direkt grafi (infiltrasyon, opasite) | 447 (86,1) | 38 (86,4) | 409 (86,1) | 1,02 (0,42 – 2,51) | *0,96* |
| Toraks BT (konsolidasyon, infiltrasyon, hava bronkogramı, tomurcuklanmış ağaç, kaldırım taşı) | 476 (69,4) | 33 (55,9) | 443 (70,7) | 0,53 (0,31 – 0,91) | *0,019* |

OR: Odds oranı, GA: Güven aralığı, ÇADA: Çeyrekler arası dağılım aralığı, BT: Bilgisayarlı tomografi
* Fischer'in kesin testi

lunmadı (Tablo IV).

Çalışma grubunda antibiyotik verilen 462 hasta bulunmaktaydı. En sık sefalosporinler (%42,5), makrolidler (%19,2) ve piperasilin-tazobaktam (%8,5) kullanılırken en az trimetoprim-sulfametoksazol (%0,3) ve fosfomisin (0.3%) kullanılmıştı.

## Tartışma

Tek merkezden retrospektif kohort tipindeki bu araştırmanın sonuçlarına göre COVID-19 hastalığı nedeniyle serviste yatan olası ikincil bakteriyel pnömonisi olan hastaların yaklaşık üçte ikisinde antibiyotik kullanılmıştır. Belirlenen olası karıştırıcılar kontrol edildiğinde istatistiksel olarak anlamlı saptanmamakla birlikte antibiyotik kullanmayan hastalarda kullananlara göre yoğun bakıma nakil riski 1,8 kat olarak belirlenmiştir.

COVID-19 salgını başladıktan sonraki ilk dönemde COVID-19 hastalarında ventilatörle ilişkili pnömoni insidansı %10 - 13 gibi düşük olarak değerlendirilse de ilerleyen dönemde geniş ve karıştırıcı kontrolü yapılan çalışmalarda kümülatif insidans %44 – 86 arasında saptanmıştır (4). Hastanede yatmakta olan COVID-19 hastalarının dahil edildiği 118 çalışmanın meta-analizinde bakteriyel koinfeksiyonun %8, süperinfeksiyonun %20 görüldüğü bildirilmiştir. Yatarak tedavi edilen COVID-19 hastalarında ikincil bakteriyel pnömoni yaygın şekilde görülmektedir (9). Antibiyotikler klinik kötüleşmenin önüne geçilmesi ve ikincil bakteriyel infeksiyonun tedavisi için kullanılmaktadır (3). Bazı istisnalar hariç antibiyotiklerin tek başına viral infeksiyonların tedavisinde yeri bulunmamaktadır (10). Alt solunum yolu infeksiyonu ile seyreden viral infeksiyonlarda ikincil bakteriyel pnömoni gelişimi ve viral hastalığın progresyonu ile klinik kötüleşme görülebilmekte ve bu iki klinik durumu ayırabilmek kolay olmayabilmektedir. Bu çalışmada pnömoni kliniğinde kanıtlanmış

**Tablo III.** Hastalara yatış sırasında verilen tedavilerin ve klinik sonuçların dağılımı

| | Toplam (N=715) | Yoğun bakıma giden (N=59) n (%) | Yoğun bakıma gitmeyen (N=656) n (%) | OR (%95 GA) | *p-değeri* |
|---|---|---|---|---|---|
| Yatışta sistemik steroid | 92 (12,9) | 12 (20,3) | 80 (12,2) | 1,84 (0,94 – 3,61) | *0,074* |
| Antiviral amaçlı tedaviler | | | | | |
| Hidroksiklorokin | 486 (68,8) | 36 (61,0) | 450 (69,6) | 0,69 (0,40 – 1,19) | *0,18* |
| Azitromisin | 312 (44,2) | 23 (39,0) | 289 (44,7) | 0,79 (0,46 – 1,37) | *0,40* |
| Favipiravir | 321 (45,5) | 29 (49,2) | 292 (45,1) | 1,18 (0,69 – 2,00) | *0,55* |
| Antibiyotik kullanma | 462 (64,6) | 33 (55,9) | 429 (65,4) | 0,67 (0,39 – 1,15) | *0,15* |
| Ciddi COVID-19 varlığı | 147 (24,3) | 17 (34,0) | 130 (23,4) | 1,68 (0,91 – 3,12) | *0,095* |
| Klinik sonuç | | | | | |
| Ortanca hastanede kalma süresi (ÇADA), gün | 399 | 6,5 (6,25) | 7,0 (6,00) | - | *0,93* |
| Ölüm | 15 (2,1) | 12 (20,7) | 3 (0,5) | 56,70 (15,45 – 208,03) | *<0,001** |

OR: Odds oranı, GA: Güven aralığı, ÇADA: Çeyrekler arası dağılım aralığı,
*Fischer'in kesin testi

**Tablo IV.** Hastaların yoğun bakım ünitesine gidiş durumuyla antibiyotik kullanımı arasındaki ilişki için oluşturulan ikili lojistik regresyon modelinin sonuçları

| | Kaba OR | %95 GA | *p-değeri* | Düzeltilmiş OR | %95 GA | *p-değeri* |
|---|---|---|---|---|---|---|
| Antibiyotik kullanımı | 0,67 | 0,39 – 1,15 | *0,15* | 0,56 | 0,30 – 1,03 | *0,063* |
| Erkek cinsiyet | 0,80 | 0,47 – 1,36 | *0,41* | 0,76 | 0,42 – 1,39 | *0,37* |
| Yaş (yıl) | 1,01 | 0,99 – 1,03 | *0,23* | 1,00 | 0,98 – 1,02 | *0,88* |
| Komorbidite varlığı | 1,33 | 0,76 – 2,32 | *0,31* | 1,09 | 0,53 – 2,26 | *0,82* |
| Ciddi COVID-19 varlığı | 1,68 | 0,91 – 3,12 | *0,098* | 1,96 | 0,96 – 3,98 | *0,064* |
| Favipiravir kullanma | 1,18 | 0,69 – 2,00 | *0,55* | 0,74 | 0,34 – 1,62 | *0,45* |
| Azitromisin kullanma | 0,79 | 0,46 – 1,37 | *0,40* | 1,23 | 0,58 – 2,61 | *0,59* |
| Hidroksiklorokin kullanma | 0,69 | 0,40 – 1,19 | *0,18* | 0,58 | 0,25 – 1,33 | *0,20* |

OR: Odds oranı, GA: Güven aralığı
Hosmer-Lemeshow *p-değeri = 0,44*, Nagelkerke $R^2$=*0,035*
Analiz 601 hasta üzerinden tamamlanmıştır.

bir bakteriyel infeksiyon tanısı koymanın zor olması nedeniyle literatürde önerilen bir tanım üzerinden olası bakteriyel pnömonisi olan COVID-19 hastaları incelenmiştir.

Literatürde kesin tanılı COVID-19 hastalarında gereğinden daha çok hastada antibiyotik kullanıldığı bildirilmektedir ancak ihtiyacı olan hastaların ne kadarının antibiyotik aldığı bilinmemektedir (11). Bu çalışmada olası bakteriyel infeksiyonu olan hastaların neredeyse üçte birinde antibiyotik başlanmamış olduğu saptanmıştır. Bu durumun viral hastalık progresyonunun dışlanamamasına bağlı olduğu değerlendirilmektedir. Öte yandan olası bakteriyel pnömoni tanımının bu klinik durumu tanımlamak için altın standart olmadığı, yapılan tanımlamaya bağlı yalancı pozitif sonuçların olabileceği akılda tutulmalıdır.

Bu çalışmada olası ikincil bakteriyel pnömonisi olan ve serviste yatan erişkin COVID-19 hastalarında antibiyotik kullanmanın yoğun bakıma nakille istatistiksel olarak anlamlı bir ilişkisi olmadığı saptanmıştır. İstatistiksel bir anlamlılık saptanmamış olsa bile yoğun bakıma gidişten koruma eğilimi olduğu görülmektedir. Beklentinin aksine istatistiksel anlamlı bir ilişkinin bulunmaması tip 2 hataya bağlı olabileceği gibi verilen her antibiyotik tedavisinin uygun olmamasıyla ilgili olabileceği değerlendirilmektedir.

Uygun bir antibiyotik tedavisinin verildiğini iddia edebilmek için uygun antibiyotiğin, uygun yoldan, uygun dozdan, uygun dozlama aralığıyla ve uygun süreyle verilme bilgilerine sahip olmak gerekmektedir (12). Uygun antibiyotik seçiminde etken bakterilerin antimikrobiyal direnç testi sonuçları önemli iken bakteriyel pnömoni varlığında bakterilerin direnç profili belirlenmesi bir tarafa etkenin tanımlanması bile mümkün olamamaktadır. Konuyla ilgili en güvenilir kanıtlara geriye dönük olarak otopsi çalışmalarından ulaşılabilmektedir. Ancak yaşayan hastalarda ve geniş hasta gruplarında yapılan çalışmalarda bakteriyel pnömoni konusunda kuvvetli kanıtlarla tanı konulması mümkün olamamaktadır (13). COVID-19 pandemisi döneminde teknik dezavantajların yanı sıra laboratuvar kapasitesinin çok sayıda SARS-CoV-2 PCR testi yapılması nedeniyle kısıtlanması, klinik örnek alınması ve takibi konusundaki zorluklar da eklenmiştir.

Bu çalışmada yatarak takip edilen olası ikincil bakteriyel

pnömonisi olan COVID-19 hastalarına en sık sefalosporinler verilmiştir. Bunu sırasıyla makrolidler, piperasilin-tazobaktam ve karbapenemler izlemiştir. Literatürde ikincil bakteriyel pnömoni etkeni olarak en sık raporlanan etkenler *Streptococcus pneumoniae, Staphylococcus aureus, Heamophilus influenzae, Legionella pneumophila, Mycoplasma pneumoniae, Chlamydophila pneumoniae*'dır (3) . Orta Asya ve Avrupa Antimikrobiyal Direnç Sürveyansı (CAESAR) 2020 raporunda kan ve beyin omurilik sıvısından izole edilen *Streptococcus pneumoniae* içinde makrolid direnci %37, sefotaksim/seftriakson direnci %8'dir. Penisiline azalmış duyarlılık %51 görülmektedir. *Esherichia coli* ve *Klebsiella pneumoniae*'da 3. kuşak sefalosporin direnci sırasıyla %50 ile %70, kinolon direnci %50 ile %65 ve karbapenem direnci *K. pneumoniae*'da %40 seviyesindedir (14). Sürveyans kapsamında incelenen etkenlerin direnç profili birebir çalışma grubuyla karşılaştırılabilir olmamakla birlikte örneğin *S. Pneumoniae*'larda görülen yüksek makrolid direnci ve azalmış penisilin duyarlılığı dikkati çekmektedir. *Acinetobacter spp., Pseudomonas spp*. ve Enterobacterales gibi Gram negatif etkenlerdeki antibiyotik direncinin daha yüksek bir düzeyde görülmesi seçilen ampirik antibiyotiklerin yetersiz kalabileceği konusunda endişeye neden olmaktadır. Ampirik olarak seçilen antibiyotiklerin etken bakterilere etkisiz kalması nedeniyle antibiyotik tedavisi kullanmanın yoğun bakıma gidişle ilişkisinin saptanamamış olabileceği değerlendirilmektedir. Antibiyotik direncinin böylesine yaygın olduğu bir durumda başlanan ampirik antibiyotik tedavilerin ön kabullerin aksine ne kadar yararlı olduğunun değerlendirilmesi gerekmektedir.

Yirmi üç ülkeden 166 hekimin katıldığı bir çalışmada Türkiye'den cevap veren 46 hekim serviste yatan COVID-19'lu hastalarda en sık seftriakson/sefotaksim ve makrolid kombinasyonunun (%32,6) kullanıldığını, bunu florokinolonların (%30,4) izlediğini belirtmiştir (15). Bu çalışmada da sefalosporinlerin ve makrolidlerin benzer şekilde sıklıkla kullanıldığı görülmüş ancak florokinolonların daha az tercih edildiği belirlenmiştir.

Bu çalışmaya dahil edilen hastalar arasında ileri yaşa sahip, sigara içme deneyimi, herhangi bir komorbiditesi, öksürük, balgam, dispnesi olan, ateş, yüksek kan basıncı, düşük oksijen saturasyonu ve ral saptanan hastalara antibiyotik daha çok verilirken, baş, kas ve eklem ağrısı, halsizlik, tat ve koku alma bozukluğu hastalara daha az verilmiştir. Baş, kas ve eklem ağrısı, tat ve koku alma bozukluğunun viral infeksiyonlarla daha uyumlu olduğu bilinmektedir (16). Antibiyotik tedavisinin viral infeksiyon tablosuyla uyumlu durumlarda daha az kullanılması beklenen bir durumdur. Klinik seyirde ikincil bakteriyel infeksiyonla uyumlu belirti ve bulgular yakın şekilde izlenmelidir.

Bu araştırmanın verileri çoğunlukla elektronik kayıt sistemi üzerinden elde edildiği için hafıza faktöründen etkilenmenin az olduğu değerlendirilmektedir. Bilinebildiği kadarıyla COVID-19 ile takipli olası ikincil bakteriyel pnömonisi olan hastalarda yoğun bakıma gidişin değerlendirildiği bir araştırma bulunmamaktadır.

Geriye dönük elektronik kayıt üzerinden veri toplanması nedeniyle kayıp veriler bulunmaktadır. Hastaneden taburculuk sonrası izlem olmadığı için yalnızca hastanede yatış süresince olan etki değerlendirilebilmektedir. Sonraki araştırmalarda ülke elektronik kayıtlarından faydalanarak erken dönem yoğun bakım ihtiyacının değerlendirilmesi önerilmektedir. Araştırmanın gücünü arttırmak için grupların büyüklüğünün eşit olması halinde en az 1255 antibiyotik alan, 1255 antibiyotik almayan olmak üzere 2510 örneğe erişilmesi hedeflenmelidir.

## Sonuç

İkincil bakteriyel pnömonisi olan serviste takipli hastalara antibiyotik tedavisi verilmesi hastaların yoğun bakıma gidişini istatistiksel olarak anlamlı şekilde azaltmasa bile yukarıda sunulan gerekçelerle var olan ilişkinin bulunamamış olabileceği düşünülmektedir. Ancak hem standardizasyonun sağlanması hem de klinik kararı desteklemek üzere bakteriyel pnömoni tanısının daha doğru şekilde konulabileceği araçlara ihtiyaç olduğu görülmektedir. Mevcut antimikrobiyal direnç profili koşullarında etken mikroorganizmaların izolasyonunun ve direnç profilinin belirlenmesinin uygun antimikrobiyal seçiminde giderek vazgeçilmez bir hal aldığı düşünülmektedir. Antimikrobiyal kullanımının optimize edildiğinin garanti edilemediği durumlarda ampirik olarak başlanan ve uygun kullanımı garanti edilemeyen antimikrobiyal kullanımının tek başına olumsuz klinik sonuçları önlenmede yeterli olamayabileceği akılda tutulmalıdır.

Araştırmanın bulguları 13-16 Mart 2023 tarihleri arasında Antalya'da düzenlenen 23. Uluslararası Türk Klinik Mikrobiyoloji ve İnfeksiyon Hastalıkları Kongresi'nde (KLİMİK 2023) sözlü bildiri olarak sunulmuştur (SS-18).

## Kaynaklar


1. https://www.who.int/europe/emergencies/situations/covid-19. (Erişim tarihi 14 Ocak 2023).
2. Gallo Marin B, Aghagoli G, Lavine K, et al. Predictors of COVID-19 severity: A literature review. Rev Med Virol 2021;31(1):1-10.
3. Mirzaei R, Goodarzi P, Asadi M, et al. Bacterial co-infections with SARS-CoV-2. IUBMB Life 2020;72(10):2097-2111.
4. Povoa P, Martin-Loeches I, Nseir S. Secondary pneumonias in critically ill patients with COVID-19: risk factors and outcomes. Curr Opin Crit Care 2021;27(5):468-473.
5. Boulos M, Bassal T, Layyous A, Basheer M, Assy N. Inflammation in COVID-19: A Risk for Superinfections. COVID. 2022;2(11):1609-1624.
6. Liu C, Wen Y, Wan W, Lei J, Jiang X. Clinical characteristics and antibiotics treatment in suspected bacterial infection patients with COVID-19. Int Immunopharmacol 2021;90:107157.
7. https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2 (Erişim tarihi: 16 Ocak 2023).
8. https://www.openepi.com/Power/PowerCohort.htm.(Erişim tarihi: 16 Ocak 2023)
9. Musuuza JS, Watson L, Parmasad V, Putman-Buehler N, Christensen L, Safdar N. Prevalence and outcomes of co-infection and superinfection with SARS-CoV-2 and other pathogens: A systematic review and meta-analysis. PLoS One 2021;16(5):e0251170.
10. Ofori-Asenso R, Agyeman AA. Irrational Use of Medicines-A Summary of Key Concepts. Pharmacy (Basel) 2016;28:4.

11. Ghosh S, Bornman C, Zafer MM. Antimicrobial Resistance Threats in the emerging COVID-19 pandemic: Where do we stand? J Infect Public Health 2021;14(5):555-560.

12. https://apps.who.int/irisbitstream/10665/66860/1/WHO_CDS_CSR DRS_2001.2.pdf (Erişim tarihi 16 Ocak 2023).

13. MacIntyre CR, Chughtai AA, Barnes M, et al. The role of pneumonia and secondary bacterial infection in fatal and serious outcomes of pandemic influenza a(H1N1)pdm09. BMC Infect Dis 2018;18(1):637.

14. https://www.who.int/europe/groups/central-asian-and-european-surveillance-of-antimicrobial-resistance-(caesar) (Erişim tarihi: 16 Ocak 2023).

15. Beovic B, Dousak M, Ferreira-Coimbra J, et al. Antibiotic use in patients with COVID-19: a 'snapshot' Infectious Diseases International Research Initiative (ID-IRI) survey. J Antimicrob Chemother 2020;75(11):3386-390.

16. https://www.cebm.net/covid-19/differentiating-viral-from-bacterial-pneumonia. (Erişim tarihi: 16 Ocak 2023).

# Does Systemic Immun Inflammation Index Predict Survival in Diffuse Large B Cell Lymphoma Patients?

**Merih Reis Aras[1], Hacer Berna Afacan Ozturk[1], Fatma Yilmaz[1], Ahmet Kursad Gunes[1], Umit Yavuz Malkan[2], Murat Albayrak[1]**

[1]Ankara Etlik City Hospital, Departmant of Hematology, Ankara, Türkiye
[2]Hacettepe University, Faculty of Medicine, Department of Hematology, Ankara, Türkiye

**Address for Correspondence:** Ankara Etlik City Hospital, Department of Hematology, Ankara, Türkiye
Email: merihreis@gmail.com

**Orcid ID:** MRA: 0000-0002-9161-5582 FY: 0000-0001-6112-3950 UYM: 0000-0001-5444-4895
HBAO: 0000-0001-9386-7604 AKG: 0000-0001-5522-8342 MA: 0000-0003-4025-741x

**Cite As:** Aras Reis M, Afacan Ozturk HB, Yilmaz F, et al. Does Systemic Immun Inflammation Index Predict Survival in Diffuse Large B Cell Lymphoma Patients? Hitit Med J 2023;5(3):170-174. https://doi.org/ 10.52827/hititmedj.1301431

## Abstract

**Objective:** The systemic immune inflammation index has been considered a novel prognostic biomarker in several malignant tumors. The aim of the current study was to determine the association between the systemic immune inflammation index and prognosis of patients with Diffuse Large B Cell Lymphoma.

**Material and Method:** The study included 101 patients diagnosed diffuse large B cell lymphoma. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off value of the systemic immune inflammation index for predicting survival.

**Results:** The results of ROC curve analysis showed a cut-off value for the systemic immune inflammation index of 500. No statistically significant difference was determined between the groups with systemic immune inflammation index ≤ 500 and >500 groups in respect of overall-survival and progression-free survival. The mortality risk was determined to be significantly higher in patients with systemic immune inflammation index ≤ 500 (*p:0.017*). There was no significant relationship between the systemic immune inflammation index values and lactat dehydrogenase, age, R-IPI risk groups,ECOG performance status, and disease stage.

**Conclusion:** The results of this study demonstrated that there is no association between the systemic immune inflammation index and survival in patients with diffuse large B cell lymphoma. Larger prospective studies are needed to investigate the association between the systemic immune inflammation index and Diffuse Large B Cell Lymphoma.

**Keywords:** Diffuse large B cell lymphoma, Lymphocyte, Neutrophil, Platelet, Survival, Systemic immune inflammation index

## Özet

**Amaç:** Sistemik immün inflamasyon indeksi, birçok malign tümörde kullanılan yeni bir prognostik biyobelirteçtir. Bu çalışmanın amacı, Diffüz Büyük B Hücreli Lenfoma hastalarında sistemik immün inflamasyon indeksi ile prognoz arasındaki ilişkiyi belirlemektir.

**Gereç ve Yöntem:** Çalışmaya Diffüz Büyük B Hücreli Lenfoma tanılı 101 hasta dahil edildi. Sağkalımı öngören optimum sistemik immün inflamasyon indeksi kesme değerini saptamak için receiver operating charecteristic curve analizi kullanıldı.

**Bulgular:** Receiver operating charecteristic curve analizi ile sistemik immün inflamasyon indeksi kesme değeri 500 saptandı. Sistemik immün inflamasyon indeksi ≤ 500 ve sistemik immün inflamasyon indeksi >500 grupları arasında progresyonsuz sağkalım ve genel sağkalım açısından istatistiksel olarak anlamlı fark yoktu. Ancak sistemik immün inflamasyon indeksi ≤ 500 olan hastalarda mortalite riski anlamlı olarak yüksekti (p:0,017). Sistemik immün inflamasyon indeksi ile laktat dehidrogenaz, yaş, R-IPI risk grupları, ECOG performans durumu ve hastalık evresi arasında anlamlı bir ilişki yoktu.

**Sonuç:** Çalışmamızın sonuçları, Diffüz Büyük B Hücreli Lenfoma hastalarında sistemik immün inflamasyon indeksi ile sağkalım arasında bir ilişki olmadığını göstermiştir. Sistemik immün inflamasyon indeksi ve DBBHL arasındaki ilişkiyi araştırmak için daha büyük prospektif çalışmalara ihtiyaç vardır.

**Anahtar Sözcükler:** Diffüz büyük B hücreli lenfoma, Lenfosit, Nötrofil, Platelet, Sağkalım, Sistemik immün inflamasyon indeksi

**Date of Submission:** 23.05.2023
**Date of Acceptance:** 10.08.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** Approval for the study was granted by the Clinical Research Ethics Committee (Approval number: 2023/138, date: 03/05/2023).
**Plagiarism Checks:** Yes - iThenticate
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: MRA, AKG, YF Design: MRA, MA, FY Data Collection/Data Processing: MRA, HBAO Data Analysis: UYM, MA Article Preparation: MRA
**Informed Consent:** Consents were obtained from the patients.
**Financial Disclosure:** No financial support has been received.

## Introduction

Diffuse large B cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma. It develops as a result of the combined effects of immunosuppression, immune stimulation, and genetic predisposition. Although 75-80% of patients achieve complete remission after first line treatment. Approximately 40% of all patients relapse (1).

Therefore, it is very important to stratify the prognosis of patients at the time of diagnosis, and to individualize the treatment according to this prognostic stratification. A more intensive or longer period of chemotherapy may be required for patients with poor prognosis (2).

Inflammation has an important role in tumor progression and treatment response. Peripheral blood count values are closely associated with the progression of malignancy and reflect the inflammation status to some degree. Previous studies have shown that inflammatory markers such as pretreatment neutrophil-lymphocyte ratio (NLR), and platelet-lymphocyte ratio (PLR) affect the outcomes of DLBCL patients. Blood biomarkers are also easier and cheaper to obtain than molecular biomarkers (3).

The systemic immune inflammation index (SII) is calculated from lymphocyte, platelet and neutrophil counts, and is a relatively new inflammatory index, which reflects the inflammatory status and correlates with circulating tumor cells. Platelets have important roles in angiogenesis, tumor cell immuneinvasion, and extravasation to other organs. There is growing evidence of the importance of SII in solid tumors. A high SII value has been associated with poor outcomes in renal cell carcinoma, hepatocellular carcinoma, small cell lung cancer, and gastrointestinal cancer, but there are limited data on SII in hematopoietic tumors (2).

The aim of this study was to evaluate the association between the systemic immune inflammation index (SII) and the prognosis of patients with DLBCL.

## Material and Method

A retrospective analysis was made of the data of patients with DLBCL diagnosed in a-tertiary-level hospital between January 2012 and September 2022. Patients treated with R-miniCHOP and R-CHOP regimens were included in the study. Patients were excluded from the study if they were aged <18 years,were pregnant, had primary central nervous system lymphoma, acquired immunodeficiency syndrome related lymphoma,HIV positivity,another concominant malignancy,heart failure,chronic kidney disease,hepatic cirrhosis,-Richter's transformation, a history of solid organ malignancy, or who were treated with a regimen other than R-CHOP or R-miniCHOP. Age,gender,disease stage,ECOG performance status,IPI score,beta-2-microglobulin,serum lactate dehydrogenase (LDH), neutrophil, platelet, and lymphocyte values were recorded at the time of diagnosis. The SII values were calculated from the laboratory values of serum neutrophil,platelet and lymphocyte counts.

Disease staging was made according to the Ann-Arbor classification Cotswold modification. The treatment regimen, treatment response and follow-up duration were recorded for all patients. Overall survival (OS) was defined as the time from diagnosis to death from any cause, and progression free survival (PFS) was defined as the time from diagnosis to progression or death.

Ethical approval and informed consent

All the study procedures complied with the principles of the Helsinki Declaration. Approval for the study was granted by the Clinical Research Ethics Committee (Approval number: 2023/138, date: 03/05/2023). Written informed consent was obtained from each patient.

## Statistical Analysis

The study data were analyzed using SPSS 21 software. Descriptive data were stated as number and percentage. Descriptive statistics and frequency tables were used. Receiver operating characteristic (ROC) curve analysis was used to identify a cut-off value for SII. The numerical variables were analyzed in terms of this cut-off value using the Student's t-test. The relationship between the SII cut-off value and categorical variables was analyzed with the Chi-square test.

The effect of the variables on survival was examined using logistic regression analysis. A value of $p<0.05$ was considered statistically significant.

## Results

The study population of 101 patients comprised, 45 (44.6%) males and 56 (55.4%) females, with a median age of 64 years (min 20-max 86 years). When the patients were analysed by age, 34 (33.7%) patients were ≤60 years old and 67 (66.3%) were older than 60 years. At the time of diagnosis, 45 (44.6%) patients had stage I-II disease, and 56 (55.4%) had stage III-IV disease. The patients were classified according to R-IPI score as very good, good, and poor-risk groups. According to the R-IPI scores, 10 (9.9%) patients were in the very good risk group, 42 (41.6%) were in the good risk group, and 49 (48.5%) were in the poor risk group. The clinical and demographic features of the patients at the time of diagnosis are given in Table I and the laboratory findings at the time of diagnosis are shown in Table II.

In ROC analysis, the cut-off value for the SII was calcula-

**Table I.** The clinical and demographic features of the patients at the time of diagnosis

| Characteristics | | n (%) |
|---|---|---|
| **Gender** | Female | 56 (55.4) |
| | Male | 45 (44.6) |
| **Age (years)** | ≤ 60 | 34 (33.7) |
| | > 60 | 67 (66.3) |
| **Ann-Arbor Stage** | 1-2 | 45 (44.6) |
| | 3-4 | 56 (55.4) |
| **ECOG PS** | 0-2 | 91 (90.1) |
| | 3-4 | 10 (9.9) |
| **LDH** | N | 39 (38.6) |
| | >N | 62 (61.4) |
| **R-IPI** | Very good (0) | 10 (9.9) |
| | Good (1-2) | 42 (41.6) |
| | Poor (3-5) | 49 (48.5) |

**ECOG PS:** Eastern Cooperative Oncology Group Performance Status
**LDH:** Lactat dehydrogenase, **R-IPI:** Revised International Prognostic Index

**Table II.** Laboratory findings of the patient at the time of diagnosis

| | Median | Min-Max |
|---|---|---|
| **White blood cell count** (x10$^6$/L) | 8493 | 1800-20550 |
| **Lymphocyte count** (x10$^6$/L) | 1574 | 300-4470 |
| **Hemoglobin** (gr/dl) | 11.9 | 6.8-16.2 |
| **Platelet count** (x10$^6$/L) | 284276 | 10000-1089000 |
| **SII** | 1373 | 38-7687 |

**SII:** Systemic Immune Inflammation Index

ted as 500 (Figure I). The patients were then separated into two groups according to the SII cut-off value. There was no significant relationship between the SII cut-off value and LDH, age, R-IPI risk groups, ECOG performance status, and disease stage. Comparisons of the parameters between the groups according to the SII cut-off value are given in Table III.

Mean OS was 33.82 months in the SII ≤ 500 group and

**Figure I.** ROC analysis acoording to the SII cut-off value

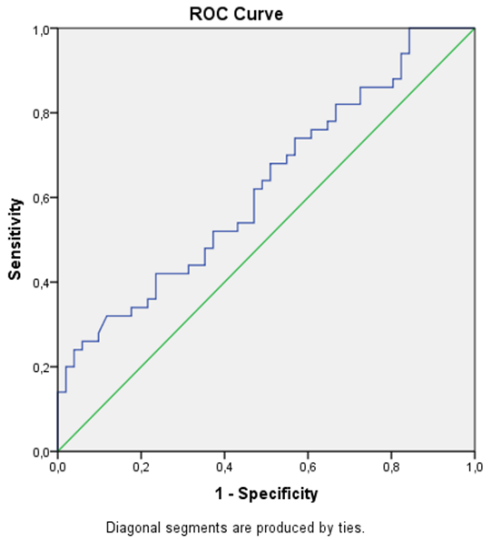



**Table III.** Comparison of parameters between the groups according to SII

| | | SII cut-off value | | | | Chi-square | *p* |
|---|---|---|---|---|---|---|---|
| | | ≤500 | | >500 | | | |
| | | n | % | n | % | | |
| **Age (years)** | ≤60 | 6 | 17.6 | 28 | 82.4 | 0.214 | *.644* |
| | >60 | 16 | 23.9 | 51 | 76.1 | | |
| **LDH** | N | 6 | 15.4 | 33 | 84.6 | 0.976 | *.323* |
| | >N | 16 | 25.8 | 46 | 74.2 | | |
| **ECOG** | 0-2 | 20 | 22.0 | 71 | 78.0 | .021 | *.886* |
| | 3-4 | 2 | 20.0 | 8 | 80.0 | | |
| **Stage** | 1-2 | 7 | 15.6 | 38 | 84.4 | 1.247 | *.264* |
| | 3-4 | 15 | 26.8 | 41 | 73.2 | | |
| **R-IPI** | very good | 0 | 0.00 | 10 | 100 | 3.097 | *.213* |
| | good | 10 | 23.8 | 32 | 76.2 | | |
| | poor | 12 | 24.5 | 37 | 75.5 | | |

SII: Systemic Immune Inflammation Index
LDH: Lactat dehydrogenase
R-IPI: Revised International Prognostic Index (very good:0, good: 1-2, poor:3-5)
ECOG: Eastern Cooperative Oncology Group

45.66 months in the SII> 500 group, with no significant difference determined between groups (*p<0.221*). The mean PFS was 21.41 months in the SII ≤ 500 group and 31.15 months in the SII> 500 group, with no significant difference determined between groups (*p<0.225*). The comprasion of overall survival and progression free survival according to the SII values are presented in Table IV.

The results of the univariate and multivariate logistic regression analyses for survival are given in Table V.

**Table IV.** Comprasion of progression free survival (PFS) and overall survival (OS) according to SII

| | SII cut-off value | | | | t | *p* |
|---|---|---|---|---|---|---|
| | ≤ 500 | | > 500 | | | |
| | Mean | SD | Mean | SD | | |
| OS (months) | 33.82 | 39.31 | 45.66 | 40.01 | -1.232 | *.221* |
| PFS (months) | 21.41 | 33.94 | 31.15 | 32.90 | -1.220 | *.225* |

SII: Systemic Immune Inflammation Index
OS: Overall survival, PFS: progression free survival
SD: Standart deviation

The univariate logistic regression analysis was performed to identify the risk factors for poor survival. Revised-IPI poor risk group,elevated LDH,age>60 years,SII ≤ 500, and stage 3-4 disease were determined to be risk factors for poor survival. The risk of mortatilty was 9.067 fold higher in the R-IPI poor risk group than in the very good risk group. Patients with an elevated LDH value were seen to be at a 4.316 fold higher risk of mortality than those with a normal LDH value. In patients older than 60 years, the mortality risk was 2.402 fold higher than for those ≤60 years. In the low SII group, the risk of mortality was 3.551 fold higher than for those in the high SII group

In the multivariate logistic regression analysis there was any significant risk factors for survival.

**Table V.** Univariate and multivariate logistic regression analysis results for survival

| | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | Odds ratio | 95 % CI | *p* | Odds ratio | 95 % CI | *p* |
| R-IPI (good) | 2.000 | 0.374_10.700 | *.418* | 1.912 | 0.151_24.139 | *.616* |
| R-IPI (poor) | 9.067 | 1.716_47.891 | *.009** | 2.117 | 0.136_33.004 | *.593* |
| LDH (>N) | 4.316 | 1.813_10.273 | *.001** | 1.694 | 0.512_5.599 | *.388* |
| SII ≤ 500 | 3,529 | 1.249_9.981 | *.017** | 3.551 | 0.815_15.470 | *.092* |
| Age (≥60) | 2.402 | 1.023_5.640 | *.044** | 1.015 | 0.240_4.287 | *.984* |
| Stage (3-4) | 2.801 | 1.243_6.312 | *.013** | 1.126 | 0.321_3.950 | *.853* |

CI: Confidence Interval, SII: Systemic Immune Inflammation Index
LDH: Lactat dehydrogenase
R-IPI: Revised International Prognostic Index (very good:0, good: 1-2, poor:3-5)

## Discussion

The host immune response and inflammatory response are closely related to cancer occurrence, progression and disease biology (4). An association between inflammation and cancer was hypothesized by Virchow in 1863 from the obervation of the presence of leukocytes in neoplastic tissues (5,6). Several prognostic parameters have been used for non-Hodgkin lymphomas, of which the International Prognostic Score (IPI) is the most commonly used (7). The hosts inflammatory response and the clinicopathological characteristics of the tumor are associated with prognosis, although, IPI does not reflects the inflammatory response (8).

Neutrophils and lymphocytes are crucial components of

the immune system. Reactive oxygen species (ROS) and nitric oxide (NO) released by neutrophils can lead to T-cell activation disorders. ROS and NO increases the incidence of tumor dissemination by downregulation of peripheral lymphocytes (9).

The first inflammatory marker from leukocyte subsets, the neutrophil-lymphocyte ratio (NLR) was first defined by Zahorec et al. (10) in oncological intensive care unit patients. Numerous studies have investigated NLR as an inflammatory and prognostic marker in malignant and benign disorders (11). Platelets play an important pro-inflammatory role, and platelet-lymphocyte ratio (PLR) was the second defined cellular immun inflammatory marker obtained from leukocyte subsets (11,12). The PLR has been shown to be an inflammatory and prognostic marker in malignant and benign disorders, similar to NLR (11).

SII was defined as the third cellular immune inflammation marker by Hu et al. Both NLR and PLR are calculated as ratios of two different blood count parameters, whereas the SII is calculated from three blood parameters (11,13). The SII is a relatively new inflammatory index that has been shown to be correlated with circulating tumor cells (2,14). Based on lymphocyte, neutrophil and platelet counts,the SII is calculated using the formula of neutrophil count × platelet count/lymphocyte count (15,16).

In a meta-analysis of 7657 cancer patients, a higher SII was reported to be correlated with poor disease free survival(DFS),poor PFS, and poor OS. In that meta-analysis, a SII value over the cut-off value was shown to predict poor OS in gastric carcinoma, esophageal squamous cell carcinoma, hepatocellular carcinoma, urinary system cancer,and small cell, and non-small cell lung cancer (15). In another meta-analysis to evaluate the prognostic role of SII in solid tumors, high SII was associated with worse OS in hepatocellulary carcinoma, urinary cancers, small cell lung lung cancer, gastrointestinal tract cancers, and acral melanoma (17). Yang et al. (18) evaluated the prognostic value of blood-based biomarkers in 28 patients with testicular DLBCL, and determined a SII cut-off value of 428. No significant associations was observed between SII and OS or PFS. However, SII was found to be significantly associated with the risk of disease progression. Similar to that study , there was no significant association between SII and OS or PFS in the current study. Only the risk of mortality was higher in the low SII group than in the high SII group Wu et al. (1) aimed to determine associations between DLBCL and SII, the lymphocytes to monocytes (LMR) ratio, the LMR to LDH (LMR/LDH) ratio, and prognosis. A total of 68 patients diagnosed with DLBCL were included in that study. The SII of patients with an Ann Arbor stage of III–IV and ECOG score of ≥ 2 was found to be significantly higher than that of patients with an Ann Arbor stage of I–II and ECOG score of < 2 ($p < 0.05$). Patients with a low SII had better PFS than those with a high SII ($p < 0.05$) .

In the current study, stage 3-4 disease, elevated LDH, R-IPI poor risk group,and age>60 years were found to be poor prognostic factors.

R-IPI and ECOG performance status are known prognostic factors for DLBCL. In this study 90.1% of the patients were in the ECOG 0-2 group and 51.2 % in R-IPI were in the very good and good risk group. This could explain why the results of this study differ from previous reports in the literature. Serum soluble interleukin-2 receptor and serum-soluble tumor necrosis factor receptor 2 levels have been used for DLBCL prognosis together with the IPI score in recent studies (19,20). The combination of serum soluble interleukin-2 receptor and serum-soluble tumor necrosis factor receptor 2 levels with the IPI score can be compared with SII in further studies.

The results of the current study are not consistent with the literature. There seen to be better survival rates in the high SII group, which was in contrast with the findings of other studies. There were some limitations to this study, primarily the retrospective, single-centre design, and small number of patients.There is a need for larger prospective studies to further investigate the association between SII and DLBCL.

## Conclusion

In conclusion,the results of this study demonstrated that elevated LDH, R-IPI poor risk group, age>60 years, and stage 3-4 disease were poor prognostic factors in patients with DLBCL. No significant relationship was determined between SII and OS or PFS. Blood cell counts are low cost parameters. There may be also other prognostic parameters that can be determined from the avaliable blood cell counts.

## References

1. Wu X-B, Hou S-L, Liu H. Systemic immune inflammation index, ratio of lymphocytes to monocytes, lactate dehydrogenase and prognosis of diffuse large B-cell lymphoma patients. World Journal of Clinical Cases 2021;9(32):9825.
2. Liu T, Ye F, Li Y, Liu A. Comparison and exploration of the prognostic value of the advanced lung cancer inflammation index, prognostic nutritional index, and systemic immune-inflammation index in newly diagnosed diffuse large B-cell lymphoma. Annals of Palliative Medicine 2021;10(9):9650-9659.
3. Wang Z, Zhang J, Luo S, Zhao X. Prognostic significance of systemic immune-inflammation index in patients with diffuse large B-cell lymphoma. Frontiers in Oncology 2021;11:655259.
4. Gupta T, Nayak P, Baviskar Y, et al. Systemic inflammatory biomarkers in primary central nervous system lymphoma versus high-grade glioma: exploratory, comparative and correlative analysis. CNS oncology 2022;11(02):CNS83.
5. Huang H, Liu Q, Zhu L, et al. Prognostic value of preoperative systemic immune-inflammation index in patients with cervical cancer. Scientific reports 2019;9(1):1-9.
6. Fest J, Ruiter R, Mulder M, et al. The systemic immune-inflammation index is associated with an increased risk of incident cancer—A population-based cohort study. International Journal of Cancer 2020;146(3):692-698.
7. Raffetti E, Donato F, Castelnuovo F, et al. The prognostic role of systemic inflammatory markers on HIV-infected patients with non-Hodgkin lymphoma, a multicenter cohort study. Journal of translational medicine 2015;13:1-8.
8. Wu J, Zhu H, Zhang Q, et al. Nomogram based on the systemic immune-inflammation index for predicting the prognosis of diffuse large B-Cell lymphoma. Asia-Pacific Journal of Clinical Oncology 2022.
9. Schietroma M, Romano L, Schiavi D, et al. Systemic inflammation response index (SIRI) as predictor of anastomotic leakage after total gastrectomy for gastric cancer. Surgical

Oncology 2022;43:101791.

10. Zahorec R. Ratio of neutrophil to lymphocyte counts-rapid and simple parameter of systemic inflammation and stress in critically ill. Bratislavske lekarske listy 2001;102(1):5-14.

11. Walzik D, Joisten N, Zacher J, Zimmer P. Transferring clinically established immune inflammation markers into exercise physiology: focus on neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and systemic immune-inflammation index. European Journal of Applied Physiology 2021;121(7):1803-1814.

12. Zarbock A, Polanowska-Grabowska RK, Ley K. Platelet-neutrophil-interactions: linking hemostasis and inflammation. Blood reviews 2007;21(2):99-111.

13. Hu B, Yang X-R, Xu Y, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. Clinical Cancer Research 2014;20(23):6212-6222.

14. Yan M, Jurasz P. The role of platelets in the tumor microenvironment: from solid tumors to leukemia. Biochimica et Biophysica Acta (BBA)-Molecular Cell Research 2016;1863(3):392-400.

15. Yang R, Chang Q, Meng X, Gao N, Wang W. Prognostic value of systemic immune-inflammation index in cancer: a meta-analysis. Journal of Cancer 2018;9(18):3295.

16. Li S, Xia Z, Cao J, et al. Proposed new prognostic model using the systemic immune-inflammation index for primary central nervous system lymphoma: A prospective-retrospective multicohort analysis. Frontiers in Immunology 2022;13.

17. Zhong J-H, Huang D-H, Chen Z-Y. Prognostic role of systemic immune-inflammation index in solid tumors: a systematic review and meta-analysis. Oncotarget 2017;8(43):75381.

18. Yang J, Guo X, Hao J, Dong Y, Zhang T, Ma X. The prognostic value of blood-based biomarkers in patients with testicular diffuse large B-cell lymphoma. Frontiers in Oncology 2019;9:1392.

19. Goto H, Tsurumi H, Takemura M, et al. Serum-soluble interleukin-2 receptor (sIL-2R) level determines clinical outcome in patients with aggressive non-Hodgkin's lymphoma: in combination with the International Prognostic Index. Journal of cancer research and clinical oncology 2005;131:73-79.

20. Goto N, Tsurumi H, Takemura M, et al. Serum-soluble tumor necrosis factor receptor 2 (sTNF-R2) level determines clinical outcome in patients with aggressive non-Hodgkin's lymphoma. European journal of haematology 2006;77(3):217-225.

# Can the Neutrophil-to-Platelet Ratio Be Used to Predict Postoperative Mortality in Geriatric Patients with Hip Fractures?

**Tugcehan Sezer Akman[1], Hatice Kusderci[2], Lokman Kehribar[3], Bahattin Cagdas Akman[4], Ahmet Sen[5]**

[1]Anesthesiology and Reanimation, Alaca State Hospital, Alaca, Corum,Türkiye
[2]Department of Anesthesiology and Reanimation, University of Samsun, Samsun, Türkiye
[3]Department of Orthopedics and Traumatology, University of Samsun, Samsun, Türkiye
[4]Orthopedics and Traumatology, Alaca State Hospital, Alaca, Corum, Türkiye
[5]Department of Anesthesiology and Reanimation, Trabzon Kanuni Training and Research Hospital, Trabzon, Türkiye

**Address for Correspondence:** Anesthesiology and Reanimation, Alaca State Hospital, Yıldızhan Neighbourhood Cengiztopel Street, No: 124 Alaca- Corum- Türkiye
Email: tgchnszr@gmail.com

**Orcid ID:** TSA: 0000-0003-4135-840 LK: 0000-0001-9799-8839 AS: 0000-0001-8981-6871
HK: 000-0002-3963-3265 BCA: 0000-0002-1439-9863

**Cite As:** Akman TS, Kusderci H, Kehribar L, et al. Can the Neutrophil-to-Platelet Ratio Be Used to Predict Postoperative Mortality in Geriatric Patients with Hip Fractures? Hitit Med J 2023;5(3): 175-179. https://doi.org/10.52827/hititmedj.1302044

## Abstract

**Objective:** Hip fracture is a condition frequently encountered in geriatric patients and is correlated with high postoperative mortality and morbidity. Numerous factors may impact mortality, but recent studies have focused on its correlation with inflammation. The neutrophil-to-platelet ratio has been evaluated as a systemic inflammation marker. The aim of our study was to examine the correlation between preoperative neutrophil-to-platelet ratio (NPR) values and postoperative one-year mortality in geriatric patients with hip fractures.

**Material and Method:** In our retrospective, multicenter study, 50 patients over 65 years of age who had undergone hip fracture surgery under spinal anesthesia were examined. Patients' preoperative neutrophil-to-platelet ratio values at the time of hospitalization, age, gender, American Society of Anesthesiologists scores, fracture types, comorbidities, durations of surgery, lengths of hospital stay, and survival in the postoperative one-year period were checked.

**Results:** The mean age of all the patients was 85.44 ± 6.93 years. Of the patients, 60% were female (n = 30), and 40% were male (n = 20). The optimal cut-off value for preoperative neutrophil-to-platelet ratio was specified as 38.286. The length of hospital stay was 8.94 ± 3.05 in the deceased patients and 6.94 ± 2.63 days ($p = 0.02$) in the surviving group. The mortality rate was higher in men than in women ($p = 0.01$).

**Conclusion:** A preoperative neutrophil-to-platelet ratio value over 38.286 is an indicator of postoperative one-year mortality in elderly hip fracture patients. Additionally, length of hospital stay and the male gender were revealed to be correlated with mortality.

**Keywords:** Geriatrics, Hip Fractures, Mortality, Inflammation

## Özet

**Amaç:** Kalça kırığı, geriatrik hastalarda sıklıkla karşılaşılan bir durumdur ve yüksek postoperatif mortalite ve morbidite ile ilişkilidir. Mortaliteyi etkileyebilecek çok sayıda faktör vardır, ancak son çalışmalar inflamasyon ile ilişkisine odaklanmıştır. Nötrofil-platelet oranı, sistemik bir inflamasyon belirteci olarak kullanılmaktadır. Çalışmamızın amacı, kalça kırığı olan geriatrik hastalarda ameliyat öncesi nötrofil-platelet oranı (NPR) değerleri ile ameliyat sonrası bir yıllık mortalite arasındaki ilişkiyi incelemektir.

**Gereç ve Yöntem:** Retrospektif, çok merkezli çalışmamızda spinal anestezi altında kalça kırığı ameliyatı geçirmiş 65 yaş üstü 50 hasta incelendi. Hastaların preoperatif hastaneye yatış anındaki nötrofil-platelet oranı değerleri, yaşları, cinsiyetleri, Amerikan Anesteziyologlar Derneği skorları (ASA), kırık tipleri, komorbiditeleri, cerrahi süreleri, hastanede kalış süreleri ve postoperatif bir yıllık dönemde sağkalımları incelendi.

**Bulgular:** Tüm hastaların ortalama yaşı 85,44 ± 6,93 idi. Hastaların %60'ı kadın (n=30), %40'ı erkekti (n=20). Ameliyat öncesi nötrofil-platelet oranı için optimal cut-off değeri 38.286 olarak belirlendi. Hastanede kalış süresi ölen hastalarda 8,94 ± 3,05, yaşayan grupta 6,94 ± 2,63 gün ($p=0,02$) bulundu. Erkeklerde ölüm oranı kadınlara göre daha yüksekti ($p=0,01$).

**Sonuç:** Ameliyat öncesi nötrofil-platelet oranı değerinin 38.286'nın üzerinde olması, yaşlı kalça kırığı hastalarında ameliyat sonrası bir yıllık mortalitenin göstergesi olarak bulundu. Ayrıca hastanede kalış süresi ve erkek cinsiyetin mortalite ile ilişkili olduğu kanıtlanmıştır.

**Anahtar Sözcükler:** Geriatri, Kalça Kırığı, Mortalite, İnflamasyon

**Date of Submission:** 24.05.2023
**Date of Acceptance:** 13.07.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** The study was approved by the Samsun University Clinical Research Ethics Committee (2023/1/18).
**Plagiarism Checks:** Yes - iThenticate
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: TSA, HK, LK, BCA, AS Design: TSA, HK, LK, BCA, AS Data Collection/Data Processing: TSA, AS Data Analysis: TSA, AS Article Preparation: TSA, AS
**Informed Consent:** Not applicable.
**Financial Disclosure:** No financial support has been received.

## Introduction

Hip fracture is a condition that is frequently seen in elderly patients and progresses with high postoperative mortality and other complications. The mortality rate is 1–7.2% in the first postoperative month, but reaches 8.4–36% in a year (1,2). The highest mortality rate after hip fractures is seen in the first six months, after which the rate decreases (3). Mortality is impacted by numerous factors, such as age, gender, functional status before fracture, type of surgery, comorbidities, length of hospital stay, preoperative hemoglobin level, a low body mass index, malnutrition, and a high American Society of Anesthesiologists (ASA) score (3-6).

Inflammation has been found to be correlated with the onset or progression of many diseases, such as cancers associated with high mortality and morbidity, atherosclerosis, and sickle cell anemia (7). In recent studies, it has been asserted that inflammatory markers may independently affect short- and long-term mortality after hip fractures (1). There are series of studies indicating the correlation between inflammation-based markers that reflect systemic inflammation, such as, , C-reactive protein (CRP), ferritin, transferrin, interleukin 6 (IL-6), soluble urokinase plasminogen activator receptor (suPAR), the prognostic nutritional index (PNI), tumor necrosis factor-alpha (TNF-alpha), the systemic immune inflammation index (SII), the CRP/PNI ratio, and the neutrophil/lymphocyte ratio (NLR), and postoperative poor prognosis and complications in patients with hip fractures (1,4,8,9). The neutrophil to platelet ratio (NPR) has been specified as a marker of systemic inflammation and has been associated with conditions such as ulcerative colitis, infective endocarditis, thromboembolic events, acute appendicitis, and hemorrhagic transformation in acute ischemic stroke (10-13). However, no publications have been found in the literature regarding its correlation with mortality in geriatric patients with hip fractures.

The aim of our study was to examine the correlation between preoperative NPR values and postoperative one-year mortality in geriatric patients with hip fractures.

## Material and Method

*1. Ethical Considerations*

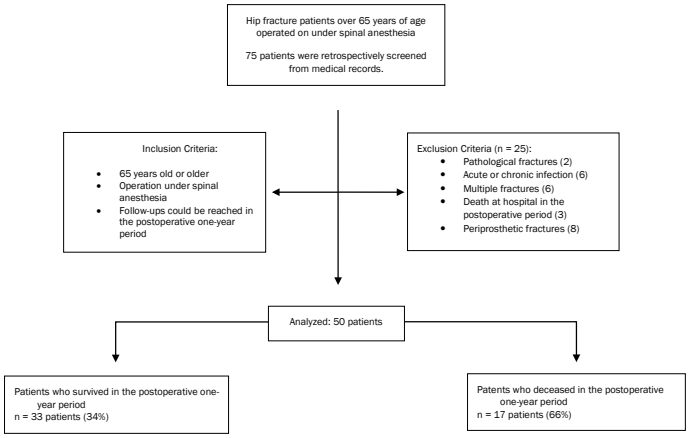
Approval from Ethics Committee was obtained for this retrospective, observational study, which was carried out in accordance with the Declaration of Helsinki.

*2. Patient Population and Data Collection*

Seventy-five patients over 65 years of age who had been operated on for hip fracture under spinal anesthesia between January 2021 and January 2022 in the two centers were retrospectively screened, and their information and follow-ups in the postoperative one-year period were acquired via medical records (computer system) and telephone. Exclusion criteria were set as patients having pathological fractures, high-energy traumas, acute or chronic infections, multiple fractures, and death at the hospital in the postoperative period. Six patients had multiple fractures, six had acute infections, three died at hospital in the postoperative period, eight had periprosthetic fractures, and two had pathological fractures. Therefore, they were excluded from consideration, and the study was conducted on the remaining 50 patients (Figure I).

The patients' ages, genders, fracture types, ASA scores, lengths of hospital stay, comorbidities, preoperative NPR values, and survival-mortality statuses in a year were recorded. When patients were admitted to the hospital, venous blood samples studied in the preoperative period were used for NPR calculation. While calculating the NPR value, the formula of neutrophil count (109/L) x 1000/platelet count (109/L) was used.

**Figure I.** Diagram of the Study Design




*Statistical Analysis*

SPSS software version 20.0 (IBM Corp., Armonk, NY) was used to conduct the statistical analyses. Descriptive statistics were presented as means, medians, standard deviations, ranges, and percentages. The normality of the data was tested using the Shapiro–Wilk test. Pearson's chi-square test was performed to analyze the categorical variables appropriately. To analyze the continuous variables, the independent samples t-test was used wherever suitable. Receiver operating characteristic (ROC) analysis was used to identify the threshold value of NPR for mortality, and thus to divide patients into high or low NPR groups. To reveal the prognostic factors predicting one-year mortality following hip fracture surgery, bilateral logistic regression was carried out for the important variables in the univariate analysis through the forward stepwise conditional method. Probability rates were calculated with 95% confidence intervals (CIs). The value of $p<0.05$ was considered statistically significant. The minimum sample size required to detect a significant difference using this test should be at least 15 in each group, (30 in total), considering type I error (alfa) of 0.05, power (1-beta) of 0.8, effect size of 1.07 and two-sided alternative hypothesis (H1). However, considering the risk of any problems with the patients, it was thought that it would be appropriate to work with a total of 50 people in the study.

## Results

In this study, in which 50 patients were involved in the analysis, the mean age of all patients was 85.44 ± 6.93 years (min: 70, max: 96; Table I). Of all the patients, 60% were female (n = 30), and 40% were male (n = 20; Table II). Furthermore, 86% (n = 43) were in the high-risk group (ASA3–4), and 14% (n = 7) were in the low-risk group (ASA1–2; Table II). The most observed type of fracture was femoral neck fracture (44%), followed by pertrochanteric (24%), intertrochanteric (18%), basicervical (8%), and subtrochanteric (6%) fractures, respectively (Table II). The mean operation time of all patients

**Table I.** Correlation Between Age, Duration of Surgery, Length of Hospital Stay and Survival of Patients

| Variable | Surviving group Mean±SD (range). | Deceased group Mean±SD (range). | Total Mean±SD (range). | *p-value* |
|---|---|---|---|---|
| Age (years) | 84.94 ± 7.03 (70–96) | 86.41 ± 5.17 (74–94) | 85.44 ± 6.44 (70–96) | *0.454* |
| Duration of surgery (minutes) | 94.61 ± 31.03 (49–160) | 95.47 ± 30.53 (49–145) | 94.9±30.56 (49–160) | *0.926* |
| Length of hospital stay (days) | 6.94 ± 2.63 (3–12) | 8.94 ± 3.05 (4–14) | 7.63 ± 2.91 (3–14) | **0.02*** |

Independent samples t-test was used. *$p < 0.05$ was considered significant.

**Table II.** Correlation Between Patients' Demographic Information and Survival

| Variable | Surviving group n (%) 33 (66) | Deceased group n (%) 17 (34) | Total n (%) 50 | *p-value* |
|---|---|---|---|---|
| **Gender** | | | | |
| Female | 24 (80) | 6 (20) | 30 (60) | *0.01** |
| Male | 9 (45) | 11 (55) | 20 (40) | |
| **ASA** | | | | |
| 1–2 (low risk) | 5 (71.4) | 2 (28.6) | 7 (14) | *0.744* |
| 3–4 (high risk) | 28 (65.1) | 15 (34.9) | 43 (86) | |
| **Comorbidity** | | | | |
| None | 7 (77.8) | 2 (22.2) | 9 (18) | *0.439* |
| 1--2 | 21 (67.7) | 10 (32.3) | 31 (62) | |
| 3 and above | 5 (50) | 5 (50) | 10 (20) | |
| **Fracture type** | | | | |
| Basicervical | 1 (25) | 3 (75) | 4 (8) | *0.162* |
| Femoral neck | 17 (77.3) | 5 (22.7) | 22 (44) | |
| Intertrochanteric | 4 (44.4) | 5 (55.6) | 9 (18) | |
| Pertrochanteric | 9 (75) | 3 (25) | 12 (24) | |
| Subtrochanteric | 2 (66.7) | 1 (33.3) | 3 (6) | |

Pearson's chi-square test was used. *$p < 0.05$ was considered significant. n: Number

was 94.9 ± 30.56 min (min: 49 min, max: 160 min), and the mean length of hospital stay was 7.63 ± 2.91 days (min: three days, max: 14 days; Table I). The most frequent comorbidities were diabetes mellitus, hypertension, and coronary artery disease, respectively (Table III).

Of all patients, 34% (n = 17) had deceased in the one-year postoperative period. The patients were categorized as surviving or deceased according to their one-year postoperative survival (Table I, Table II). According to the ROC curve analysis, the optimal cut-off value for preoperative NPR was found to be 38.286 (sensitivity: 66.7%, specificity: 64.7%) (Figure 2). The NPR value was 58.07 ± 44.14 (min: 15.47, max: 202.83) in the deceased patient group and 33.34 ± 17.64 (min: 10.70, max: 76.83) in the surviving patient group.

The mean age of the surviving patients was 84.94 ± 7.03 years (min: 70, max: 96), while the mean age of the deceased patients was 86.41 ± 5.17 years (min: 74, max: 94). No statistical difference was observed (p = 0.454; Table I). When the two groups were categorized as low risk (ASA1–2) and high risk (ASA3–4) groups according to the ASA score, five people from the surviving group were assessed to be in the low-risk group, and 28 people were assigned to the high-risk group. From the deceased group, two people were evaluated in the low-risk group, and 15 people were assigned to the high-risk group. No statistical difference was determined between the two groups ($p = 0.744$).

**Figure II.** ROC curve of NPR for predicting 1-year mortality. Data presented as area under the curve (AUC) with 95% confidence interval (CI)

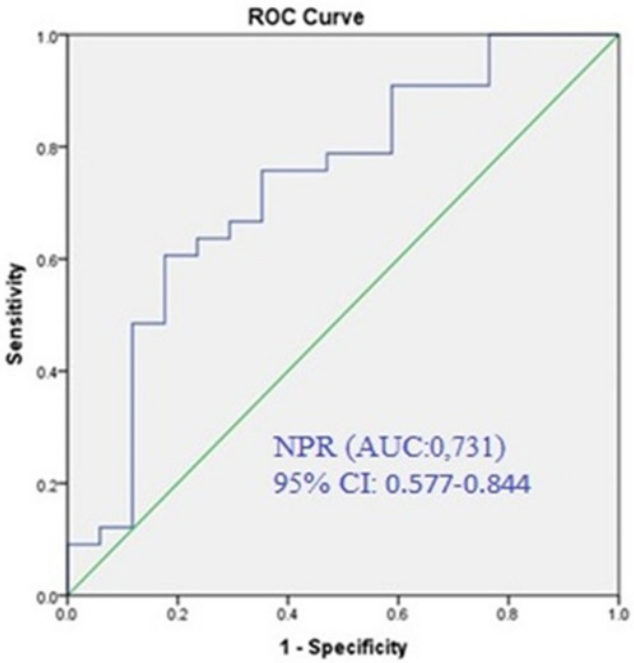



**Table III.** Accompanying Comorbid Diseases

| Comorbid diseases | N (%) |
|---|---|
| Diabetes mellitus | 15 (20.3) |
| Hypertension | 16 (21.6) |
| Coronary artery diseases | 10 (13.5) |
| Cerebrovascular disease | 9 (12.2) |
| Chronic obstructive pulmonary disease | 5 (6.8) |
| Chronic renal failure | 5 (6.8) |
| Alzheimer's disease | 5 (6.8) |
| Congestive heart failure | 8 (10.8) |
| Parkinson's disease | 1 (1.4) |

The patients were classified into three groups based on whether their number of comorbidities was 1–2, three, or above, and there was no statistical difference between the surviving and deceased groups in this respect ($p = 0.439$; Table II). The mean length of hospital stay was 6.94 ± 2.63 days (min: 3, max: 12 days) in the surviving group and 8.94 ± 3.05 days (min: 4, max: 14 days) in the deceased group. The length of hospital stay was found to be significantly higher in deceased patients (p = 0.02; Table I). When the gender distribution of the surviving and deceased patients was examined, the mortality rate was found to be 4.889 times higher in men than in women, and a significant difference was observed (p = 0.01; Table II). When the mean operation time and fracture types of the surviving and deceased patients were checked, no significant difference was seen between the two groups (Table I, Table II). The mean operation time of the surviving group was 94.61 ± 31.03 min, and the corresponding value was 95.47 ± 30.56 min in the deceased group (Table I).

## Discussion

Hip fracture is one of the leading issues associated with serious mortality and morbidity rates in elderly patients. In our study, we found that a preoperative NPR value of over 38.286 was associated with postoperative one-year mortality in elderly hip fracture patients. In addition, length of hospital stay and the male gender were also associated with one-year mortality.

Neutrophils are known as the group of cells that create the first response to inflammation (14). Stress-induced hormonal changes, such as cortisol secretion, increase neutrophil counts through vascular demargination in hip fracture patients (15). Platelets play an important role in inflammation and its resolution process, despite the fact that they are known to be mainly involved in hemostasis and immunothrombosis. There is also the view that hemostasis and inflammation are closely correlated pathophysiological processes (14). The NPR has been suggested as a systemic inflammation marker that can be calculated with a complete blood count; it is also low cost, easily accessible, and can quickly provide results (10). However, there are no publications in the literature on the correlation between the NPR and postoperative prognosis and mortality of patients with hip fractures.

Muscle injury caused by hip fractures may produce an excessive inflammatory response (8). Recently, more attention has been paid to the correlation between inflammation and prognosis, particularly in elderly individuals (1). In rat models, the correlation between high systemic inflammation observed after hip fracture and acute lung injury has been demonstrated, and lung injury has been found to be more severe in the elderly than in the young (16). It has also been shown that the IL-6 level is correlated with one-year mortality in hip fractures over 80 years of age, and systemic inflammation-associated markers, such as CRP, suPAR, and ferritin, are linked with 30-day mortality after hip fracture (1). Capkın et al. suggested that a CRP/albumin ratio above 2.49 was correlated with postoperative one-year mortality in elderly patients who underwent hemiarthroplasty due to hip fractures (4). In the study by Sökmen et al., in patients over 65 years of age who had undergone hemiarthroplasty for hip fracture, a CRP/albumin ratio of ≥ 29, being over 85 years old, and having three or more comorbidities were associated with mortality (17). Temiz et al. also checked the correlation between postoperative survival and the NLR at the time of admission to the hospital in patients over 65 years of age who had hip fractures and underwent hemiarthroplasty, and it was shown that a high NLR value was correlated with mortality.

The NLR value has been defined as a marker of systemic inflammation (2). Wang et al. investigated the correlation between the SII, a value calculated over peripheral neutrophils, platelets, and lymphocytes, and postoperative one-year and total mortality; in this case, they found a correlation between the SII and mortality (1). Like these parameters, the NPR is also considered a marker of systemic inflammation. There are publications on various inflammation-associated diseases showing that the NPR can be used as a prognostic factor and a mortality marker. For instance, an increased NPR was found to be correlated with long-term mortality outcomes during hospital stays in infective endocarditis patients (13,18). Likewise, the NPR exhibited superior diagnostic performance in ulcerative colitis patients with clinical and endoscopic activity compared to other serum biomarkers (CRP, albumin, and ESR) and could identify these patients without the need for expensive biomarkers or colonoscopy (10). Our study revealed that the NPR could also be used in such a way, like the inflammation biomarkers used in previous publications on the elderly population with hip fractures, and determined a correlation between the NPR and the one-year mortality of the geriatric patient population undergoing hip fracture surgery. With the ROC curve analysis, the cut-off value for the preoperative NPR was specified as 38.286, which was found to be significantly higher in patients who died in the postoperative one-year period.

In the systematic literature review by Yu Xu et al. on hip fractures, it was found that the male gender was correlated with poor prognosis and mortality in most studies. Moreover, it has been asserted that there are many predictive factors associated with poor functional outcomes and mortality (19). In a study conducted by Bicen et al. on patients undergoing hip fracture surgery, it was reported that age, male gender, preoperative hemoglobin level, and comorbidities affected mortality (20). Likewise, in our study, postoperative one-year mortality was higher in male patients, and mortality was found to be 4.889 times higher in men than in women.

Yoo et al. investigated the relationship between the length of hospital stay and one-year mortality after hip fracture operations and reported that 604 (14.3%) of 4,213 patients died within one year, and the mortality rate (21.7%) was the highest in patients hospitalized for 10 days or less (21). In a cohort study conducted in the United States, however, a low number of hospital stay days was correlated with reduced postoperative 30-day mortality (22). In our study, the length of hospital stay was observed to be significantly longer in the deceased group. Some studies have identified a relationship between advanced age, extracapsular fractures, and mortality. Despite the presence of studies that have found a link between a high ASA score and mortality, there are also publications indicating that the ASA score is not a determinant of mortality (19). In our study, no correlation was revealed between age, duration of surgery, ASA score, number of comorbidities, fracture type, and postoperative one-year mortality. These differences between the studies most likely result from the fact that mortality is impacted by multifactorial causes.

The limitations of our study consist of the non-inclusion of some variables that might affect survival, such as the level of albumin, the time between the occurrence of the fracture and hospital admission, and body mass index. Our patients' complete blood count values only at the time of admission to the hospital were used, and NPR values in other postoperative periods could be included in further studies. Since our study was carried out retrospectively with medical records and telephone calls, the reasons why the patients had deceased were not exactly known. Therefore, this factor was not included in the study.

## Conclusion

In conclusion, our study found that a preoperative NPR value above 38,286 can be an indicator for predicting the mortality of patients over 65 undergoing hip fracture surgery in the postoperative one-year period. Male gender and length of hospital stay were also correlated with postoperative 1-year mortality. Based on our data, NPR can be used as a simple and economical biomarker in predicting prognosis in geriatric

hip fracture patients.

This study was presented as an oral presentation at the 7th Rize Thematic Anesthesia Symposium.

## References

1. Wang ZC, Jiang W, Chen X, Yang L, Wang H, Liu YH. Systemic immune-inflammation index independently predicts poor survival of older adults with hip fracture: a prospective cohort study. BMC Geriatr 2021;21(1):155.

2. Temiz A, Ersözlü S. Admission neutrophil-to-lymphocyte ratio and postoperative mortality in elderly patients with hip fracture. Ulus Travma Acil Cerrahi Derg 2019;25(1):71-74.

3. Mutlu T, Daşar U. Hip fracture surgery in patients older than 90 years : evalution of factors that affect 30-day mortality in a particularly risky group. Turkish Journal of Geriatrics 2018;21 (2):279-284.

4. Capkin S, Guler S, Ozmanevra R. C-reactive protein to albumin ratio may predict mortality for elderly population who undergo hemiarthroplasty due to hip fracture. J Invest Surg 2021;34(11):1272-1277.

5. Temizel F, Uckun S, Kuzucuoglu T, Arslan G, Çevik B. The effects of comorbidities on intensive care admission in elderly patients undergoing hip surgerious. Turkish Journal of Geriatrics 2018;21 (2):109-114.

6. Kasıkara H, Lafcı A. Evaluation of factors affecting mortality in geriatric hip fracture surgery: a retrospective study. Turkish Journal of Geriatrics 2022;25(3): 452-464.

7. Stokes KY, Granger DN. Platelets: a critical link between inflammation and microvascular dysfunction. J Physiol 2012; 590(5):1023-1034.

8. Norring-Agerskov D, Bathum L, Pedersen O et al. Biochemical markers of inflammation are associated with increased mortality in hip fracture patients: the Bispebjerg hip fracture biobank. Aging Clin Exp Res 2019;31(12):1727-1734.

9. Saribal D, Hocaoglu-Emre FS, Erdogan S, Bahtiyar N, Caglar Okur S, Mert M. Inflammatory cytokines IL-6 and TNF-α in patients with hip fracture. Osteoporos Int. 2019;30(5):1025-1031.

10. Yamamoto-Furusho JK, Mendieta-Escalante EA. Diagnostic utility of the neutrophil-platelet ratio as a novel marker of activity in patients with ulcerative colitis. PLoS One 2020;15(4):e0231988.

11. Somaschini A, Cornara S, Demarchi A, et al. Neutrophil to platelet ratio: a novel prognostic biomarker in ST-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention. Eur J Prev Cardiol 2020;27(19):2338-2340.

12. He W, Ruan Y, Yuan C, et al. High neutrophil-to-platelet ratio is associated with hemorrhagic transformation in patients with acute ischemic stroke. Front Neurol 2019;10:1310.

13. Li Z, Gao Q, Ren Z, Zhou H, Qian Z, Peng J. Nomogram based on neutrophil-to-platelet ratio to predict in-hospital mortality in infective endocarditis. Biomark Med. 2021 Oct;15(14):1233-1243

14. Margraf A, Zarbock A. Platelets in inflammation and resolution. J Immunol 2019;203(9):2357-2367.

15. Karahan MA. The effect of spinal anesthetic technique on neutrophil to lymphocyte ratio and postoperative mortality in elderly patients with coronary artery disease undergoing hip replacement surgery. Turkish Journal of Geriatrics 2019;22(3):305-314

16. Gan L, Sun T, Li B, et al. Serum miR-146a and miR-150 as potential new biomarkers for hip fracture-induced acute lung injury. Mediators Inflamm 2018;2018:8101359

17. Sokmen FC, Ulucakoy C. Can the c-reactive protein to albumin ratio predict mortality due to hemiarthroplasty performed after hip fracture in the elderly population? Turkish Journal of Geriatrics 2021;24(1): 79-86

18. Wei XB, Liu YH, He PC, et al. The impact of admission neutrophil-to-platelet ratio on in-hospital and long-term mortality in patients with infective endocarditis. Clin Chem Lab Med 2017;55(6):899-906.

19. Xu BY, Yan S, Low LL, Vasanwala FF, Low SG. Predictors of poor functional outcomes and mortality in patients with hip fracture: a systematic review. BMC Musculoskelet Disord. 2019;20(1):568.

20. Biçen Ç, Akdemir M, Türken MA, Çekok K, Ekin A, Turan AC. Analysis of risk factors affecting mortality in elderly patients operated on for hip fractures: A retrospective comparative study. Acta Orthop Traumatol Turc. 2021;55(6):493-499.

21. Yoo J, Lee JS, Kim S, et al. Length of hospital stay after hip fracture surgery and 1-year mortality. Osteoporos Int. 2019;30(1):145-153.

22. Nikkel LE, Kates SL, Schreck M, Maceroli M, Mahmood B, Elfar JC. Length of hospital stay after hip fracture and risk of early mortality after discharge in New York state: retrospective cohort study. BMJ. 2015;351:h6246.

# Tiroid Kanserlerinde Histomorfolojik Bulguların Değerlendirilmesi ve Diyabet ile Birlikteliği

**Havva Hande Keser Şahin[1], Orhan Aslan[2], Yılmaz Baş[1]**

[1]Hitit Universitesi, Erol Olçok Eğitim ve Araştırma Hastanesi, Patoloji Ana Bilim Dalı, Çorum, Türkiye
[2]Hitit Universitesi, Erol Olçok Eğitim ve Araştırma Hastanesi, Genel Cerrahi Ana Bilim Dalı, Çorum, Türkiye

**Yazışma Adresi:** Hitit Üniversitesi Tıp Fakültesi Genel Cerrahi Anabilim Dalı, Çorum, Türkiye
e-posta: drorhanaslan@gmail.com

**Orcid NO:** HHKŞ: 0000-0003-1827-1039 YB: 0000-0002-4229-8568
OA: 0000-0002-1982-0792

**Atıf:** Keser Şahin HH, Aslan O, Baş Y. Tiroid Kanserlerinde Histomorfolojik Bulguların Değerlendirilmesi ve Diyabet ile Birlikteliği. Hitit Med J 2023;5(3):180-184. https://doi.org/ 10.52827/hititmedj.1301998

## Özet

**Amaç:** Bu çalışmada tiroid kanseri türleri ile diabetes mellitus arasındaki ilişkinin araştırılması amaçlanmıştır.

**Gereç ve Yöntemler:** 2016-2018 yılları arasında Hitit Üniversitesi Erol Olçok Eğitim ve Araştırma Hastanesi Patoloji bölümünde tanı alan 406 tiroidektomi olgusu retrospektif olarak hastane bilgisayar kayıt sisteminden ve Patoloji kliniği arşivinden tarandı. Bu vakalar içerisinden tiroid kanseri tanısı alanlar belirlendi. Tiroid kanserli olgulardan Diyabetes Mellitus tanılı olanlar hastane bilgi sisteminden tespit edildi. Olgular tanılarına, cinsiyet, yaş, tümör tipi, tümör lokalizasyonu, tümör çapı, lenf nodu metastazı ve uzak organ metastazı açısından sınıflandırıldı. İmmünohistokimyasal HBME1, Galaktin 3 ve Sitokeratin-19 ekspresyonu incelendi.

**Bulgular:** Tiroid karsinomu tanısı alan 109 olgu vardı. Bu olguların yaş ortalaması 51,1'di. Kadın/erkek oranı 2,9'du. Kanser olguları 4. dekatta en yüksek oranda görülmekteydi. Tiroid papiller karsinom 55 (%50,5), mikrokarsinom 48 (%44,0), folliküler karsinom 3 (%2,8) ve medüller karsinom tanısı alan 3 (%2,8) olgu vardı. Olguların 12'inde (%11,0) vasküler invazyon ve kapsül invazyonu vardı. Tiroid papiller karsinom tanısı alan 2 (%1,8) olguda lenf nodu metastazı vardı. Tiroid kanserli 109 hastanın 14'ünde (%12,8) diyabetes mellitus vardı. Çalışma grubumuzdaki hastaların diyabet oranı ile genel popülasyon diyabet oranı karşılaştırıldığında istatistiksel olarak anlamlı farklılık saptanmamıştır (*p=0,519*).

**Sonuç:** Çalışmamızda diyabetin tiroid kanseri için bir risk faktörü olmadığı görülmüştür. Diyabetin düşük orandaki birlikteliği nedeniyle, diyabetli hastalarda tiroid bezi kontrolünün yapılmasının gerekliliği ortaya çıkmıştır. Diyabetin tiroid kanseri için bir risk faktörü olduğunu belirtmek için daha çok veriye ihtiyaç vardır.

**Anahtar Sözcükler:** Diyabet, Kanser, Tiroid

**Geliş Tarihi:** 25.05.2023
**Kabul Tarihi:** 07.09.2023
**Yayım Tarihi:** 10.10.2023

**Hakem Değerlendirmesi:** Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
**Etik Beyanı:** Çalışma Hitit Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulundan onay almıştır. (Onay Numarası: 2018/175)
**İntihal Kontrolleri:** Evet - intihal.net
**Çıkar Çatışması:** Yazarlar arasında çıkar çatışması belirtilmemiştir.
**Şikayetler:** hmj@hitit.edu.tr
**Katkı Beyanı:** Fikir/Hipotez: HHKŞ, YB Tasarım: HHKŞ, YB Veri Toplama/Veri işleme: HHKŞ, OA Veri Analizi: HHKŞ, OA Makalenin Hazırlanması: OA, YB, HHKŞ
**Hasta Onamı:** Onama gerek yoktur.
**Finansal Destek:** Finansal destek alınmamıştır.

# Evaluation of Histomorphological Findings in Thyroid Cancers and Association with Diabetes

**Havva Hande Keser Sahin[1], Orhan Aslan[2], Yilmaz Bas[1]**

[1]Hitit University, Faculty of Medicine, Corum Erol Olcok Training and Research Hospital, Department of Pathology, Corum, Türkiye
[2]Hitit Üniversity Faculty of Medicine, Department of General Surgery, Corum, Türkiye

**Adress for Correspondence:** Hitit Üniversity Faculty of Medicine, Department of General Surgery, Corum, Türkiye
**e-posta:** drorhanaslan@gmail.com

**Orcid ID:** HHKŞ: 0000-0003-1827-1039 YB: 0000-0002-4229-8568
OA: 0000-0002-1982-0792

**Cite As:** Keser Sahin HH, Aslan O, Bas Y. Evaluation of Histomorphological Findings in Thyroid Cancers and Association with Diabetes. Hitit Med J 2023;5(3):180-184. https://doi.org/ 10.52827/hititmedj.1301998

## Abstract

**Objective:** This study aimed to investigate the relationship between thyroid cancer types and Diabetes Mellitus (DM).

**Material and Methods:** Between 2016-2018, 406 thyroidectomy cases diagnosed in the Pathology department of Hitit University Erol Olçok Training and Research Hospital were retrospectively reviewed from the hospital computer registration system and the archive of the Pathology clinic. Among these cases, patients diagnosed with thyroid cancer were identified. Among the thyroid cancer cases, those diagnosed with DM were identified using hospital records. Cases were classified based on diagnosis, gender, age, tumor type, tumor localization, tumor diameter, lymph node metastasis, and distant organ metastasis. HBME1, Galactin 3, and Cytokeratin-19 expression were analyzed immunohistochemically.

**Results:** There were 109 patients diagnosed with thyroid carcinoma. The mean age of these patients was 51.1 years, and the male/female ratio was 2.9. Cancer cases were most common in the fourth decade. There were 55 (50.5%) cases of thyroid papillary carcinoma, 48 (44.0%) cases of microcarcinoma, 3 (2.8%) cases of follicular carcinoma and 3 (2.8%) cases of medullary carcinoma. Vascular invasion and capsular invasion were observed in 12 cases (11.0%). Lymph node metastasis was present in 2 (1.8%) patients diagnosed with thyroid papillary carcinoma. DM was present in 14 (12.8%) of 109 patients with thyroid cancer. When the DM rate of the patients in our study group was compared with the DM rate in the general population, no statistically significant difference was found ($p=0.519$).

**Conclusion:** In our study, DM was not found to be a risk factor for thyroid cancer. Due to the low association rate of DM, it is necessary to check the thyroid gland in patients with diabetes mellitus. More data and further studies are needed to indicate that diabetes is a risk factor for thyroid cancer.

**Keywords:** Diabetes, Cancer, Thyroid

**Date of Submission:** 25.05.2023
**Date of Acceptance:** 07.09.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** Ethical approval for the study was granted by the Research Ethics Committee of Hitit University (Approval No: 2018/175).
**Plagiarism Checks:** Yes - intihal.net
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: HHKS, YB Design: HHKS, YB Data Collection/Data Processing: HHKS, OA Data Analysis: HHKS, OA Article Preparation: OA, YB, HHKS
**Informed Consent:** Not applicable.
**Financial Disclosure:** No financial support has been received.

## Giriş

Kanser ve Diyabetes Mellitus (DM) çağımızın mücadele ettiği en önemli sağlık sorunlarının başında gelmektedir. Bu iki kronik hastalık türünde endüstrileşme, sedatif yaşam, obezite, yaş, cinsiyet gibi bazı çevresel risk faktörlerin ortak olması düşündürücüdür. Global olarak, DM ve kanserin artışı, DM'li hastalarda kanser gelişim insidansının artışı ve kanser prognozu üzerine etkisi, araştırmacıları DM-kanser komorbiditesi üzerine çalışmalar yapmaya yönlendirdi (1).

DM tanılı erkeklerde, özellikle kolorektal ve prostat kanseri olmak üzere genel olarak kanser gelişme riskinin %39 arttığı bildirilmiştir (1). 2003 yılında araştırmacılar, DM tanısı olan kadınlarla olmayanlar kıyaslandığında, DM'li kadınlarda %17 oranında artmış meme kanseri insidansı riski bildirmişlerdir (2). Ancak bunun aksini belirten çalışmalar da literatürde mevcuttur (3-5). DM-kanser komorbiditesi çalışmalarında görülen bu tutarsız sonuçlar, en sık görülen endokrin kanser olan tiroid kanserinde de mevcuttur. Son yıllarda küresel olarak tiroid kanseri insidansında artış görülmektedir (6). DM'nin tiroid kanseri riskini artırdığı hipotezini destekleyen bazı çalışmalar bulunmaktadır (7-9). Ancak bazı çalışmalar herhangi bir ilişki saptanmadığını raporlamıştır (10-13). Literatürdeki bu farklı sonuçlara rağmen, DM ve kanser gelişimindeki benzer mekanizmaların varlığı, konunun güncelliğini koruması için yeterli görünmektedir. DM-kanser ilişkisinin hiperglisemi, hiperinsülinemi ve inflamasyona bağlı olduğu yaygın olarak kabul edilmektedir (14-16). Çevresel risk faktörlerinin benzerliğine mekanizma benzerliğinin eşlik etmesi bu iki hastalık arasında olası yakın ilişkiyi araştırmaya değer kılmaktadır.

Biz bu çalışmada patoloji kliniğimizde tiroid kanseri tanısı konulan hastalarda DM varlığını ve DM ile Tiroid kanseri türleri arasındaki korelasyonu analiz etmeyi amaçladık.

## Yöntem ve Gereçler

Çalışmamızda Hitit Üniversitesi Erol Olçok Eğitim ve Araştırma Hastanesi'nde 01.01.2016 - 30.04.2018 yılları arasında opere edilmiş 406 tiroidektomi olgusu retrospektif olarak Patoloji Kliniği arşivinden tarandı. Bu olgulardan 18 yaş üstü olan, tiroid kanseri tanısı alan 109'u çalışmaya dahil edildi. 18 yaş altı olanlar ve tiroid bezine metastaz olan vakalar, çalışma dışı bırakıldı. Olgulara ait yaş, cinsiyet ve patolojik tanılar patoloji raporlarından elde edildi. Hitit Üniversitesi Girişimsel Olmayan Etik Kurulundan etik onayı alındı(Karar no:2018-174).

Tümörlere ait formalin fikse parafine gömülü dokulardan elde edilen Hematoksilen ve Eozin boyalı kesitleri ve immünohistokimyasal olarak Galaktin-3, HBME1 ve sitokeratin-19 boyalı lamlar 2 patoloji uzmanı tarafından tekrar incelendi (HHKŞ ve YB). Tümör içeren olgular, tanılarına, cinsiyet, yaş, tümör tipi, tümör lokalizasyonu, tümör çapı, vasküler invazyon, kapsül invazyonu, lenf nodu metastazı ve uzak organ metastazı açısından sınıflandırıldı.

Hastanemiz bilgi işlem sisteminden tiroid kanseri olan olguların kan biyokimya bulgularının dökümü alındı ve DM olan olgular belirlendi.

*İstatistiksel Analiz*

Sonuçlar uygun olarak medyan veya ortalama standart sapma olarak ifade edildi. Gruplar arası değişkenler arasındaki farklar Ki-kare testi ve SigmaStat 2.03 (Systat Software Inc., Point Richmond, CA) kullanılarak Student t testi ile analiz edildi. İstatistiksel analizler SPSS 20.0 kullanılarak yapıldı. *P <0,05* değeri istatistiksel olarak anlamlı kabul edildi.

## Bulgular

Kriterlere uygun karsinom tanısı alan 109 olgu vardı. Bu olguların yaş ortalaması 51,1'di. Kadın/erkek oranı 2,9'du. Kanser olguları 4. dekatta en yüksek oranda görülmekteydi. Opere edilen guatrlı olgular içinde tiroid kanser oranı %26,9'dur.

Tiroid papiller karsinom(TPK) 55 (%50,5), mikrokarsinom 48 (%44,0), folliküler karsinom 3 (%2,8) ve medüller karsinom tanısı alan 3 (%2,8) olgu vardı(Tablo I). Anaplastik karsinom tanısı alan olgu yoktu.

Bilateral yerleşimli olgu sayısı 21 (%19,3), sağ lob yerleşimli 60 (%55,0), sol lob yerleşimli 26 (%23,9), ve isthmus yerleşimli 2 (%1,8) olgu vardı. Tümör çapı mikrokarsinom olgularında ortalama 0,54 cm, tiroid papiller karsinom olgularında 2,5 cm, folliküler karsinom olgularında 5,5 cm ve medüller karsinom olgularında 1,8 cm'di. 12 (%11,0) olguda vasküler invazyon ve kapsül invazyonu vardı. Tiroid papiller karsinom tanısı alan 2 (%1,8) olguda lenf nodu metastazı vardı. Uzak organ metastazı saptanmadı.

**Tablo I.** Tiroid kanser türlerinin dağılımı ve DM ile ilişkisi

| | TPK | Mikrokarsinom | Folliküler karsinom | Medüller karsinom | |
|---|---|---|---|---|---|
| DM(+) | 6 | 8 | - | - | |
| DM(-) | 49 | 40 | 3 | 3 | |
| Toplam | 55(%50,5) | 48(%44) | 3(% 2,8) | 3(%2,8) | 109 (%100) |

Diyabetli olguların oranı %12,8'di (n=14). Bu olgularda ortalama yaş 57 (45-72) iken K/E oranı (11/3) 3,7 idi. 8 olguda mikrokarsinom ve 6 olguda tiroid papiller karsinom saptandı. Diğer histolojik kanser tiplerinde DM'li olgu yoktu. Çalışma grubumuzdaki hastaların DM oranı ile genel popülasyon DM oranı karşılaştırıldığında istatistiksel olarak anlamlı farklılık saptanmamıştır (p=0,519) (Tablo II).

**Tablo II.** Normal populasyonu temsil eden grup ile çalışma grubunun diyabet oranlarının karşılaştırılması

| Değişkenler | | Normal Populasyon* (n=100) | Çalışma Grubu (n=109) | İstatistiki Anlamlılık |
|---|---|---|---|---|
| Diyabet Durumu | Non-Diyabetik | 90 (%90) | 95 (%87,16) | 0,519 |
| | Diyabetik | 10 (%10) | 14 (%12,84) | |

*Temsil grubu Satman ve ark. 2013 yılındaki çalışması baz alınarak oluşturulmuştur(33)

## Tartışma

Son yirmi yıldır Türkiye'de tiroid malignitesinin görülme sıklığı artmaktadır. Bu artış Çernobil nükleer kazası, endemik iyot eksikliği, artan tanısal inceleme, patoloji analizlerinin gelişmesi ve değişen cerrahi teknikler ile açıklanabilir (17).

Endokrin maligniteler içinde tiroid kanseri en sık görülür ve toplam yeni endokrin kanserlerin %96'sını ve endokrin kanserlerine bağlı ölümlerin %66,8'ini oluşturmaktadır. ABD'de, en sık tipi TPK'dir ve olgularda ortalama yaş 50'dir. Çalışmamızda da yaş ortalaması 51,1'dir. Tiroid kanser insidansı kadınlarda 3 kat fazladır (18). Çalışmamızda kanserli

olgularda kadınların oranı erkeklere göre yaklaşık 3 kat fazlaydı. TPK gelişiminde etyolojik faktörler arasında DM'nin de olduğu belirtilmektedir (19). DM'li hastalarda meme kanseri, endometriyum, mesane, karaciğer, kolorektal ve pankreas kanseri riskinin yüksek olduğu bilinmektedir(20). DM'nin kanser gelişimine nasıl katkıda bulunduğunun patofizyolojisi, aktif bir araştırma alanıdır. Hiperinsülineminin, insülin reseptörünün veya insülin benzeri büyüme faktörü-I reseptörünün aktivasyonu yoluyla mitojenik etkisi, hücresel proliferasyonu uyarması ve hücresel apopitozu inhibe etmesi patofizyolojik olarak en sık üzerinde durulan mekanizmalardır (21,22). Bir başka olası mekanizma ise hiperglisieminin, oksidatif stresi artırarak karsinogenezi teşvik etmesidir (20). Yeo ve arkadaşlarının çalışmasında DM ile birlikteliği olan az sayıda tiroid kanser olgusu saptanmış ve eldeki sonuçların tutarlı olmadığı vurgulanmıştır (7). Shyang ve arkadaşlarının derleme yazısında DM ve tiroid kanseri riskinin tartışmalı olduğu ve kanıt düzeyinin yeterince güçlü olmadığı belirtilmiştir(23). Balasubramaniam ve Tseng çalışmalarında, DM'li hastalarda tiroid kanseri prevalansında anlamlı bir artış tespit etmemişlerdir (24,11). Wang ve arkadaşlarının 2937 tiroid kanserli hasta içeren çalışmasında tiroid kanserli hastalardaki DM oranı yaklaşık % 10 bulunmuş ve DM ile tiroid kanseri riski arasında anlamlı bir ilişki bulunmadığı belirtilmiştir (25). Benzer olarak, çalışmamızda tiroid kanserli hastalarda DM oranı %12,8' dir.

Türkiye, IDF(Uluslararası Diyabet Federasyonu) 2015 Diyabet atlasına göre Avrupa ülkeleri arasında en yüksek prevelansa sahiptir (26). Türkiye'de normal populasyonda tip II DM prevalansı 12 yıl içinde %7,2'den %16,5'e yükselmiştir (27). Bu çalışmamızda belirlediğimiz %12,8 oranı normal popülasyondaki DM prevalansı ile de uyumludur. Bulgularımız Yeo Y, Tseng, Shyang-RongShih, Balasubramaniam, ile Wang ve arkadaşlarının çalışmalarıyla da uyumlu sonuçlar içermektedir (7,11,23-25).

Çalışmamızın başlıca kısıtlılıkları retrospektif olması, iki yıllık bir süre boyunca tek merkezde değerlendirilen tiroid kanseri hastalarını içermesi ve vaka sayısının az olmasıdır. Ayrıca, DM'li hastaların tanı süreleri ve antidiyabetik tedavi içeriklerine ait verilerin bulunmaması da çalışmayı sınırlamaktadır.

Sonuçta, çalışmamızda DM ile tiroid kanser türleri arasında anlamlı bir ilişki olmadığı görülmüştür. Bulgularımızın normal popülasyondaki DM oranı ile yakın değerleri nedeniyle, DM'nin tiroid kanseri için bir risk faktörü olup olmadığını belirtmek için, daha çok veriye ihtiyaç olduğu anlaşılmaktadır.

## Kaynaklar


1. Steenland K, Nowlin S, Palu S. Cancer incidence in the National Health and Nutrition Survey I. Follow-up data: diabetes, cholesterol, pulse and physical activity. Cancer Epidemiol Biomarkers Prevention 1995;4:807–811.
2. Michels KB, Solomon CG, Hu FB et al. Nurses' Health Study. Type 2 diabetes and subsequent incidence of breast cancer in the Nurses' Health Study. Diabetes Care 2003;26: 1752–1758.
3. Rastad H, Parsaeian M, Shirzad N, Mansournia MA, Yazdani K. Diabetes mellitus and cancer incidence: the Atherosclerosis Risk in Communities (ARIC) cohort study. J Diabetes Metab Disord 2019;18:65–72.
4. Chen Y, Wu F, Saito E et al. Association between type 2 diabetes and risk of cancer mortality: a pooled analysis of over 771,000 individuals in the Asia Cohort Consortium. Diabetologia 2017;60: 1022–1032.
5. Pladys A, Couchoud C, LeGuillou A, Siebert M, Vigneau C, Bayat S. Type 1 and type 2 diabetes and cancer mortality in the 2002–2009 cohort of 39,811 French dialyzed patients. PLoS One 2015;10(5):e0125089.
6. Kim J, Gosnell JE, Roman SA. Geographic influences in the global rise of thyroid cancer. Nat Rev Endocrinol 2020;16:17–29
7. Yeo Y, Ma SH, Hwang Y et al. Diabetes Mellitus and risk of thyroid cancer : a meta-analysis. PLoSOne 2014;9(6):e98135.
8. Aschebrook-Kilfoy B, Sabra MM, Brenner A et al. Diabetes and thyroid cancer risk in the National Institutes of HealthAARP Diet and Health Study. Thyroid 2011;21(9):957–963.
9. Liu X, Hemminki K, Försti A, Sundquist K, Sundquist J, Ji J. Cancer risk in patients with type 2 diabetes mellitus and their relatives. Int J Cancer 2015; 137:903–910.
10. Kitahara CM, Platz EA, Beane Freeman LE et al. Physical activity, diabetes, and thyroid cancer risk: a pooled analysis of five prospective studies. Cancer Causes Control 2012;23:463–471.
11. Tseng CH. Thyroid cancer risk is not increased in diabetic patients. PLoSOne 2012;7:e53096.
12. Seo YG, Choi HC, An AR et al. The Association between Type 2 Diabetes Mellitus and Thyroid Cancer. J Diabetes Res 2017; 2017:5850879.
13. Luo J, Phillips L, Liu S, Wactawski-Wende J, Margolis KL. Diabetes. Diabetes Treatment, and Risk of Thyroid Cancer. J Clin Endocrinol Metab 2016;101:1243–1248.
14. Jee SH, Ohrr H, Sull JW, Yun JE, Ji M, Samet JM. Fasting serum glucose level and cancer risk in Korean men and women. JAMA 2005;293:194–202.
15. Giovannucci E, Harlan DM, Archer MC et al. Diabetes and cancer: a consensus report. Diabetes Care 2010;33(7): 1674–1685.
16. Tabák AG, Jokela M, Akbaraly TN, Brunner EJ, Kivimäki M, Witte DR. Trajectories of glycaemia, insulin sensitivity, and insulin secretion before diagnosis of type 2 diabetes: an analysis from the Whitehall II study. Lancet 2009;373(9682):2215–2221
17. Yildiz SY, Berkem H, Yuksel BC, Ozel H, Kendirci M, Hengirmen S. The rising trend of papillary carcinoma in thyroidectomies: 14-years of experience in a referral center of Turkey. World J Surg Oncol 2014;12:34.
18. Siegel R, Naishadham D, Jemal A. Cancer statistics,2013. CA Cancer J. Clin 2013;63:11-30.
19. WHO Classification of Tumours of Endocrine Organs, Edited by Ricardo V. Lloyd, Robert T. Osamura, Günter Klöppel, Juan Rosai, IARC, Lyon, 2017;p81.
20. Noto H, Tsujimoto T, Sasazuki T, Noda M. Significantly increased risk of cancer in patients with diabetes mellitus: a systematic review and meta-analysis. Endocr Pract 2011;17:616–628.
21. Malaguarnera R, Belfiore A. The insulin receptor: a new target for cancer therapy. Front Endocrinol (Lausanne)

2011;2:93.

22. Djiogue S, NwaboKamdje AH, Vecchio L, et al. Insulin resistance and cancer: the role of insulin and IGFs. Endocr Relat Cancer 2013;20:1–17.

23. Shyang RS, Chiu WY, Chang TC, Tseng CH. Diabetes and Thyroid Cancer Risk: Literature Review. Hindawi Publishing Corporation Experimental Diabetes Research Volume 2012, Article ID 578285.

24. Balasubramaniam S, Ron E, Gridley G, Schneider AB, Brenner AV. Association between benign thyroid and endocrine disorders and subsequent risk of thyroid cancer among 4,5 million U.S male veterans. J.Clin Endocrinol Metab 2012;97:2661-2669.

25. Wang M, Gong WW, Lu F, Hu RY, He QF, Yu M. The association between diabetes and thyroid cancer risk: a hospital-based case-control study in China. BMC Endocr Disord 2021 Jan 28;21:21.

26. International Diabetes Federation Diabetes Atlas. 7th edition.(2015) http://www.diabetesatlas.org. (Erişim tarihi: 15.08.2018).

27. Satman I, Omer B, Tutuncu Y et al. Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. Eur J Epidemiol 2013;28:169–180.

# Sezaryen Oranlarının Robson On Grup Sınıflandırılması ile Değerlendirilmesi: Sezaryen Oranları Azaltılabilir mi?

**Mehmet Unsal[1], Uğurcan Zorlu[2], Gizem Aktemur[1], Nazan Vanlı Tonyalı[1], Elif Gülşah Diktaş[1], Ayşe Gülçin Baştemur[1], Şadıman Kıykaç Altınbaş[1], Tuğba Ensari[1]**

[1]Sağlık Bilimleri Üniversitesi, Etlik Zübeyde Hanım Kadın Hastalıkları ve Doğum EAH, Jinekoloji Bölümü, Ankara, Türkiye
[2]Sağlık Bilimleri Üniversitesi, Bilkent Şehir Hastanesi, Jinekoloji Bölümü, Ankara, Türkiye

**Yazışma Adresi:** Sağlık Bilimleri Üniversitesi, Etlik Zübeyde Hanım Kadın Hastalıkları ve Doğum EAH, Jinekoloji Bölümü, Posta Kodu: 06010, Ankara / Türkiye
e-posta: munsal174@hotmail.com

**Orcid No:** MU: 0000-0002-9920-6804 GA: 0000-0001-6824-881X EGD: 0000-0002-2869-6914 ŞKA: 0000-0003-2773-9641
UZ: 0000-0002-8912-0812 NVT: 0000-0002-7284-6887 AGB: 0000-0001-8362-7324 TE: 0000-0002-7819-5325

**Atıf:** Unsal M, Zorlu U, Aktemur G, ve ark. Sezaryen Oranlarının Robson On Grup Sınıflandırılması ile Değerlendirilmesi: Sezaryen Oranları Azaltılabilir mi? Hitit Med J 2023;5(3):185-189. https://doi.org/10.52827/hititmedj.1304323

## Özet

**Amaç:** Üçüncü basamak bir doğum hastanesinde bir yılda gerçekleşen sezaryen doğumların Robson On Gruplu Sınıflandırma Sistemi kullanılarak analiz edilmesi amaçlanmıştır.

**Gereç ve Yöntem:** 1 Ocak 2019 - 31 Aralık 2019 tarihleri arasında hastanemiz doğum salonuna kabul edilip, hastanemizde doğum yapmış olan ve herhangi bir obstetrik risk faktörü olmayan gebeler çalışmaya dahil edilmiştir. Çalışmamız retrospektif olarak dizayn edilmiştir.

**Bulgular:** Çalışmada 10781 doğuma ait veriler incelendi. Bu doğumların 4391'i sezaryen doğum ile gerçekleşmiştir. Tüm doğumlar içerisinde sezaryen doğum oranı %40,7'dir. Sezaryen doğum yapan gebelerin %9,3'lük kısmı Robson sınıflandırmasına göre birinci grupta, %13,6'sı Robson sınıflandırılmasına göre ikinci grupta yer almıştır. Sezaryen doğum yapan gebelerin %12,1'lik kısmı Robson sınıflandırmasına göre üçüncü grupta, %10,8'i dördüncü gruptadır. Grup 5, grup 6 ve grup 7'nin tüm sezaryen doğumlardaki oranları sırasıyla % 47,7, %2,5 ve %2,6'dır. Robson sınıflandırmasına göre Grup 9 'un tüm sezaryen doğumlar arasındaki oranı ise %1,4'tür.

**Sonuç:** Sonuç olarak, hastanelerin yıllık Robson On Gruplu Sınıflandırma Sistemi Formundaki yüzdelere göre sezaryen doğumlarının izlenmesi ve değerlendirilmesi, kendi sezaryen eylem planlarını hazırlamaları ve belirledikleri sezaryen hedefine göre kalite notlarının değerlendirilmesi de sezaryen oranının azaltılması hedefine katkı sağlayacaktır.

**Anahtar Sözcükler:** Gebelik, Robson On Grup Sınıflandırması, Sezaryen

**Geliş Tarihi:** 28.05.2023
**Kabul Tarihi:** 08.08.2023
**Yayım Tarihi:** 10.10.2023

**Hakem Değerlendirmesi:** Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
**Etik Beyanı:** Çalışma izni 10.10.2019 tarih ve 90057706-799 sayılı TÜEK kararı ile alınmıştır
**İntihal Kontrolleri:** Evet - iThenticate
**Çıkar Çatışması:** Yazarlar arasında çıkar çatışması belirtilmemiştir.
**Şikayetler:** hmj@hitit.edu.tr
**Katkı Beyanı:** Fikir/Hipotez: MU, UZ, GA Tasarım: NVT, EGD, TE Veri Toplama/Veri İşleme: AGB, SKA, TE Veri Analizi: MU, TE, UZ Makalenin Hazırlanması: TE, MU, UZ, GA, NVT, EGT, AGB, ŞKA
**Hasta Onamı:** Onama gerek yoktur.
**Finansal Destek:** Finansal destek alınmamıştır.

# Evaluatıon Of Cesarean Sectıon Rates Using The Robson Ten-Group Classıfıcatıon: Can Cesarean Section Rates Be Reduced?

**Mehmet Unsal[1], Ugurcan Zorlu[2], Gizem Aktemur[1], Nazan Vanli Tonyali[1], Elif Gulsah Diktas[1], Ayse Gulcin Bastemur[1], Sadıman Kiykac Altinbas[1], Tugba Ensari[1]**

[1]Health Sciences University, Etlik Zubeyde Hanim Women's Health Teaching and Research Hospital, Gynecology Clinic, Ankara, Türkiye
[2]Health Sciences University, Bilkent City Hospital, Gynecology Clinic, Ankara, Türkiye

**Adress for Correspondence:**Etlik Zubeyde Hanim Women's Health Teaching and Research Hospital, Gynecology Clinic, Etlik Street, Post code: 06010, Ankara / TURKEY
e-mail: munsal174@hotmail.com

**Orcid ID:** MU: 0000-0002-9920-6804 GA: 0000-0001-6824-881X EGD: 0000-0002-2869-6914 ŞKA: 0000-0003-2773-9641
UZ: 0000-0002-8912-0812 NVT: 0000-0002-7284-6887 AGB: 0000-0001-8362-7324 TE: 0000-0002-7819-5325

**Cite As:** Unsal M, Zorlu U, Aktemur G, et al. Evaluatıon Of Cesarean Section Rates Using The Robson Ten-Group Classıfıcatıon: Can Cesarean Sectıon Rates Be Reduced?? Hitit Med J 2023;5(3):185-189. https://doi.org/10.52827/hititmedj.1304323

## Abstract

**Objective:** The aim of this study was to analyze cesarean deliveries performed within one year at a tertiary level maternity hospital using the Robson Ten-Group Classification System.

**Material and Method:** Pregnant women who were admitted to our hospital's delivery ward and gave birth at our hospital between January 1, 2019, and December 31, 2019, without any obstetric risk factors were included in the study. The study was designed retrospectively.

**Results:** A total of 10,781 deliveries were included in the study. Out of these births, 4,391 were performed via cesarean section. The overall cesarean section rate among all deliveries was 40.7%. Among the women who underwent cesarean section, 9.3% were classified in the first group according to the Robson classification, while 13.6% were classified in the second group. In terms of the Robson classification, 12.1% of the women belonged to the third group, and 10.8% belonged to the fourth group. The rates of Group 5, Group 6, and Group 7 in all cesarean deliveries were 47.7%, 2.5%, and 2.6%, respectively. The rate of Group 9 among all cesarean deliveries according to the Robson classification was 1.4%.

**Conclusion:** In conclusion, monitoring and evaluating cesarean deliveries based on the percentages in the Robson Ten-Group Classification System form on an annual basis can contribute to reducing the cesarean section rate by enabling hospitals to prepare their own cesarean action plans and assessing their quality scores according to the determined cesarean section rate target.

**Keywords:** Cesarean section, Pregnancy, Robson Ten-Group Classification.

**Date of Submission:** 28.05.2023
**Date of Acceptance:** 08.08.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** The work permit was obtained by TUEK decision dated 10.10.2019 and numbered 90057706-799
**Plagiarism Checks:** Yes - iThenticate
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: MU, UZ, GA Design: NVT, EGD, TE Data Collection/Data Processing: AGB, SKA, TE Data Analysis: MU, TE, UZ Article Preparation: TE, MU, UZ, GA, NVT, EGT, AGB, SKA
**Informed Consent:** Not applicable.
**Financial Disclosure:** No financial support has been received.

## Giriş

Sezaryen doğum tıbbi gerekçelerle yapıldığında maternal ve perinatal, mortalite ve morbiditeyi azaltmaktadır. Herhangi bir cerrahi işlemde olduğu gibi, sezaryen doğum sonrasında da kısa ve uzun vadeli riskler mevcuttur (1). Pek çok çalışmada %10'un üzerindeki sezaryen doğum oranlarının anne ve yeni doğan ölüm oranlarında azalma ile ilişkili olmadığı gösterilmiştir (2). Sezaryen ile doğum oranı son on yılda giderek artmaktadır. Türkiye Nüfus Sağlık Araştırması-2008'e göre Türkiye'de % 37 olan sezaryen doğum oranı 5 yıl içinde hızla artarak %48'e ulaşmıştır (3). Sezaryen doğum oranlarındaki artışın nedenlerini ortaya koymak, sezaryen doğum hızlarını belirlemek ve tıbben gereksiz işlemlerden kaçınarak, gerekli durumlarda yapılan en düşük sezaryen doğum hızını hesaplamak önemli ancak bir o kadar da güç bir konudur.

Dünya Sağlık Örgütü (DSÖ), sezaryenle doğum oranlarını azaltmak amacıyla uluslararası düzeyde kullanılabilir, klinikte uygulanabilir ve anlamlı bir sınıflama sistemi önermiştir (4). Bu sınıflama sistemi, basit, sağlam, tekrarlanabilir ve geleceğe yönelik olmalıdır. Aynı zamanda, tartışmalı ve net olmayan durumları ortadan kaldıracak şekilde doğru ve kapsamlı olmalıdır. Robson On Gruplu Sınıflaması (ROGSS) ise bu amaçlar doğrultusunda geliştirilmiştir ve doğum öncesi, intrapartum ve doğum sonrası verilere dayanmaktadır. Gebeleri 10 farklı grupta sınıflandırmak için 5 temel obstetrik parametre kullanılır (5). Bu parametreler şunlardır: parite (nullipar, multipar), geçirilmiş sezaryen öyküsü, doğum eyleminin başlangıcı (spontan, indüklenmiş veya eylem başlamadan sezaryen), gebelik süresi (preterm veya term), fetal prezantasyon (baş, makat veya transvers) ve fetus sayısı (tekil veya çoğul). ROGSS, gebelerin obstetrik özelliklerine göre sınıflandırılmasını sağlar ve böylece gruplar arasında sezaryen doğum oranlarının karşılaştırılmasına ve sezaryen doğuma neden olan faktörlerin belirlenmesine yardımcı olur (6, 7). ROGSS, objektif, tekrarlanabilir, kolay anlaşılabilir ve klinikte kullanıma uygun bir yapıya sahiptir ve doğum eylemine ilişkin riskleri belirlemede önemli bir araç oluşturur.

Robson On Gruplu Sınıflama Sistemi, 2015 yılında uluslararası kurumlar ve resmi kılavuzlar tarafından onaylandıktan sonra, dünya genelinde birçok ülke tarafından hızla benimsenerek kullanılmaya başlanmıştır. Türkiye Cumhuriyeti Sağlık Bakanlığı da Mayıs 2012'den itibaren "ROGSS"nin kliniklerde kullanılmasına karar vermiştir.

Bu çalışmada, Ankara Etlik Zübeyde Hanım Kadın Hastalıkları Eğitim ve Araştırma Hastanesi'nde 1 Ocak 2019 - 31 Aralık 2019 tarihlerinde gerçekleşen sezaryen doğumlar, ROGSS kullanılarak analiz edilmeyi amaçlamaktadır.

## Gereç ve Yöntemler

Çalışma grubumuz, 1 Ocak 2019 - 31 Aralık 2019 tarihlerinde hastanemiz doğum salonuna kabul edilmiş, hastanemizde doğum yapmış olan ve herhangi bir obstetrik risk faktörü olmayan gebeleri kapsamaktadır. Çalışmamız retrospektif olarak dizayn edilmiştir. Çalışma izni 10.10.2019 tarih ve 90057706-799 sayılı TÜEK kararı ile alınmıştır.

Hastalara ait veriler, hastane bilgi sistemi ve doğum kayıtları kullanılarak incelendi. Doğum salonuna ait kayıtlardan hastaların listesine ve doğum şekillerine ulaşıldı. Bu hastaların hastane bilgi sistemindeki kayıtlı özellikleri (demografik özellikler, özgeçmiş, soygeçmiş, eski sonografik ve laboratuvar sonuçları, takip özellikleri, yenidoğan ve doğuma ait nicel veriler) ve doğum kayıtlarında olan bilgileri kullanılarak veri seti oluşturuldu. Hastanemiz Perinatoloji Kliniği tarafından takip edilen; preeklampsi, gestasyonel diyabet, çoğul gebelikler, preterm eylem ve matermal komorbiditesi gibi ek özellikleri olan riskli gebelik olarak sınıflandırılan gebeler ise çalışmamız dışında bırakılmıştır. Belirlenen çalışma süresi boyunca sezaryen ile doğum yapan hastalar Robson On Gruplu Sınıflamasına göre gruplandırılmıştır (Tablo I).

*İstatistik Yöntemler*

Bu çalışmada veri analizinde, IBM SPSS Statistics versiyon 23.0 (Armonk, NY: IBM Corp.) yazılım paketi kullanıldı. Sayısal değişkenlerin normal dağılıma uygun olduğu durumlarda ortalama ± standart sapma şeklinde tanımlayıcı istatistikler verildi. Normal dağılıma uymayan sayısal değişkenler için ise ortanca ve minimum-maksimum değerleri kullanılarak ifade edildi. Kategorik değişkenler ise sayı ve yüzde cinsinden belirtilmiştir. Sürekli değişkenlerin normal dağılımı, Kolmogorov-Smirnov testi gibi analitik yöntemler kullanılarak belirlendi.

**Tablo I.** Robson On Gruplu Sınıflama Sistemi

| ROBSON ON GRUPLU SINIFLAMA SİSTEMİ<br>ROBSON SEZARYEN GRUPLAMASI | |
|---|---|
| Robson Grup | GRUPLAR |
| 1 | Nullipar, tekil, baş geliş, ≥37 hafta, travayı spontan başlamış |
| 2 | Nullipar, tekil, baş geliş, ≥37 hafta, indüklenmiş ya da travay başlamadan önce sezaryen yapılmış |
| 3 | Multipar (eski sezaryenli değil), tekil, baş geliş, ≥37 hafta, travayı spontan başlamış |
| 4 | Multipar (eski sezaryenli değil), tekil, baş geliş, ≥37 hafta, indüklenmiş ya da travaydan önce sezaryen yapılmış |
| 5 | Eski sezaryenli, tekil, baş geliş, ≥37 hafta |
| 6 | Tüm nullipar makatlar |
| 7 | Tüm multipar makatlar (eski sezaryenliler dahil) |
| 8 | Tüm çoğul gebelikler (eski sezaryenliler dahil) |
| 9 | Tüm transvers-oblikler (eski sezaryenliler dahil) |
| 10 | Tüm tekil baş pr. ≤36 hafta (eski sezaryenliler dahil) |

## Bulgular

Çalışmada 10781 doğuma ait veriler incelendi. Bu doğumların 4391'i sezaryen doğum ile gerçekleşmiştir. Tüm doğumlar içerisinde sezaryen doğum oranı %40,7'dir (Tablo II).

Sezaryen ile doğum gerçekleştiren gebelerin %9,3'lük kısmı Robson sınıflandırmasına göre birinci grupta (Nullipar, baş geliş, ≥37 hafta, tekil, travayı spontan başlamış), %13,6'sı Robson sınıflandırılmasında ikinci grupta (nullipar, baş geliş, ≥37 hafta, indüklenmiş ya da travay başlamadan önce sezaryen yapılmış, tekil) yer almıştır. Sezaryen ile doğum gerçekleştiren gebelerin %12,1'lik kısmı Robson sınıflandırmasında üçüncü grupta [Multipar (eski sezaryenli değil), baş geliş, tekil, ≥37 hafta, travayı spontan başlamış], %10,8'i dördüncü gruptadır [Multipar (eski sezaryenli değil), baş geliş, ≥37 hafta, indüklenmiş ya da travay başlamadan önce sezaryen yapılmış başlamış, tekil,]. Grup 5 (Eski sezaryenli, baş geliş, tekil, ≥37 hafta gebelikler), grup 6 (Tüm nullipar makatlar) ve grup 7 (Tüm multipar makatlar, eski sezaryenliler dahil)'nin

**Tablo II.** : 2019 Yılı Robson On Gruplu Sınıflamasına Göre Sezaryen Olgularının Sınıflaması

| Robson Grup | Sezaryen Olan Vaka Sayısı | Toplam Doğum Sayısı | Sezaryen Oranı % | C/S içinde ağırlık |
|---|---|---|---|---|
| 1 | 411 | 2021 | %20,3 | %9,3 |
| 2 | 599 | 2358 | %25,4 | %13,6 |
| 3 | 535 | 2527 | %21,1 | %12,1 |
| 4 | 478 | 1506 | %31,7 | %10,8 |
| 5 | 2076 | 2076 | %100 | %47,7 |
| 6 | 112 | 112 | %100 | %2,5 |
| 7 | 118 | 119 | %99,1 | %2,6 |
| 8 | 0 | 0 | 0 | 0 |
| 9 | 62 | 62 | %100 | %1,4 |
| 10 | 0 | 0 | 0 | 0 |
| GENEL TOPLAM | 4391 | 10781 | %40,7 | |

tüm sezaryen doğumlardaki oranları sırasıyla % 47,7, %2,5 ve %2,6'dır. Robson sınıflandırmasına göre Grup 9 (Tüm multipar makatlar, eski sezaryenliler dahil)'un tüm sezaryen doğumlar arasındaki oranı ise %1,4'tür.

Grupların kendi içlerinde sezaryen doğum oranlarına bakıldığında, grup 5, grup 6 ve grup 9'da bu oran %100'dür. Grup 7'de bu oran %99,1'dir. Diğer gruplar içerisinde oranlara sırasıyla bakıldığında grup 1 %20,3, grup 2 %25,4, grup 3 %21,2, grup 4 %31,7'dir.

Grup 8 ve Grup 10'daki hasta grupları perinataloji kliniğinde takipli olup yüksek riskli gebelikler olduğundan çalışma dışı bırakılmıştır.

## Tartışma

Hastanemizde gerçekleşen %40,7'sinin sezaryen doğum olduğu ve 10781 doğumun incelendiği çalışmamızda sezaryen doğum oranları Robson On Gruplu sınıflandırması ile değerlendirilmiştir. Dünya Sağlık Örgütü, sağlık kuruluşlarında %10- %15 arasında bir sezaryen oranı önermektedir (8). Türkiye Sağlık İstatistikleri datalarına (2019) Türkiye geneli sezaryen doğum oranı % 54,4, primer sezaryen doğum oranı %26,5 olarak hesaplanmıştır (3). Endikasyon dışı sezaryen doğum sonrasında maternal morbidite ve mortalite ile perinatal morbidite riski artmakta ve bu durum hem anne hem yenidoğan sağlığı hem de ekonomik açıdan olumsuz sonuçlara yol açmaktadır (2).

DSÖ tarafından önerilen sezaryen oranlarına ulaşmak için ROGSS gruplarının etkin bir şekilde yönetilmesi gerekmektedir. Sezaryen oranının azaltılması hedefine yönelik olarak, düşük riskli gruplarda (Grup 1 ve 3) azalma, benzer özelliklere sahip gruplarda (Grup 2 ve 4) artış gözlemlenmiştir. Sezaryen oranındaki en büyük katkıyı Grup 5 (geçirilmiş uterin cerrahisi) yapmaktadır. Bu nedenle, çözüm odaklı bir yaklaşımla primer sezaryen oranlarının düşürülmesi, hedefe ulaşmak için en kritik adım olarak kabul edilmektedir. Bu amaca ulaşmak için fetal distress, ilerlemeyen eylem, baş-pelvis uyumsuzluğu gibi endikasyonlar daha net ve objektif kriterlere oturtulmalı, Grup 4 ve 2 için doğum indüksiyonu denenme oranı artırılmalı, makat prezentasyonlarda ve çoğul gebeliklerde uygun gebelerde vajinal doğum şansı denenmeli ve operatif vajinal doğum oranları artırılmalıdır (6).

Bu araştırmada toplam sezaryen doğum oranı %40,7 olarak belirlenmiştir. Farklı merkezlerde yapılan bir çalışmada Souza ve ekibi, sezaryen doğum oranının %30 olduğunu bulmuştur (9). Sezaryen doğum endikasyonları üzerine yapılan tüm çalışmalarda, geçirilmiş uterin cerrahinin en önemli endikasyon olduğu belirtilmiştir (10). Yine, kendi araştırmamızda da en yaygın görülen sezaryen endikasyonu, tüm sezaryenlerin %47,7'sini oluşturan geçirilmiş uterin cerrahidir (grup 5). ACOG'nun 2010 kriterlerine göre, daha önce bir veya iki alt segment transvers insizyon ile sezaryen geçiren hastaların, uygun bir pelvis anatomisine sahip olmaları, fetüsün 4000 gramdan hafif olması, başka bir uterin cerrahi veya uterin rüptür öyküsü olmaması, hasta aktif eylem sırasında monitörize edilebilme ve acil koşullarda sezaryenin uygulanabilme durumlarında vajinal doğumun mümkün olabileceği belirtilmiştir. Ancak, ülkemizde şartlarında, medikolegal endişeler nedeniyle, sezaryen sonrası vajinal doğum seçeneğinin ne yazık ki yetersiz kaldığı belirtilmiştir (11). Buhur ve ekibinin yaptığı bir çalışmada, Grup 6 ve Grup 7'nin sırasıyla %93,81 ve %84,92 olan sezaryen doğum oranları, kendi çalışmamızda da literatüre uygun olarak %100 ve %99,1 olarak bulunmuştur. Bu yüksek oranların, kliniğimizde eksternal sefalik versiyon uygulanmaması ve makat doğumlarında yanlış uygulama korkusunun nedeni olduğu düşünülmektedir (12).

2023 de ülkemizde yapılan bir çalışmada Robson grup 1 %21,31 sezaryen doğum oranına sahiptir. Çalışmamızda da benzer şekilde grup 1 de %20,3 sezaryen doğum oranı vardır (13). Grup 1' deki artış baş pelvis uyumsuzluğu, fetal distres, ilerlemeyen travay gibi endikasyonların tüm doğumlar içerisindeki oranlarının yıllar içerisindeki artışından dolayı kaynaklanmaktadır.

Araştırmamızda bir diğer sık primer sezaryen endikasyonu olarak fetal distress (fetal sıkıntı) saptanmıştır. Altuntaş ve arkadaşlarının yaptığı çalışmada 2000-2007 yılları arasında geçirilmiş sezaryen oranının artışından fetal distres nedeniyle yapılan sezaryenların sorumlu olduğu bulunmuştur (14). Elektronik fetal izlemin artmasıyla birlikte, fetal distress nedeniyle gerçekleştirilen sezaryen doğum sayısında bir artış gözlemlenmiştir. 2012 yılında yapılan bir sistematik analizde, düşük riskli gebeliklerde devamlı elektronik fetal izlemin perinatal mortalite ve morbidite açısından ek fayda sağlamadığı, aksine sezaryen doğum oranını yaklaşık %20 kadar arttırdığı tespit edilmiştir. (15). Antepartum değerlendirmede yaygın olarak kullanılan non stres test (NST), yüksek yanlış pozitiflik oranına sahiptir ve neonatal yoğun bakım ihtiyacını öngörmede güvenilir değildir (16). Ancak literatürde latent fazda kullanılan NST ile fetal iyilik halinin değerlendirilmesinin fetal komplikasyonların öngörülmesinde güvenilir olduğunu belirten çalışmalar da mevcuttur (17). Sezaryen oranlarındaki artışı azaltmak uğruna, fetal takibin özensizce ve yetersiz yapılması da kötü obstetrik sonuçlar doğuracaktır.

Anne adaylarının vajinal doğum, sezaryenin faydaları ve dezavantajları hakkında bilgilendirilmesi ve vajinal doğuma teşvik edilmesi; anne isteğine bağlı sezaryen oranının azaltılmasında önemli bir rol oynayacaktır (18). Robson Grup 1-3'te sezaryen oranının azaltılması için kullanılan stratejiler, ülkeye özgü faktörlerin varlığından ciddi şekilde etkilenir. Türkiye'de isteğe bağlı sezaryen sağlık politikası gereği yapılmamasına rağmen son 10 yılda yaklaşık %50 artış

göstermiştir. Bu artışın nedeni olarak; yüksek tazminatlı malpraktis davalarındaki %35'e varan artışın etkisi olduğunu düşünmekteyiz. Bu süreç ister istemez kadın hastalıkları ve doğum uzmanların tutumlarını, davranışlarını ve uygulamalarını değiştirmiş olabilir. Kadın hastalıkları ve doğum uzmanlarının diğer branşlara göre medikolegal korkular nedeniyle daha defansif davrandıkları Küçük M'nin çalışmasında da gösterilmiştir (19). Tıbbi prosedürler, bu defansif yaklaşımdan önemli ölçüde etkilenir. Örneğin, eksternal sefalik versiyon ve vakum-forseps uygulamaları gibi manevraların kullanımının önemli ölçüde azaldığı görülmektedir (20, 21) Bu yasal düzenlemelerin sağlanması ilerleyen süreçte yükselen sezaryen oranlarının azalmasına yardımcı olabilir. Başer ve ark. da çalışmalarında sezaryen oranlarının azalması için yasal süreçlerin, devlet politikalarının da kadın hastalıkları ve doğum hekimlerinin tutumlarıyla birlikte son derece etkili olabileceğini söylemişlerdir (22).

Çalışmamızın güçlü yanları olarak; tersiyer bir doğum hastanesinde bir yıldaki gerçekleşen doğumların tamamının alınmış olması ve yüksek hasta sayımızı sayabiliriz. Çalışmamızın kısıtlılıkları arasında ise retrospektif bir çalışma olmasını ve riskli gebeliklerin alınmamış olmasını sayabiliriz.

## Sonuç

Sonuç olarak, hastaneler, yıllık Robson On Gruplu Sınıflandırma Sistemi Formu'ndaki oranlara dayanarak sezaryen doğumların izlenmesi ve değerlendirilmesiyle birlikte kendi özgün sezaryen eylem planlarını oluşturmalı ve belirledikleri sezaryen hedefine uygun olarak kalite notlarını gözden geçirmelidir. Bu yaklaşım, sezaryen oranlarının azaltılma hedefine önemli katkılar sağlayacaktır.

## Kaynaklar


1. Betrán AP, Ye J, Moller AB, Zhang J, Gülmezoglu AM, Torloni MR. The Increasing Trend in Caesarean Section Rates: Global, Regional and National Estimates: 1990-2014. PLoS One. 2016;11(2):e0148343.
2. Betran AP, Torloni MR, Zhang J, et al. What is the optimal rate of caesarean section at population level? A systematic review of ecologic studies. Reprod Health. 2015;12:57.
3. Çavlin A. Türkiye Nüfus ve Sağlık Araştırması 2018. 2019.
4. Betran AP, Torloni MR, Zhang JJ, Gülmezoglu AM. WHO Statement on Caesarean Section Rates. Bjog 2016;123(5):667-670.
5. Robson MS. Classification of caesarean sections. Fetal and Maternal Medicine Review 2001;12(1):23-39.
6. Robson M, Hartigan L, Murphy M. Methods of achieving and maintaining an appropriate caesarean section rate. Best Pract Res Clin Obstet Gynaecol 2013;27(2):297-308.
7. Robson M. The Ten Group Classification System (TGCS) - a common starting point for more detailed analysis. Bjog. 2015;122(5):701.
8. WHO statement on caesarean section rates. World Health Organization; 2015.
9. Souza JP, Betran AP, Dumont A, et al. A global reference for caesarean section rates (C-Model): a multicountry cross-sectional study. Bjog 2016;123(3):427-436.
10. Betrán AP, Vindevoghel N, Souza JP, Gülmezoglu AM, Torloni MR. A systematic review of the Robson classification for caesarean section: what works, doesn't work and how to improve it. PLoS One 2014;9(6):e97769.
11. ACOG Practice bulletin no. 115: Vaginal birth after previous cesarean delivery. Obstet Gynecol 2010;116(2 Pt 1):450-463.
12. Buhur A, Öncü N, Erdem D. Analysis of Caesarean Section Rates with the Robson 10 Group Classification. Turkish Journal of Health and Sport Volume. 2022;3(2):53.
13. Buhur A, Erdem D. Changing trends in cesarean section deliveries in a tertiary hospital using the Robson Ten Group Classification. Journal of Contemporary Medicine. 2023;13(2):301-314.
14. Altuntaş H, Dansuk R, Köse O. Sezaryen oranlarının çeşitli değişkenlere bağlı olarak değerlendirilmesi. Kırıkkale Üniversitesi Tıp Fakültesi Dergisi. 2013;15(2):1-7.
15. Devane D, Lalor JG, Daly S, McGuire W, Cuthbert A, Smith V. Cardiotocography versus intermittent auscultation of fetal heart on admission to labour ward for assessment of fetal wellbeing. Cochrane Database Syst Rev. 2017;1(1):Cd005122.
16. Moghimi N, Vahdani-Rashvanlouyi N, Rahmani R, Farazmand T, Nezami H, Chamani V. Fetal Health Assessment by Nonstress Test and its relationship with Neonatal Hospitalization at Birth. Journal of Isfahan Medical School 2021;39(642):697-701.
17. Raouf S, Sheikhan F, Hassanpour S, Bani S, Torabi R, Shamsalizadeh N. Diagnostic value of non stress test in latent phase of labor and maternal and fetal outcomes. Glob J Health Sci 2014;7(2):177-182.
18. Wu JM, Hundley AF, Visco AG. Elective primary cesarean delivery: attitudes of urogynecology and maternal-fetal medicine specialists. Obstet Gynecol 2005;105(2):301-306.
19. Küçük M. Defensive medicine among obstetricians and gynaecologists in Turkey. J Obstet Gynaecol 2018;38(2):200-205.
20. Rauf B, Nisa M, Hassan L. External cephalic version for breech presentation at term. J Coll Physicians Surg Pak 2007;17(9):550-553.
21. Shaaban MM, Sayed Ahmed WA, Khadr Z, El-Sayed HF. Obstetricians' perspective towards cesarean section delivery based on professional level: experience from Egypt. Arch Gynecol Obstet 2012;286(2):317-323.
22. Başer E, Kırmızı Aydoğan D, Özdemirci Ş, et al. An evaluation of cesarean rate in turkey by the Robson ten group classification system: How to reduce cesarean rates? Journal of Surgery and Medicine 2020;4(11):1031-1035.

# Evaluation of Plasma Lipid Levels in Intrahepatic Cholestasis of Pregnancy

**Merve Ozturk Agaoglu[1], Zahid Agaoglu[1], Sevki Celen[2]**

[1]Turkish Ministry of Health Ankara City Hospital, Department of Perinatology, Ankara, Türkiye
[2]Etlik City Hospital, Department of Perinatology, Ankara, Türkiye

**Adres for Correspodence:** Department of Perinatology, Turkish Ministry of Health Ankara City Hospital, Universiteler Mahallesi Bilkent Cad. No: 1 Cankaya/Ankara/Türkiye
e-mail: drmerveoz@gmail.com

**Orcid ID:** MOA: 0000-0002-1283-4032 SC: 0000-0001-7033-3474
ZA: 0000-0001-8726-1075

**Cite As:** Agaoglu Ozturk M, Agaoglu Z, Celen S. Evaluation of Plasma Lipid Levels in Intraheptaic Cholestasis of Pregnancy. Hitit Med J 2023;5(3): 190-194. https://doi.org/10.52827/hititmedj.1321034

## Abstract

**Objective:** To investigate the total cholesterol, triglyceride, LDL, VLDL, and HDL levels of pregnant women diagnosed with intrahepatic cholestasis of pregnancy and to examine the association with disease severity.

**Material and Method:** A total of 80 pregnant women, 40 of whom were diagnosed with intrahepatic cholestasis of pregnancy, and 40 age-matched controls, were prospectively enrolled in this study. Lipid levels were compared among the case and controls, and their association with disease severity was analyzed. Birth weight, birth week, and neonatal outcomes were studied.

**Results:** LDL and VLDL were significantly higher, and HDL levels were lower in the intrahepatic cholestasis of the pregnancy group than in the healthy pregnancies ($p<0.05$). Total cholesterol and triglyceride levels did not differ among the two groups. Birth weight, birth week, and 1-5-minute Apgar scores were lower, and the neonatal intensive care unit admission and the rate of primary cesarean section were higher in the group with intrahepatic cholestasis in pregnancy ($p<0.05$). In correlation analysis, a positive correlation was found between serum LDL and bile acids levels ($r=0.349$, $p=0.027$). LDL levels were significantly higher in severe disease than in mild disease ($p=0.009$)

**Conclusion:** There are significant changes in lipid homeostasis in intrahepatic cholestasis of pregnancy. Abnormal lipid levels, such as high LDL and VLDL levels, could have a role in the pathogenesis, and in particular high LDL levels may contribute to the prediction of disease severity.

**Keywords:** Bile acids, Cholesterol, Intrahepatic cholestasis of pregnancy, Triglycerides

## Özet

**Amaç:** Çalışmamızın amacı, intrahepatik gebelik kolestazı tanılı gebelerde total kolesterol, trigliserid, LDL, VLDL, HDL düzeylerini araştırmak ve hastalık şiddeti ile ilişkisini incelemektir.

**Gereç ve Yöntem:** İntrahepatik gebelik kolestazı tanılı 40 ve benzer yaş grubunda 40 kontrol olmak üzere toplam 80 gebe prospektif olarak çalışmaya dahil edildi. Vaka ve kontrol grubu arasında lipid parametreleri karşılaştırıldı ve hastalık şiddeti ile ilişkisi analiz edildi. Doğum ağırlığı, doğumdaki gebelik haftası ve yenidoğan sonuçları incelendi.

**Bulgular:** İntrahepatik gebelik kolestazı tanılı grupta sağlıklı gebelere göre LDL, VLDL düzeyleri anlamlı olarak daha yüksek ve HDL düzeyleri daha düşük saptandı ($p<0,05$). Total kolesterol ve trigliserid seviyeleri iki grupta benzerdi. Gebelik kolestazı grubunda doğum haftası, doğum kilosu ve 1-5.dakika Apgar skorları daha düşük, yenidoğan yoğun bakıma yatış ve primer sezaryen oranları daha yüksekti ($p<0,05$). Korelasyon analizinde, serum LDL ile safra asiti seviyeleri arasında pozitif yönde korelasyon saptandı ($r=0,349$, $p=0,027$). LDL düzeyi, şiddetli hastalık grubunda hafif hastalık grubuyla karşılaştırıldığında anlamlı olarak yüksekti ($p=0,009$).

**Sonuç:** İntrahepatik gebelik kolestazında lipid homeostazında önemli değişiklikler meydana gelmektedir. LDL ve VLDL yüksekliği gibi anormal lipid düzeyleri gebelik kolestazı patogenezinde rol oynayabilir ve özellikle yüksek LDL kolesterol düzeyi kolestaz şiddetinin tahminine katkıda bulunabilir.

**Anahtar Sözcükler:** Gebeliğin intrahepatik kolestazı, Kolesterol, Safra asitleri, Triglseridler

**Date of Submission:** 30.06.2023
**Date of Acceptance:** 20.08.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** The study was ethically approved by Zekai Tahir Burak Hospital ethics committee (23/2019).
**Plagiarism Checks:** Yes - intihal.net
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: MOA, SC Design: MOA, ZA, SC Data Collection/Data Processing: MOA, ZA Data Analysis: MOA, ZA, SC Article Preparation: MOA, ZA, SC
**Informed Consent:** Informed consents were obtained from the patients.
**Financial Disclosure:** There is no financial support used in the study

## Introduction

Intrahepatic cholestasis of pregnancy (ICP) is a liver disorder characterized by elevated serum liver enzymes and bile acids and widespread pruritus that begins in the second and third trimester of pregnancy (1). The etiology of ICP is not clearly known. Autosomal inheritance, hypersensitivity to estrogen, hormonal changes, environmental factors, and dietary type may play a role in pathogenesis (2-4). Elevated aminotransferase and bile acid levels help diagnose ICP. It is associated with maternal conditions such as postpartum hemorrhage, preeclampsia, preterm delivery, and neonatal conditions such as a higher risk of meconium-stained amnion (1).

The higher prevalence of cholelithiasis is thought to be due to changes in lipid profiles in ICP (5-9). However, it is unclear whether dyslipidemia is the leading cause of ICP or a secondary consequence of liver dysfunction. It is more likely that lipid metabolism plays a role in the pathophysiology of cholestasis, as lipoproteins and their components generate oxidative stress and impair cell membrane fluidity and hepatobiliary transporter and receptor activity, thereby increasing the formation of cholestatic metabolites of placental steroid hormones (4, 10, 11).

This study aims to investigate low-density lipoproteins (LDL), very low-density lipoproteins (VLDL), the total cholesterol, triglycerides (TG), and high-density lipoproteins (HDL) levels of pregnant women diagnosed with ICP and to examine the association with disease severity.

## Material and Method

This prospective study was conducted with 80 patients aged 18-42 between June 2019 and September 2019 at Zekai Tahir Burak Women's Health and Research Hospital, Gynecology and Obstetrics Department. Zekai Tahir Burak Hospital ethics committee approved the study (Decision number: 23/2019). The Declaration of Helsinki was followed, and all participants gave written informed consent.

80 pregnant women, 40 of whom were diagnosed with ICP, and age-matched 40 controls between 28 and 37 weeks gestation, were included in the study. Multiple pregnancies, fetal structural abnormalities, chronic liver disease, viral or nonviral hepatitis, diseases, conditions that block the bile ducts, such as cholelithiasis, hypertensive diseases such as preeclampsia, chorioamnionitis, chronic cardiac, renal, or pulmonary diseases were excluded from the study. ICP diagnosis was made with elevated serum bile acids higher than 10 mmol/L or elevated liver function tests and the presence of pruritus. Pruritus, characterized by exacerbations and abrasions due to nocturnal itching, was usually confined to the palms and feet without any known skin disease or rash. Ultrasonography of the upper abdomen was performed to rule out hepatobiliary disease. ICP patients were divided into 2 groups due to bile acid levels. At range of 10-40, mmol/L were defined as moderate ICP, whereas serum bile acids >40 mmol/L were defined as severe ICP. Maternal blood samples for TG, total cholesterol, aspartate transaminase (AST), alanine transaminase (ALT), LDL, VLDL, and HDL were obtained at diagnosis of cholestasis and measured with the Architect Autoanalyzer (Abbott Park, IL, USA). TBA concentrations were measured in millimoles per liter by a spectrophotometric method.

*Statistical Analysis*

SPSS (IBM SPSS Statistics 24) was used for statistical analysis. Means and standard deviations were used for descriptive variables. The independent-sample t-test was used for parametric distribution, and for nonparametric distribution, the Mann-Whitney U test was performed. The chi-square test was used to analyze the relationship between categorical data. The Spearman correlation test was performed to investigate the correlations. *P-value <0.05* indicates a significant difference.

## Results

A total of 80 patients were enrolled in the study, 40 in the ICP group and 40 in the control group. Table I shows the maternal characteristics and laboratory parameters. When the groups were compared, no statistically significant differences were found in age, gravidity, parity, week of gestation at diagnosis (at the time of blood collection), and body mass index. LDL, VLDL, total bilirubin levels, ALT, and AST, were significantly higher in the ICP group than in healthy pregnancies ($p<0.05$). TG and total cholesterol levels didn't differ in the two groups (Table I).

Birth weight, birth week, and 1-5 minutes Apgar scores were lower in the ICP group, while rates of neonatal intensive care unit (NICU) admission and primary cesarean section rates were higher ($p<0.05$). The rate of meconium-stained amnion was found to be 17.5% in the ICP group and 5% in the control group, with no statistical difference between the groups ($p=0.067$) (Table II).

Correlation analysis revealed a positive correlation betwe-

**Table I.** Characteristics and laboratory parameters of case and control groups

| | Intrahepatic cholestasis of pregnancy group (n=40) | Control group (n=40) | *p -value* |
|---|---|---|---|
| Age, year | 32±5.9 | 30±4.6 | *0.801* |
| Gravida (n) | 2 [1-4] | 2 [1-5] | *0.512* |
| Parity (n) | 1[0-5] | 0 [0-3] | *0.223* |
| Body mass index (kg/m$^2$) | 30 [22-43] | 25 [24-38] | *0.625* |
| Gestational week at diagnosis | 32±2.1 | 31±1.9 | *0.764* |
| Triglyceride (mg/dL) | 262±109 | 255±114 | *0.659* |
| Total cholesterol (mg/dL) | 253±49 | 238±43 | *0.164* |
| LDL (mg/dL) | 165±40 | 145±29 | ***0.015*** |
| VLDL (mg/dL) | 63±28 | 52±15 | ***0.021*** |
| HDL (mg/dL) | 31±14 | 40±12 | ***0.002*** |
| AST (U/L) | 84±14 | 27±8 | ***0.024*** |
| ALT (U/L) | 120 ±23 | 36 ±11 | ***0.001*** |
| Total bilirubin (mg/dL) | 0.70 ±0.30 | 0.21± 0.14 | ***0.042*** |

mean ± standard deviation , median (min-max)
ALT, alanine transaminase; AST, aspartate transaminase; HDL, high-density lipoproteins; LDL, low-density lipoproteins; VLDL, very low-density lipoproteins
*p < 0.05* considered statistically significant

**Table II.** Comparison of pregnancy and neonatal outcomes of study groups

| | ICP group (n=40) | Control group (n=40) | p-value |
|---|---|---|---|
| **Apgar 1.min** | 7 [6-8] | 8 [7-9] | **0.042** |
| **Birth weight (gr)** | 2670±577 | 3050±640 | **0.031** |
| **Birth week** | 36±2.2 | 38±2.4 | **0.043** |
| **Apgar 1.min** | 7 [6-8] | 8 [7-9] | **0.042** |
| **Apgar 5.min** | 9 [7-10] | 10 [9-10] | **0.036** |
| **NICU admission** | 9/40 (22.5%) | 2/40 (5%) | **0.045** |
| **Primary CS rate** | 13/40 (32.5%) | 4/40 (10%) | **0.014** |
| **Meconium stained amnion** | 7/40 (17.5%) | 2/40 (5%) | 0.067 |

mean ± standard deviation, median (min-max), number (%),
CS, cesarean section; NICU, neonatal intensive care unit
Significant at $p < 0.05$

en LDL and serum bile acids (*r=0.349, p=0.027*) (Table III). A positive correlation was also detected between ALT, AST, and serum bile acids (*r=0.512, p=0.001; r=0.345, p=0.043*, respectively). There were 18 patients in the severe ICP group and 22 pregnant women in the mild ICP group. When comparing lipid levels between groups according to disease severity, LDL levels were significantly higher in severe disease than in mild ICP (*p=0.009*) (Table IV).

## Discussion

**Table III.** Correlation of laboratory characteristics and serum bile acid

| ICP (n=40) | Serum bile acid | |
|---|---|---|
| | *r*[a] | *p-value* |
| **LDL (mg/dL)** | *0.349* | *0.027* |
| **VLDL (mg/dL)** | *0.192* | *0.241* |
| **HDL (mg/dL)** | *-0.158* | *0.332* |
| **AST (U/L)** | *0.345* | *0.043* |
| **ALT (U/L)** | *0.512* | *0.001* |

ALT, alanine transaminase; AST, aspartate transaminase; HDL, high-density lipoproteins; Intrahepatic cholestasis of pregnancy; LDL, low-density lipoproteins; VLDL, very low-density lipoproteins
[a] Spearman's correlation coefficient
Significant at $p < 0.05$

**Table IV.** Comparison of lipid levels in groups with mild and severe ICP

| | Mild ICP (n=22) | Severe ICP (n=18) | *p-value* |
|---|---|---|---|
| Total cholesterol (mg/dL) | 232(133-310) | 264 (177-336) | *0.192* |
| Triglyceride (mg/dL) | 300 (184-480) | 278 (119-664) | *0.505* |
| LDL (mg/dL) | 147 (35-208) | 190 (104-251) | *0.009* |
| VLDL (mg/dL) | 65 (36-100) | 60 (23-132) | *0.781* |
| HDL (mg/dL) | 32 (21-67) | 34 (8-60) | *0.227* |

Median (min-max)
HDL, high-density lipoproteins; ICP, intrahepatic cholestasis of pregnancy; LDL, low-density lipoproteins; VLDL, very low-density lipoproteins
$p < 0.05$ considered statistically significant

In this study, we investigated the lipid profile in ICP and its relationship to disease severity. Our results suggest that the lipid profile is impaired in ICP compared with healthy pregnancies and that abnormal lipid levels may have a role in the ICP pathogenesis. In particular, LDL levels might be related to disease severity.

Cholesterol is an essential structural element of the cell membrane and serves as a precursor of bile acids and steroid hormones. Bile acids have a toxic effect on the fetus, and their accumulation in the vascular bed of the placenta is thought to increase the risk of meconium-stained amnion and intrauterine exitus in cases with ICP (12, 13). Because of this relationship between total cholesterol and bile acid, attention has been focused on lipid levels in pregnant women with cholestasis, and there are conflicting results in the literature (7, 14). A recent study found that total cholesterol levels in pregnancies with cholestasis were significantly elevated than in the control group and increased during pregnancy (15). In our study, total cholesterol level was higher in ICP than healthy pregnancies, but this was not statistically significant. The mechanisms behind these changes in lipid metabolism remain unknown. The most likely cause is a disturbance of the hepatobiliary transport system (6, 16). It is not known whether ICP causes the changes in lipid metabolism or whether these changes are due to ICP. In a recent study, plasma LDL concentrations were found to be higher in cholestasis than in pruritis gravidarum patients, and the increase in bile acid levels from 28 weeks of gestation was probably due to an increase in LDL cholesterol (15). These data support our finding that LDL levels were significantly elevated in the group with severe ICP compared with those with mild ICP.

A recent study shows ICP may be part of metabolic disease (17). A growing body of research suggests that the farnesoid X receptor (FXR), the major bile acid receptor, may influence lipid metabolism. Bile acid is now recognized as a signaling molecule, and there is strong evidence that it modulates glucose and lipid balance via FXR (18). Activation of FXR inhibits endogenous bile acid production and lowers plasma levels of TG, cholesterol, and glucose (19). Cholestasis was associated with decreased FXR expression and activity (20). Increased levels of the 3-sulfated progesterone metabolite antagonize FXR in ICP pregnancies, as shown by another study (21). Consequently, decreased FXR activity could play a role in ICP and affect the maternal lipid profile. However, the relationship between ICP and imbalanced lipid profiles needs to be better understood and convoluted, and it could include additional findings such as intestinal flora changes in ICP (22). This close relationship between the bile acid receptor and lipid metabolism may be one of the reasons for the high lipid levels in ICP in our study.

In the current study, LDL and VLDL levels were significantly elevated, while HDL levels were significantly lower in the case group. High levels of cholesterol, especially elevated LDL and TG levels, are one of the main risk factors for atherosclerosis (23). LDL causes atherosclerosis by several mechanisms, such as cytotoxicity to smooth muscle cells. In placental atherosclerosis, there is a decrease in fetal blood flow, which can lead to fetal hypoxia, distress, and intrauterine loss, as well as a decrease in the transfer of oxygen nutrients in the blood (24, 25). Similar to previous studies, the ratio of primary

cesarean section and NICU acceptance were found to be higher, while 1 and 5-minute Apgar scores were lower in the case group (26, 27). An analysis of patients with ICP found an increased risk of meconium-stained amniotic fluid (OR 2.60) (26). The incidence of meconium-stained amniotic fluid was reported to range from 15% to 25% in the intrapartum period in a normal pregnancies and may be a potential indicator of fetal distress (1). Animal studies have shown that fetal colonic motility is increased due to high maternal bile acid, resulting in meconium in amniotic fluid (28). In a study of 713 women with bile acid levels of 40 micromol/L or more, researchers discovered that this group of patients had a higher preterm delivery risk and higher maternal age than healthy pregnancies (27). Although it was not statistically significant, the meconium-stained amniotic fluid rate increased in current study. The advantage of the current study is to evaluate the relationship between lipid profile and severe ICP. Although there are other publications showing worsening of the lipid profile in ICP, the main strength of our article lies in showing the association between high LDL levels and severe cholestasis. Our study's limitation is that apolipoproteins that may play a role in pathogenesis were not included in the lipid profile analysis. Further studies with larger lipid panels may help elucidate the relationship between bile acid and lipid metabolism.

## Conclusion

In conclusion, we demonstrated that LDL and VLDL were higher in ICP than in healthy pregnancies suggesting abnormal lipid levels may play a role in the pathogenesis of ICP. There are significant changes in lipid homeostasis in ICP, and in particular, a high LDL cholesterol level may help predict the severity of the disease.

## References


1. Girling J, Knight CL, Chappell L, Gynaecologists RCo-Oa. Intrahepatic cholestasis of pregnancy: Green-top Guideline No. 43 June 2022. BJOG. 2022;129(13):e95-e114.
2. Yamamoto Y, Moore R, Hess HA, Guo GL, Gonzalez FJ, Korach KS, et al. Estrogen receptor alpha mediates 17alpha-ethynylestradiol causing hepatotoxicity. J Biol Chem 2006;281(24):16625-16631.
3. Rathi U, Bapat M, Rathi P, Abraham P. Effect of liver disease on maternal and fetal outcome--a prospective study. Indian J Gastroenterol. 2007;26(2):59-63.
4. Reyes H, Simon FR. Intrahepatic cholestasis of pregnancy: an estrogen-related disease. Semin Liver Dis 1993;13(3):289-301.
5. Dalén E, Westerholm B. Occurrence of hepatic impairment in women jaundiced by oral contraceptives and in their mothers and sisters. Acta Med Scand 1974;195(6):459-463.
6. Johnson P. Studies in cholestasis of pregnancy with special reference to lipids and lipoproteins. Acta Obstet Gynecol Scand Suppl 1973;27:1-80.
7. Reyes H. The spectrum of liver and gastrointestinal disease seen in cholestasis of pregnancy. Gastroenterol Clin North Am. 1992;21(4):905-21.
8. Nikkilä K, Riikonen S, Lindfors M, Miettinen TA. Serum squalene and noncholesterol sterols before and after delivery in normal and cholestatic pregnancy. J Lipid Res 1996;37(12):2687-2695.
9. Wojcicka J, Sienko J, Smolarczyk R, Romejko E, Grymowicz M, Czajkowski K. Alpha-hydroxybutyrate dehydrogenase activity in intrahepatic cholestasis of pregnancy. Int J Gynaecol Obstet 2005;89(3):247-250.
10. Schachter D. Fluidity and function of hepatocyte plasma membranes. Hepatology 1984;4(1):140-151.
11. Vore M. Estrogen cholestasis. Membranes, metabolites, or receptors? Gastroenterology 1987;93(3):643-649.
12. Sepúlveda WH, González C, Cruz MA, Rudolph MI. Vasoconstrictive effect of bile acids on isolated human placental chorionic veins. Eur J Obstet Gynecol Reprod Biol 1991;42(3):211-215.
13. Monte MJ, Morales AI, Arevalo M, Alvaro I, Macias RI, Marin JJ. Reversible impairment of neonatal hepatobiliary function by maternal cholestasis. Hepatology. 1996;23(5):1208-1217.
14. Johnson P, Samsioe G, Gustafson A. Studies in cholestasis of pregnancy. I. Clinical aspects and liver function tests. Acta Obstet Gynecol Scand 1975;54(1):77-84.
15. Dann AT, Kenyon AP, Wierzbicki AS, Seed PT, Shennan AH, Tribe RM. Plasma lipid profiles of women with intrahepatic cholestasis of pregnancy. Obstet Gynecol. 2006;107(1):106-114.
16. Svanborg A, Vikrot O. Plasma lipids in recurrent jaundice of pregnancy. Acta Med Scand. 1967;181(1):83-7.
17. de Aguiar Vallim TQ, Tarling EJ, Edwards PA. Pleiotropic roles of bile acids in metabolism. Cell Metab 2013;17(5):657-669.
18. Fiorucci S, Mencarelli A, Palladino G, Cipriani S. Bile-acid-activated receptors: targeting TGR5 and farnesoid-X-receptor in lipid and glucose disorders. Trends Pharmacol Sci 2009;30(11):570-580.
19. Chiang JYL, Ferrell JM. Bile acid receptors FXR and TGR5 signaling in fatty liver diseases and therapy. Am J Physiol Gastrointest Liver Physiol 2020;318(3):G554-G573.
20. Keitel V, Dröge C, Häussinger D. Targeting FXR in Cholestasis. Handb Exp Pharmacol 2019;256:299-324.
21. Abu-Hayyeh S, Papacleovoulou G, Lövgren-Sandblom A, Tahir M, Oduwole O, Jamaludin NA, et al. Intrahepatic cholestasis of pregnancy levels of sulfated progesterone metabolites inhibit farnesoid X receptor resulting in a cholestatic phenotype. Hepatology 2013;57(2):716-726.
22. Zhan Q, Qi X, Weng R, Xi F, Chen Y, Wang Y, et al. Alterations of the Human Gut Microbiota in Intrahepatic Cholestasis of Pregnancy. Front Cell Infect Microbiol. 2021;11:635680.
23. National Cholesterol Education Program. Second Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). Circulation 1994;89(3):1333-1445.
24. Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. World J Gastroenterol 2009;15(17):2049-2066.
25. Lammert F, Marschall HU, Glantz A, Matern S. Intrahepatic cholestasis of pregnancy: molecular pathogenesis, diagnosis and management. J Hepatol 2000;33(6):1012-1021.
26. Ovadia C, Seed PT, Sklavounos A, Geenes V, Di Ilio C, Chambers J, et al. Association of adverse perinatal outcomes of intrahepatic cholestasis of pregnancy with biochemical markers: results of aggregate and individual patient data meta-analyses. Lancet 2019;393(10174):899-909.
27. Geenes V, Chappell LC, Seed PT, Steer PJ, Knight M, Williamson C. Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: a pros-

pective population-based case-control study. Hepatology 2014;59(4):1482-1491.

28. Blackwell SC, Wolfe HM, Redman ME, Hassan SS, Berry SM, Treadwell MC, et al. Relationship between meconium staining and amniotic fluid volume in term pregnancies. Fetal Diagn Ther 2002;17(2):78-82.

# Exploring Women's Perspectives on Oral Contraceptives: The Role of Pharmacists in Shaping Attitudes

**Muhammed Yunus Bektay[1], Pınar Nur Demirci[1], Muhammed Atak[2]**

[1]Bezmialem Vakif University, Faculty of Pharmacy, Department of Clinical Pharmacy, Istanbul, Türkiye
[2]Istanbul University, Faculty of Medicine, Department of Public Health, Istanbul, Türkiye

**Adres for Correspodence:** Department of Clinical Pharmacy, Faculty of Pharmacy, Bezmialem Vakif University, 34093, Istanbul, Türkiye
e-mail: yunusbektay@gmail.com

**Orcid ID:** MYB: 0000-0003-2032-9957 MA: 0000-0002-8545-3660
PND: 0009-0001-3982-589X

**Cite As:** Bektay MY, Demirci PN, Atak M. Exploring Women's Perspectives on Oral Contraceptives: The Role of Pharmacists in Shaping Attitudes. Hitit Med J 2023;5(3): 195-201. https://doi.org/ 10.52827/hititmedj.1345245

## Abstract

**Objective:** Over the past two decades, oral contraceptives have emerged as the predominant choice for contraception globally. This study explores women's knowledge, attitudes, and behaviors regarding oral contraceptives and the pharmacist's possible role.

**Material and Method:** From November 2020 to January 2021, we conducted a cross-sectional observational study in Turkey. To assess the women's knowledge attitudes and knowledge level about oral contraceptives, we developed an online questionnaire utilizing Google Forms. The data were gathered through an exponential non-discriminative snowball sampling method. The reliability of the questionnaire was measured by Cronbach α value. The data obtained from the participants were statistically analyzed using principal component factor analysis and chi-square test.

**Results:** This study involved 140 participants, with a mean age of 32.31±14.21. Most participants (77, 55%) reported being single. Among the participants, a notable majority (93, 66.4%) were not utilizing any contraceptive methods, and a statistically significant discrepancy was observed between the married and single women ($p<0.001$, $\chi^2=21.968$). Nearly half of the participants (75, 53.6%) indicated lack of usage of any contraception methods. According to our findings, a substantial portion (76, 54.3%) of participants gathered information about oral contraceptives from sources with lower reliability, including sources like television, Internet, social media, friends, and relatives.

**Conclusion:** The knowledge and attitudes regarding oral contraceptives among different age groups within the Turkish population are not at the desired level. The involvement of community pharmacists, who serve as accessible healthcare professionals, educating women about contraception and family planning, would yield favorable results.

**Keywords:** Contraception, Family planning, Oral contraceptives, Pharmaceutical care, Pharmacist.

## Özet

**Amaç:** Son yirmi yılda, oral kontraseptifler tüm dünyada doğum kontrolü için sık tercih edilen seçenek olarak kullanılmaktadır. Bu çalışmanın amacı, kadınların oral kontraseptiflere ilişkin bilgi, tutum ve davranışlarını ve eczacının olası rolünü araştırmaktır.

**Gereç ve Yöntem:** Kasım 2020-Ocak 2021 tarihleri arasında Türkiye'de kesitsel gözlemsel bir çalışma yürütülmüştür. Kadınların oral kontraseptifler hakkındaki bilgi, tutumlarını ve bilgi düzeylerini değerlendirmek için Google Forms kullanarak çevrimiçi bir anket uygulanmıştır. Veriler, ayrımcı olmayan kartopu örnekleme yöntemiyle toplanmıştır. Anket güvenilirliği Cronbach α değeriyle ölçülmüştür. Katılımcılardan elde edilen veriler faktör analizi ve ki-kare testiyle istatistiksel olarak analiz edilmiştir.

**Bulgular:** Bu çalışmada yaş ortalaması 32,31±14,21 olan 140 katılımcı yer almıştır. Katılımcıların büyük bir kısmı (77, %55) bekâr olduğunu bildirmiştir. Katılımcıların önemli bir çoğunluğu (93, %66,4) herhangi bir kontraseptif yöntem kullanmamaktadır. Evli ve bekar kadınların doğum kontrol yöntemi kullanımları istatistiksel olarak anlamlı düzeyde farklı bulunmuştur ($p<0,001$, $\chi^2=21,968$). Katılımcıların yaklaşık yarısı (75, %53,6) şimdiye kadar herhangi bir doğum kontrol yöntemi kullanmadığını belirtmiştir. Bulgularımıza göre, katılımcıların önemli bir kısmı (76, %54,3) oral kontraseptifler hakkında bilgiyi televizyon, internet, sosyal medya, arkadaşlar ve akrabalar gibi güvenilirliği düşük kabul edilen kaynaklardan edinmiştir.

**Sonuç:** Türk toplumunda farklı yaş gruplarında oral kontraseptiflere ilişkin bilgi ve tutumların istenen düzeyde olmadığı aşikardır. Erişilebilir bir sağlık profesyoneli olarak hizmet veren toplum eczacılarının, kadınları doğum kontrolü ve aile planlaması konusunda eğitmesi olumlu sonuçlar verecektir.

**Anahtar Sözcükler:** Aile planlaması, Eczacı, Farmasötik bakım, Kontraseptif yöntemler, Oral kontraseptif

**Date of Submission:** 18.08.2023
**Date of Acceptance:** 03.10.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** The study has been approved by the Bezmialem Vakif University local Ethics Committee with decision number 19/377.
**Plagiarism Checks:** Yes - iThenticate
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: MYB Design: MYB, PND Data Collection/Data Processing: MYB, PND Data Analysis: MYB Article Preparation: MYB, PND, MA
**Informed Consent:** An electronically signed informed consent was obtained from all individual participants included in the study.
**Financial Disclosure:** The authors declared that this study has received no financial support.

## Introduction

Each year, significant number of women, approximately 80 million, encounter undesired or unplanned pregnancies (1). This leads to around 45 million pregnancies being terminated, with 19 million terminations occurring under unsafe conditions. Notably, 40 percent of these terminations involve women under the age of 25, and tragically, approximately 68,000 women lose their lives due to unsafe abortion practices. In pursuing national development objectives, bolstering and maintaining women's empowerment is a crucial endeavor (1, 2). This empowerment is pivotal for enabling women to fulfill their responsibilities and practices for their fundamental human rights. Empirical evidence points out the association between women's status, empowerment, and critical reproductive outcomes. Notably, enhanced women's status and empowerment correlate with extended birth intervals, reduced rates of unintended pregnancies, and a lower fertility rate. Consequently, ensuring that women and their families have accurate and comprehensive family planning information improves quality of life and community well-being (2, 3).

Family planning initiatives have played a pivotal role in offering women access to contemporary contraceptive methods. These resources empower women to align their fertility preferences effectively, prevent unintended pregnancies, and mitigate potential complications associated with such pregnancies (1–4). Nowadays, family planning has become an integral component of comprehensive women's health initiatives and programs focused on ensuring safe motherhood. Family planning encompasses a range of practices that empower individuals to safeguard themselves against undesired pregnancies, manage the timing between successive pregnancies, exercise control over the number of children they have, and facilitate parenthood for those who have not yet experienced it (4, 5). The utilization of family planning methods has significant implications for advancing the well-being of women, children, and society. By curbing excessive fertility rates that have adverse repercussions on the health of mothers and infants, family planning methods play a pivotal role in safeguarding and enhancing women's and children's health. This, in turn, contributes to the overall health and vitality of the community (2, 4–7).

There are two methods of family planning: modern and traditional. Traditional methods have been used for many years, mostly in less developed countries. Modern methods, on the other hand, are the methods that are being used more frequently day by day with the development of technology. The use of modern contraceptive methods use by women varies according to their sociodemographic characteristics. According to Turkey Demographic and Health Survey (TDHS) 2018 data, the rate of modern contraceptive use among married women in the 15-49 age group is 49% (2). While modern method use is 52.6% in the 40-44 age group, it decreases to 37.4% in the 45-49 age group (2). It is observed that the use of modern methods is higher among women who live in urban areas and have a higher level of education and welfare (2).

Oral contraceptives (OCs) have become the most common contraceptive method in many countries in the last 20 years. In order to reduce the side effects and risks of OCs, the amounts of estrogen and progesterone derivatives contained have been reduced, and new progesterone derivatives have been developed. Thus, OCs have become a safe method since their beneficial effects outweigh their side effects and problems. Today, in developed countries, approximately 24 million married women, or in other words, 14 percent of married women of childbearing age, use oral contraceptives. In developing countries, about 38 million married women (about 6 percent of women of childbearing age) use the OCs pill (6, 7).

The fact that health services that patients receive from pharmacies are more easily accessible and trustworthy positions pharmacists in an important role as health service providers (8). Community pharmacist are valued healthcare team members trained to provide medication therapy management and a range of healthcare and prevention activities. Pharmacists' services could fill the gap in the family planning. Different studies have investigated the role of pharmacists in contraception, and the pharmacist's patient counseling and audit were found beneficial in many aspects (9–13).

The aim of our study is to investigate the possible benefits of the pharmacist by analyzing the level of knowledge, attitudes, and behaviors of women applying to a community pharmacy about OCs.

## Material and Method

From November 2020 to January 2021, a cross-sectional observational study was conducted in Turkey with the participation of women. The participants were selected based on their voluntary participation. The research protocol obtained ethical approval from the Bezmialem Vakif University local Ethics Committee (decision number 19/377). The exponential non-discriminative snowball sampling method was employed to recruit participants, and the study adhered to the reporting standards outlined by the CROSS (A Consensus-Based Checklist for Reporting of Survey Studies) guidelines (14).

The Raosoft sample size calculator software was utilized to determine the sample size. The target population for this study comprised Turkish women residing in Turkey, with an anticipated response rate of around 50%. Under these conditions and considering a 95% confidence interval and 5% margin of error, the calculated minimum sample size required to achieve with a Type 1 error (α) of 5% and a Type II error (β) of 80% was 105 participants. When accounting for a 15% non-response rate across the total sample, the necessary sample size was adjusted to 122 participants (15, 16).

2.2. Questionnaire, Survey Distribution, and Data Collection

To examine women's knowledge, attitudes, and behaviors concerning oral contraceptive (OC) medicines, an online questionnaire was developed using Google Forms. The questionnaire was disseminated through diverse communication channels, including email, direct messages, and social media platforms, accompanied by study details. Respondents were encouraged to share the survey link within their social circles to promote broader participation. The questionnaire consisted of four sections encompassing demographics, OCs' knowledge and behavior, information sources, and trust related to OCs, with 52 items. Respondents provided an electronic consent before participation and a hyperlink of the consent form was embedded in the online survey for individual reference.

The questionnaire was designed based on existing literature and incorporated with dichotomous and five-point Likert scale items (ranging from 1 Strongly Disagree to 5 Strongly

Agree). The main dependent variable was marital status (married or single), assessed through a dichotomous item. The study encompassed multiple independent variables exploring knowledge level, attitude, trust, and information sources concerning OCs.

A panel of three experts provided insights into the survey's language, structure and design, leading to revisions in accordance with their recommendations. Additionally, the questionnaire underwent pre-testing with two individuals experienced in behavior change education. This evaluation involved retrospective cognitive interviews to assess content, format, and wording structure of the questionnaire. A pilot study involving ten participants which were not included in the initial evaluation provided valuable feedback, contributing to improved clarity and comprehensibility.

Following this, a separate group of twelve participants, distinct from the original dataset, completed the questionnaire over two weeks. Survey completion time ranged between 10 to 15 minutes. To assess test-retest reliability, a subset of 12 participants underwent evaluation using the Spearman's rank correlation coefficient, Wilcoxon test, and intraclass correlation coefficient (ICC). The results revealed an insignificantly low correlation of 0.493 ($p>0.05$) and an ICC of 0.872 (95% CI: 0.837-0.903, F: 7,818, $p<0.001$). Furthermore, the questionnaire's reliability was evaluated through Cronbach's alpha test, yielding a value of 0.872 for the survey instrument employed in this study.

*Statistical Analysis*

Continuous variables were summarized using descriptive statistics, including mean, median, standard deviation, and interquartile range (IQR), while categorical variables were presented as frequencies and percentages. The normality of continuous variables was assessed through Kolmogorov-Smirnov, Shapiro-Wilk tests, Q-Q plots, histogram and density analysis, skewness, and kurtosis values. Missing data were excluded from analysis, and Statistical Package for Social Science (SPSS) version 26® and Jamovi version 1.6 software were used for statistical analysis. Statistical significance was defined as $p < 0.05$. The internal consistency of the questionnaire's reliability was evaluated using Cronbach's alpha coefficient. A principal component analysis (PCA) with varimax rotation was performed to assess the 19-item questionnaire. The determination of the number of components was accomplished by considering factors such as total variance explained, scree plot analysis, assumptions tests, factor loadings, and component loadings. The Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy and Bartlett's test of sphericity were employed as well. The data were deemed suitable for the principal component analysis, meeting the following conditions: matrix coefficient ≥ 0.40, KMO sampling adequacy > 0.60, and Bartlett's test of sphericity ≤ 0.05. The mean and standard deviation for each item and determinant component were computed. Both items and components received scores ranging from 1 to 5, following established criteria. Negative-phrased items were reversed in scoring.

## Results

3.1. Sociodemographic Characteristics of Study Participants

This study involved 140 participants with a mean age of 32.31±14.21. Most of the participants (77, 55%) were Single. A large proportion of participants (80 57.1%) were unemployed. Most of the sample had university degrees (114, 81.4%), and the majority had monthly income between 2500 to 10000 Turkish lira (80, 57.14%). Only 29 (14.3%) of the participants reported history of any chronic disease. The majority of the participant who had a child was married individuals (33, 23.6%), and the mean number of children for the total sample was 0.73±1.26. On the other hand, around one-third of the total sample size was not planning to have a child in the near future (92, 65.7). The family structure of the sample is mainly a nuclear family (109, 77.9%); however, a substantial number of the participants lived within their extended family (26, 18.6%). The demographic characteristics of the sample are presented in Table I.

3.2. Preferred contraception methods and Knowledge level of participants about contraception.

According to the results we obtained, the participants' preferred contraception methods and knowledge levels have been presented in Table 2. The most of the women who participated the questionnaire were not using any contraceptive

**Table I.** Sociodemographic Characteristics of Participants (n=140).

| Parameter | Total N, % | Married N, % | Single N, % | *p* |
|---|---|---|---|---|
| | **140, 100%** | **63, 45%** | **77, 55%** | ***NA*** |
| **Age (Mean±SD)** | 32.31±14.21 | 43.2±14.9 | 23.4±2.95 | |
| **Employment Status** | | | | *$\chi^2$=19,347* |
| Employed | 60, 42.9% | 32, 22.9% | 28, 20% | |
| Unemployed | 80, 57.1% | 31, 22.1% | 49, 35% | |
| **Level of Education** | | | | *<0.001* $\chi^2$=24,718* |
| Primary School | 5, 3.6% | 5, 3.6% | 0, 0% | |
| Secondary School | 8, 5.7% | 7, 5% | 1, 0.7% | |
| High School | 13, 9.3% | 11, 7.9% | 2, 1.4% | |
| Graduate | 114, 81.4% | 40, 28.6% | 74, 52.9% | |
| **Comorbidity** | | | | *<0.016* $\chi^2$=6,098* |
| Yes | 20, 14.3% | 14, 10.1% | 6, 4.3% | |
| No | 119, 85% | 48, 34.5% | 71, 51.1% | |
| **Monthly Income (TL)** | | | | *<0.001* $\chi^2$=25,530* |
| 0-2500 | 47, 33.6% | 10, 7.5% | 37,27.8% | |
| 2500-5000 | 51, 36.4% | 22, 16.5% | 29, 21.8% | |
| 5000-10000 | 29, 20.7% | 22, 16.5% | 7, 5.3% | |
| >10000 | 6, 4.3% | 5, 3.8% | 1, 0.8% | |
| **Having a Child** | | | | |
| Yes | 33, 23.6% | 31, 22.1% | 2, 1.4% | *<0.001* $\chi^2$=41,783* |
| No | 107, 76.4% | 32, 22.9% | 75, 53.6% | |
| **Number of Children (Mean±SD)** | 0.73±1.26 | | | |
| 0 | 90, 64.3% | 13, 9.3% | 77, 55% | *<0.001* $\chi^2$=66.872* |
| 1 | 15, 10.7% | 15, 10.7% | | |
| 2 | 20, 14.3% | 20, 14.3% | | |
| 3 | 8, 5.7% | 8, 5.7% | | |
| 4 | 4, 2.9% | 4, 2.9% | | |
| 5 | 3, 2.1% | 3, 2.1% | | |
| **Planning to have Child** | | | | *<0.001* $\chi^2$=14,392* |
| Yes | 48, 34.3% | 11, 7.9% | 37, 26.4% | |
| No | 92, 65.7% | 52, 37.1% | 40, 28.6% | |
| **Smoking** | | | | *>0.05** |
| Yes | 43, 30.7% | 22, 15.7% | 21, 15% | |
| No | 97, 69.3% | 41, 29.3% | 56, 40% | |
| **Alcohol** | | | | *>0.05** |
| Yes | 41, 29.3% | 13, 9.4% | 28, 20.1% | |
| No | 98, 70% | 49, 35.3% | 49, 35.3% | |
| **Family Structure** | | | | *>0.05** |
| Nuclear Family | 109, 77.9% | 53, 39.3% | 56, 41.5% | |
| Extended family | 26, 18.6% | 9, 6.7% | 17, 12.6% | |

* Chi-Square test. NA: Not Applicable.

methods (93, 66.4%), and a statistically significant difference was observed between the married and single women ($p<0.001$, $\chi^2=21,968$). Half of the married women were not using any medical contraception methods. Instead, traditional methods were specified for contraception. On the other hand, almost half of the single women (63, 46%) were not using contraception either. Another interesting finding of our study was that nearly half of the participants did not use any contraception methods 75 (53.6%). The reason for using contraception methods was mainly answered as not to get pregnant 41 (29.28%). Among married women, 11 (42.3%) of them do not need any contraception due to various reasons, tube ligation, menopause, not being sexually active, etc. ($p<0.001$, $\chi^2=40,635$). The question regarding "Have you ever heard OCs" were mainly answered as yes (111, 79.3%). However, only 53 (37.9%) of them ever used oral contraceptive medicine ($p<0.001$, $\chi^2=15,251$). The most common reason for the OCs usage was to prevent pregnancy (81, 57.9%) and OCs use due to any a health-related issues (27, 19.3%), respectively ($p<0.005$, $\chi^2=11,669$). Hence around one out of five participants had no information about the OCs usage (32, 22.9%) (Table II).

3.3. Information sources about contraception and contraception behavior.

Table III presents the obtained results about the information sources about contraception and contraception behavior. According to our results, more than half (76.2%) of the participants get informed about the OCs through less reliable sources such as TV, Internet, social media, friends, and relatives (76, 54.3%). Only 40 (28.6%) participants answered yes to the question, "Does OCs should be prescribed by a physician." Hence about one-third of the participants recommended the OCs to someone else without any doctor visit (50, 35.7%), and 60 (42.9 %) of them did not know what to do about these kinds of recommendations ($p<0.005$, $\chi^2=11,906$). Most of the participant correctly answered the question of when to take OCs during the day (61, 43.6%) ($p<0.01$, $\chi^2=6,848$). One hundred and two of the participants did not quit OCs due to the side effects ($p<0.001$, $\chi^2=25.721$). The participant women's responses regarding the knowledge, attitude, and trust about OC have been summarized in Table 4. In line with the PCA findings, the KMO measure of sampling adequacy was determined to be 0.787, and Bartlett's test exhibited significance ($p < 0.001$). The derived three-factor model explained 53.95% of the overall variance. The Cronbach's alpha coefficients for each component were 0.842, 0.817, and 0.735, respectively.

## Discussion

One hundred and forty women participated in this study, attitudes, behaviors, and knowledge levels of married and single women about OCs were investigated. Married women especially had higher levels of knowledge and attitudes about

**Table II.** Preferred contraception methods and Knowledge level of participants about contraception (n=140).

| Parameter | Total N, % | Married N, % | Single N, % | p |
|---|---|---|---|---|
| | 140, 100% | 63, 45% | 77, 55% | NA |
| **Do you use a type of contraception method?** | | | | <0.001* $\chi^2=21,968$ |
| Yes | 44, 31.4% | 33, 24.1% | 11, 8% | |
| No | 93, 66.4% | 30, 21.9% | 63, 46% | |
| **The reason for contraception** | | | | >0.05* |
| Not to get pregnant | 41, 29.28% | 30, 62.5% | 11, 22.9% | |
| Health-related issues | 3, 2.14% | 4, 8.3% | 3, 6.3% | |
| **Have you ever used any contraception?** | | | | >0.05* |
| Yes | 53, 37.9% | 43, 33.6% | 10, 7.8% | |
| No | 75, 53.6% | 18, 14.1% | 57, 44.5% | |
| **What is the reason for not contraception?** | | | | <0.001* $\chi^2=40,635$ |
| Having a Children | 5, 3.6% | 5, 19.2% | 0 ,0% | |
| Not needed | 19, 13.6% | 11, 42.3% | 8, 30.8% | |
| Other | 2, 1.4% | 1, 3.8% | 1, 3.8% | |
| **Have you ever heard of oral contraceptive medicines?** | | | | >0.05* |
| Yes | 111, 79.3% | 53, 37.9% | 58, 41.4% | |
| No | 29, 20.7% | 10, 7.1% | 19, 13.6% | |
| **Have you ever used any oral contraceptive medicines?** | | | | <0.001* $\chi^2=15,251$ |
| Yes | 53, 37.9% | 35, 25% | 18, 12.9% | |
| No | 87, 62.1% | 28, 20% | 59, 42.1% | |
| **What are the OCs used for?** | | | | <0.005* $\chi^2=11,669$ |
| Not to get pregnant | 81, 57.9% | 46, 32.9% | 35, 25% | |
| Health-related issues | 27, 19.3% | 6, 4.3% | 21, 15% | |
| Do not know | 32, 22.9% | 11, 7.9% | 21, 15% | |
| **What are the benefits of the OCs?** | | | | <0.001* $\chi^2=13,365$ |
| Contraception | 55, 39.3% | 35, 25% | 20, 14.3% | |
| Diseases | 46, 32.9% | 17, 12.1% | 29, 20.7% | |
| Do not know | 39, 27.9% | 11, 7.9% | 28, 20% | |

* Chi-Square test, OCs: Oral contraceptives, NA: Not Applicable.

**Table III.** Information sources about contraception and contraception behavior (n=140).

| Parameter | Total N, % | Married N, % | Single N, % | p |
|---|---|---|---|---|
| | 140, 100% | 63, 45% | 77, 55% | NA |
| **Source of knowledge about oral contraceptive medicines** | | | | >0.05* |
| Physician | 32, 22.9% | 19 14.6% | 13, 10% | |
| Pharmacist | 22, 15.7% | 6, 4.6% | 16, 12.3% | |
| TV, Internet, social media | 30, 21.4% | 12, 9.2% | 18, 13.8% | |
| Relatives and friends | 46, 32.9% | 19, 14.6% | 13, 10% | |
| **Should OCs be prescribed by a doctor?** | | | | >0.05* |
| Yes | 40, 28.6% | 19, 13.6% | 21, 15% | |
| No | 88, 62.9% | 41, 29.3% | 47, 33.6% | |
| Do not know | 12, 8.6% | 3, 2.1% | 9, 6.4% | |
| **Do you recommend OCs for someone else?** | | | | <0.005* $\chi^2=11,906$ |
| Yes | 50, 35.7% | 23, 16.4% | 27, 19.3% | |
| No | 30, 21.4% | 21, 15% | 9, 6.4% | |
| Do not know | 60, 42.9% | 19, 13.6% | 41, 29.3% | |
| **Do you know what is the proper time of the day to take OCs?** | | | | <0.01* $\chi^2=6,848$ |
| Yes | 61, 43.6% | 35, 25.4% | 26, 18.8% | |
| No | 77, 55% | 27, 19.6% | 50, 36.2% | |
| **Have you ever stopped taking OCs due to any side effect?** | | | | <0.001* $\chi^2=25.72$ |
| Yes | 31, 22.1% | 26, 18.6% | 5, 3.6% | |
| No | 102, 72.9% | 35, 25% | 67, 47.9% | |
| Never used | 7, 5% | 2, 1.4% | 5, 3.6% | |

* Chi-Square test, OCs: Oral contraceptives, NA: Not Applicable, TV: Television.

**Table IV.** Participants response regarding the knowledge, attitude, and trust about Oral Contraceptives (n=140)

| | Mean [SD] | Strongly Disagree [n, %] | Disagree [n, %] | Neither Agree nor Disagree [n, %] | Agree [n, %] | Strongly Agree [n, %] |
|---|---|---|---|---|---|---|
| **Knowledge Cronbach's alpha: 0.842** | **2.38 [0.95]** | | | | | |
| *Oral contraceptives cause infertility.* | 2.15 [1.33] | 67 [47.86] | 20 [14.29] | 35 [25] | 6 [4.29] | 12 [8.57] |
| *Oral contraceptives cause hair growth.* | 2.7 [1.46] | 46 [32.86] | 21 [15] | 30 [21.43] | 19 [13.57] | 24 [17.14] |
| *Oral contraceptives cause breast cancer.* | 2.25 [1.37] | 46 [32.86] | 21 [15] | 30 [21.43] | 19 [13.57] | 24 [17.14] |
| *Oral contraceptives cause uterine/ovarian cancer.* | 2.04 [1.27] | 46 [32.86] | 21 [15] | 30 [21.43] | 19 [13.57] | 24 [17.14] |
| *Oral contraceptives cause menstrual irregularities.* | 2.1 [1.5] | 71 [50.71] | 27 [19.29] | 24 [17.14] | 9 [6.43] | 9 [6.43] |
| *Oral contraceptives cause sexual reluctance.* | 2.12 [1.41] | 84 [60] | 10 [7.14] | 18 [12.86] | 11 [7.86] | 17 [12.14] |
| *Oral contraceptives cause weight gain.* | 3 [1.47] | 76 [54.29] | 22 [15.71] | 20 [14.29] | 7 [5] | 15 [10.71] |
| *Oral contraceptives cause depression.* | 2.63 [1.51] | 35 [25] | 21 [15] | 30 [21.43] | 27 [19.29] | 27 [19.29] |
| *Oral contraceptives should not be used continuously.* | 2.93 [1.64] | 51 [36.43] | 24 [17.14] | 25 [17.86] | 16 [11.43] | 24 [17.14] |
| **Attitude Cronbach's alpha: 0.817** | **2.53 [1.18]** | | | | | |
| *It is difficult for women who use contraception to have children again.* | 1.92 [1.39] | 31 [22.14] | 20 [14.29] | 36 [25.71] | 22 [15.71] | 31 [22.14] |
| *I avoid using oral contraceptives.* | 2.43 [1.63] | 81 [57.86] | 22 [15.71] | 9 [6.43] | 7 [5] | 14 [10] |
| *I am afraid of the side effects of oral contraceptives.* | 2.7 [1.52] | 65 [46.43] | 8 [5.71] | 23 [16.43] | 8 [5.71] | 27 [19.29] |
| *I think oral contraceptives are harmful to the body because they contain artificial hormones.* | 3.11 [1.44] | 49 [35] | 12 [8.57] | 25 [17.86] | 17 [12.14] | 37 [26.43] |
| **Trust Cronbach's alpha: 0.735** | **2.82 [0.99]** | | | | | |
| *I believe oral contraceptives are more effective than IUD.* | 2.43 [1.4] | 40 [28.57] | 25 [17.86] | 27 [19.29] | 14 [10] | 26 [18.57] |
| *I believe oral contraceptives are more effective than condoms.* | 3.09 [1.48] | 49 [35] | 19 [13.57] | 35 [25] | 6 [4.29] | 17 [12.14] |
| *I believe oral contraceptives are more effective than pills containing progestogen alone.* | 2.75 [1.42] | 30 [21.43] | 15 [10.71] | 31 [22.14] | 23 [16.43] | 32 [22.86] |
| *I believe oral contraceptives are more effective than withdrawal.* | 3.34 [1.63] | 34 [24.29] | 18 [12.86] | 40 [28.57] | 10 [7.14] | 23 [16.43] |
| *I believe oral contraceptives are less effective than sterilization.* | 2.36 [1.43] | 28 [20] | 13 [9.29] | 23 [16.43] | 11 [7.86] | 54 [38.57] |
| *I believe smokers can use oral contraceptives.* | 2.98 [1.68] | 41 [29.29] | 14 [10] | 15 [10.71] | 20 [14.29] | 40 [28.57] |

IUD: Intrauterine Device, n: Number, SD: Standard Deviation.

OCs. On the other hand, it is observed that women have confidence in OCs in terms of protection but have some concerns about possible side effects. The results of this study pointed out that, there is a need for improvements in the level of knowledge of the women included in our sample, especially those who are single. In addition, it was observed that myths are prevalent among society, and individuals recommending OCs to their friends and relatives without a prescription are other important issues.

It was determined that 42.85% of the women in the study were between the ages of 18-25, 19.64% between 26-35, 15.47% between 36-45, 11.9% between 46-55, 10.11% between 56 and above, respectively. In the study, the average of the female population of reproductive age was 87.96%. In TDHS 2018, it was found that 58.33% of the women were university graduates, 13.09% were master's, doctorate, etc., 10.71% were high school graduates, 10.11% were secondary school graduates, 4.16% were primary school graduates and 3.57% were illiterate. At the same time, according to the results of TDHS 2018, it was observed that the level of knowledge about contraceptive methods and oral contraceptives increased with increasing education levels. When compared with our study, it was observed that the level of education and the level of knowledge progressed in parallel, and it was found to be in common with the results of TDHS 2018 (2). These results show that a significant proportion of women in the 15-49 age group in our country have primary school education. However, as seen in our results, their educational status was high. In our sample women with graduate and postgraduate degrees are at the top of the list. Ahmad et al. (2006) also reported that individuals had a more positive perspective on family planning methods with increasing educational levels. As a result, higher education levels of women may positively affect their attitudes toward family planning and method selection. In addition, many studies in the literature, obtained a significant difference between educational status and contraceptive method use ($p<0.05$) (17–19).

It was found that 76.4% of the participants in the study had no children, 10.7% had one child, 1.34% had two children, 5.7% had three children, and 5% had four or more children. In another study, it was found that families had two children with a rate of 34.8% (20). Different results were obtained in two studies on the number of children selected in accordance with today's economic conditions. The fact that more people who do not have children participated in our study is parallel with the fact that they have not been married. Tehrani et al. found that the number of pregnancies decreased as the educational level of women increased (21). It was found that

the higher the monthly income and education level, the lower the number of pregnancies. This is thought to be because couples postpone having children until the period when their financial status improve (22).

In this study, the utilization of any form of contraceptive method was evaluated and revealed that 31.4% of the participants were using any kind of contraceptive method. According to the results of TDHS, 71% employed contraceptive methods, with 28.5% favoring traditional methods and 42.5% adopting modern approaches. In comparison with our research, a notable disparity emerged, with a higher prevalence of modern methods and a reduced reliance on traditional methods in the TDHS results (2). The results of existing literature reveals a spectrum of contraceptive utilization rates by women, spanning from 57% to 83% (21, 23, 24). The contraceptive usage rate in our results (41%) was found to be beneath both the literature's range and the TDHS 2018 results.

Participants were asked regarding their sources of knowledge or information regarding the oral contraceptives they utilized, revealing that a mere 45.6% were informed by a medical professional such as a physician or pharmacist. In a study by Mayda SA et al. (25), it was found that 55.6% of participants obtained knowledge about oral contraceptives from the general environment, 13.4% from doctors, and 12.3% from pharmacists. Consequently, there exists a clear need for comprehensive education aimed at women, encompassing family planning, contraceptive methods, and, specifically, oral contraceptives. The indispensable role of pharmacists in facilitating informed usage of oral contraceptives and contraception, therefore, becomes evident. Pharmacists should diligently undertake pharmaceutical care activities such as patient education and counselling related to family planning, contraceptive methods, and oral contraceptives. As a result of these cognitive pharmacy services an enhancement in adherence, reduction of side effects, increase in illness perception and optimization of treatment duration can be achieved.

Community pharmacists are responsible for providing family planning services and they should perform comprehensive patient counseling regarding oral contraceptives. This counseling serves the dual purpose of evaluating the appropriateness of the contraceptive method for individual women and providing essential information to those considering the use of oral contraceptives. Eligible women can then acquire the prescribed oral contraceptives from pharmacies or other healthcare facilities, excluding subsequent follow-up visits. If discontinuation of the method is necessary for any reason, consultation with pharmacist would be beneficial. Given that pharmacists constitute easily accessible healthcare providers, their pivotal role in this process is important (26).

Roughly fifty percent of the women participated in the survey believed that OCs might have potential harm to the body due to their content as synthetic hormones, while the remaining half did not share this perspective. This indicates an equipoise of opinion among women on this matter. It is noteworthy that the existing literature does not provide specific evidence regarding potential harm arising from the synthetic hormone nature of these drugs, although prior research has highlighted that synthetic hormones tend to exhibit a higher incidence of side effects compared to natural hormones (17).

A study undertaken at the NHMRC Centre for Research Excellence in Women's Sexual and Reproductive Health in Primary Care (SPHERE) at Monash University in Australia was aimed at investigating the role of community pharmacists in providing contraception (27). The study sought to ascertain the extent of pharmacy services, their feasibility, acceptability, and overall efficacy. The findings of this study suggest that contraception services offered in community pharmacies have the potential to address prevailing sexual and reproductive health disparities on a global scale and enhance patient access to contraception. While pharmacy-based initiatives may not entirely eliminate all barriers to access or drastically reduce unintended pregnancy rates, they undoubtedly hold substantial significance for both pharmacists and patients (27). While some patients might exhibit hesitancy in seeking contraceptive advice from pharmacists, they frequently express contentment with the convenience and approachability of pharmacy services. Overall, these interventions have succeeded in bolstering access to contraceptive options, even though they may not consistently alleviate disparities. It's notable that the health advantages of pharmacy interventions, if present, tend to be modest or unreported in the existing literature. Consequently, further research is warranted to delineate the health outcomes associated with routine contraceptive provision, contraceptive counseling, accessibility, and service delivery. Such endeavors will serve to better elucidate the advantages and efficacy of pharmacy-based interventions in this domain.

This study has some limitations. Initially, given the reliance on self-reported information, individual viewpoints might have influenced the responses received. Secondly, the design of the questionnaires may have elicited reticence in acknowledging misconceptions; nevertheless, the emphasis on safeguarding participants' anonymity and responses helped alleviate this potential predisposition.

## Conclusion

Considering the results, we obtained and the existing literature, the level of knowledge and attitude about OCs in the Turkish women for different age groups is not at the desired level. There is a need for community-wide information programs for a healthier structuring of attitudes and behaviors about contraception and contraceptives, especially in young individuals. The active involvement of community pharmacists, in issues such as contraception and family planning would enhance to better practice. The benefits of pharmaceutical care and counselling services provided by community pharmacists on women's knowledge and attitudes about OCs should be investigated in more detailed studies are necessary to explore this issue in detail.

## Acknowledgment

The authors thank Bezmialem Vakif University for the opportunity. The authors declare no conflict of interest.

## References

1. Teal S, Edelman A. Contraception Selection, Effectiveness, and Adverse Effects: A Review. Amer. Medical Assoc 2021;326(24):2507-2518.
2. Nüfus Etütleri Enstitüsü. 2018 Türkiye Nüfus ve Sağ-

lık Araştırması. Published 2018. https://hips.hacettepe.edu.tr/tr/2018_turkiye_nufus_ve_saglik_arastirmasi-55

3. Skaritanov E, Wilkie G, Kovell LC. Selection, Effectiveness, and Adverse Effects of Contraception. Amer. Medical Assoc 2022;327(15):1504.

4. Simmons RG, Jennings V. Fertility awareness-based methods of family planning. Best Pract Res Clin Obstet Gynaecol 2020;66:68-82.

5. Ganti AK, Hillard PJA. Family planning in adolescents. Curr Opin Obstet Gynecol 2019;31(6):447-451.

6. Black A, Guilbert E, Costescu D, et al. Canadian Contraception Consensus (Part 1 of 4). J Obstet Gynaecol Canada JOGC = J d'obstetrique Gynecol du Canada JOGC 2015;37(10):936-942.

7. Black A, Guilbert E, Costescu D, et al. Canadian Contraception Consensus (Part 3 of 4): Chapter 7, Intrauterine Contraception. J Obstet Gynaecol Canada J d'obstetrique Gynecol du Canada, JOGC 2016;38(2):182-222.

8. Bektay MY, Sancar M, Jadoo SAA, Izzettin FV. Time to change to improve health: clinical pharmacy and pharmaceutical care education in Turkey. J Ideas Heal 2020;3(1):130-134.

9. Kennedy CE, Yeh PT, Gonsalves L, et al. Should oral contraceptive pills be available without a prescription? A systematic review of over-the-counter and pharmacy access availability. BMJ Glob Heal 2019;4(3):e001402.

10. Landau SC, Tapias MP, McGhee BT. Birth control within reach: a national survey on women's attitudes toward and interest in pharmacy access to hormonal contraception. Contraception 2006;74(6):463-470.

11. Irwin AN, Stewart OC, Nguyen VQ, Bzowyckyj AS. Public perception of pharmacist-prescribed self-administered non-emergency hormonal contraception: An analysis of online social discourse. Res Social Adm Pharm 2019;15(6):650-655.

12. Hilverding AT, DiPietro Mager NA. Pharmacists' attitudes regarding the provision of sexual and reproductive health services. J Am Pharm Assoc (2003) 2017;57(4):493-497.

13. Norman W V, Soon JA, Panagiotoglou D, Albert A, Zed PJ. The acceptability of contraception task-sharing among pharmacists in Canada the ACT-Pharm study. Contraception 2015;92(1):55-61.

14. Sharma A, Minh Duc NT, Luu Lam Thang T, et al. A Consensus-Based Checklist for Reporting of Survey Studies (CROSS). J Gen Intern Med 2021;36(10):3179-3187.

15. Hashemi F, Hoepner L, Hamidinejad FS, et al. A comprehensive health effects assessment of the use of sanitizers and disinfectants during COVID-19 pandemic: a global survey. Environ Sci Pollut Res Int 2023;30(28):72368-72388.

16. Sümbül-Şekerci B, Bildik O, Bektay MY, İzzettin FV. Attitudes of medicine, pharmacy, and dentistry students about psychostimulant use to enhance cognition. Int J Clin Pract 2021;75(10):e14608.

17. Dinç A. 40 Yaş Üzeri Evli Kadınların Kontraseptif Tercihlerinin İncelenmesi. Zeynep Kamil medical journal 2018;49(3):251-255.

18. Ezire O, Idogho O, Theophilus A, Ikani S, Oluigbo O. Study on the patterns and trend in contraceptive use in South-South and North-Western zones of Nigeria: 2003–2011. Open Access J Contracept 2014;5:65-72.

19. Adeyemi AS, Olugbenga-Bello AI, Adeoye OA, Salawu MO, Aderinoye AA, Agbaje MA. Contraceptive prevalence and determinants among women of reproductive age group in Ogbomoso, Oyo State, Nigeria. Open access J Contracept 2016;7:33-41.

20. Karabulutlu GO. 15-49 yaş grubundaki kadınların doğum oncesi bakım alma sıklığı ve etkileyen faktorleri belirleme, verilen hizmetin uygunluğunu değerlendirme. Journal of Nursology 2021;24(4):520-530.

21. Tehrani FR, Farahani FK, Hashemi M. Factors influencing contraceptive use in Tehran. Fam Pract 2001;18(2):204-208.

22. Toprak Evcik D, Gokseven Y, Oztürk GZ. Üreme Çağındaki KadınlardaKontrasepsiyon Bilgi Düzeyinin, Tutum ve Davranışlarının Değerlendirilmesi. The Turkish Journal of Family Practice 2020;24(4):203-212.

23. Gotmark F, Andersson M. Human fertility in relation to education, economy, religion, contraception, and family planning programs. BMC Public Health 2020;20(1):265.

24. Gürkaş E MK. Gaziantep İstasyon Aile Sağlığı Merkezi Bolgesindeki 15–49 Yaş Kadınların Aile Planlaması Yontemi Kullanım Düzeyinin Belirlenmesi. Konuralp Medical Journal 2013;5(2):1-3.

25. Mayda As, Bozkurt HB, Arslan T, Dedeli İ, Ozkan MO. Düzce ili kalıcı konutlar bolgesinde 15-49 yaş arası kadınlarda yontem kullanma oranları ve tercih nedenleri. TSK Koruyucu Hekim Bülteni 2005;4(5):265-279.

26. Gorvett Z. The strange truth about the pill. BBC, Futur. Published online 2018. https://www.bbc.com/future/article/20180822-the-birth-control-pill-can-have-male-side-effects

27. SPHERE Centre of Research Excellence. Driving better sexual and reproductive health outcomes for women through primary care. https://www.spherecre.org/

# A Pilot Study: The Effect of COVID-19 on Sonographic Optic Nerve Sheath Diameter Measured for Critical Patient Management

**Seval Komut[1], Nurdan Fidan[2]**

[1] Department of Emergency Medicine, Faculty of Medicine, Hitit University, Corum, Türkiye
[2] Department of Radiology, Faculty of Medicine, Hitit University, Corum, Türkiye

**Address for Correspondence:** Department of Emergency Medicine, Faculty of Medicine, Hitit University, 19040, Corum, Türkiye
e-posta: drsevalkomut@hotmail.com

**Orcid ID:** KS: 0000-0002-9558-4832
FN: 0000-0002-2995-6220

**Cite As:** Komut S, Fidan N. A Pilot Study: The Effect of COVID-19 on Sonographic Optic Nerve Sheath Diameter Measured for Critical Patient Management. Hitit Med J 2023;5(3):202-208 https://doi.org/10.52827/hititmedj.1344000

## Abstract

**Objective:** The aim of this study is to evaluate the effects of the Coronavirus disease 2019 on sonographic optic nerve sheath diameter measurement and thus avoid possible misleading results in clinical practice.

**Material and Method:** Each volunteer was first evaluated using carotid system color Doppler ultrasonography. Patients with a history of PCR-confirmed Coronavirus disease 2019 infection were classified as group 1 and patients without a history of Coronavirus disease 2019 infection were classified as group 2, and sonographic optic nerve sheath diameter values of both groups were analyzed.

**Results:** Of the 123 patients included in the study, 70 (56.9%) were female and 58 (43.1%) were male. 83 (67.5%) of the patients included in the study were in group 1 and 40 (32.5%) were in group 2. The mean sonographic optic nerve sheath diameter values for the groups were 3.53 mm and 3.46 mm, respectively. The sonographic optic nerve sheath diameter differences between the two eyes for the groups were determined to be 0.203±0.139 mm and 0.282±0.2 mm.

**Conclusion:** Due to the variable effects of Severe Acute Respiratory Syndrome Coronavirus-2, the use of sonographic optic nerve sheath diameter measurement in current standards for critical patient management may lead to false-positive or false-negative results.

**Keywords:** COVID-19, Critical patient, Optic nerve, Pandemic, Ultrasonography

## Özet

**Amaç:** Bu çalışmanın amacı, Coronavirüs hastalığı 2019'un merkezi sinir sistemi üzerindeki etkileri ile ilişkili olarak; sonografik optik sinir kılıf çapı ölçümünün güvenilirliğini değerlendirmek ve böylece klinik pratikte olası yanıltıcı sonuçları önlemektir.

**Gereç ve Yöntem:** Her gönüllü öncelikle karotis sistemi renkli Doppler ultrasonografi kullanılarak değerlendirildi. PCR ile doğrulanmış Coronavirüs hastalığı 2019 enfeksiyonu öyküsü olan hastalar grup 1, Coronavirüs hastalığı 2019 enfeksiyonu öyküsü olmayan hastalar ise grup 2 olarak sınıflandırılarak her iki grubun sonografik optik sinir kılıfı çapı değerleri analiz edildi.

**Bulgular:** Çalışmaya dahil edilen 123 hastanın 70'i (%56,9) kadın, 58'i (%43,1) erkekti. Çalışmaya dahil edilen hastaların 83'ü (%67,5) grup 1'de, 40'ı (%32,5) grup 2'de yer aldı. Grupların ortalama sonografik optik sinir kılıfı çapı değerleri sırasıyla 3,53 mm ve 3,46 mm idi. Gruplar için iki göz arasındaki sonografik optik sinir kılıf çapı farkları 0,203±0,139 mm ve 0,282±0,2 mm olarak belirlendi.

**Sonuç:** Severe Acute Respiratory Syndrome Coronavirus-2'nin değişken etkileri nedeniyle, kritik hasta yönetimi için mevcut standartlarda sonografik optik sinir kılıf çapı ölçümünün kullanılması yanlış pozitif veya yanlış negatif sonuçlara yol açabilir.

**Anahtar Sözcükler:** COVID-19, Kritik hasta, Optik sinir, Pandemi, Ultrasonografi

**Date of Submission:** 15.08.2023
**Date of Acceptance:** 23.09.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** Ethical approval for the study was granted by the Non-Interventional Research Ethics Committee of Hitit University (decision no: 13, dated: 31.05.2022)
**Plagiarism Checks:** Yes - iThenticate
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: SK Design: SK Data Collection/Data Processing: SK, NF Data Analysis: SK, NF Article Preparation: SK, NF
**Informed Consent:** Consent was obtained from the patients.
**Financial Disclosure:** No financial support has been received.

## Introduction

The optic nerve, showing continuity with the central nervous system (CNS), protrudes from the diencephalon towards the orbita during embryogenesis and is in the form of three layers, the pia, dura, and arachnoid mater, enclosed in a meningeal sheath (1, 2). The cerebral spinal fluid (CSF) in the subarachnoid space circulates freely in the intraorbital and intracranial compartments. Therefore, changes in intracranial pressure (ICP) are observed with variability in the subarachnoid space around the optic nerve in the orbital compartment (3). When ICP increases, an increase in optic nerve sheath diameter (ONSD) is expected. This measurement of transorbital sONSD is used as a preferred marker for non-invasive monitoring of ICP (4-8). However, it has been emphasized in many studies that for this method to be used safely, the patient should have no history of glaucoma, trauma, or tumor affecting ophthalmic anatomy, endocrinopathy, electrolyte imbalance, or the use of drugs that can affect ICP (1, 9-11). It has also been reported that atherosclerotic or micro embolic processes that can affect the internal carotid artery (ICA)-origin vascularity of the optic nerve, affect sONSD measurements (12). The efficacy of the method will increase with the elimination of these factors or the use of corrected values, thereby preventing misdiagnosis in the critical patient group who need ICP monitoring.

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the agent of coronavirus disease 2019 (COVID-19), first emerged in Wuhan, China in December 2019, and has had profound effects throughout the world (13). A broad range of symptoms are caused by COVID-19, and no specific pathophysiology has yet been revealed. However, it has been reported that the penetration of the CNS by the virus leads to neurological symptoms and complications (14-16). Thromboembolism and microthromboembolic events as well as neural and neurovascular hyperinflammation, are evaluated as the basic neurological effects of COVID-19. Therefore, it is probable that just as all CNS elements are affected, the optic nerve is also affected in patients who have contracted COVID-19 (17, 18). The aim of this study was to evaluate the reliability of the sONSD measurement, which has become more widely used and valuable in recent years, associated with the effects of COVID-19 on the CNS, and to thereby prevent possible misleading results in clinical practice.

## Material and Method

Ethical approval for the study was granted by the Non-Interventional Research Ethics Committee of Hitit University (decision no: 13, dated: 31.05.2022). This study was conducted in the Emergency Medicine and Radiology Clinics of Erol Olçok Training and Research Hospital between June 2022 and January 2022. The study sample comprised healthy hospital employees who volunteered to participate in the study. Volunteers who had undergone cranial Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) imaging for at least 2 months for any reason and no intracranial pathology that can affect ICP, were included in the study. Patients with a history of PCR-confirmed Coronavirus disease 2019 infection were classified as group 1 and patients without a history of Coronavirus disease 2019 infection were classified as group 2, and sonographic optic nerve sheath diameter values of both groups were analyzed.

Exclusion criteria were defined as a history of glaucoma, any surgery affecting the orbital anatomy, electrolyte imbalance, or the use of any medical agent that could cause a change in ICP (19). A record was made for each participant of age, sex, smoking status, COVID-19 positivity confirmed with a polymerized chain reaction (PCR) test, current or pre-COVID-19 use of antiaggregant or anticoagulant drugs, the presence of neurological symptoms at the time of the last PCR positivity, and the pattern of symptoms (visual impairment, loss of sense of smell, vertigo, confusion- dizziness, cephalgia, etc). Hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), and other diseases were defined as comorbidities.

Carotid System Color Doppler Ultrasonography (CD) Technique

Each volunteer was first evaluated using carotid system color Doppler ultrasonography (CD) to exclude significant stenosis and occlusion of the common carotid artery (CCA) and internal carotid artery (ICA). The right and left carotid CD examinations were performed with the subject positioned supine, the head in extension, and the neck turned 30°-45° towards the side being evaluated. Narrowings and occlusions were discounted using B-mode US examination, CD examination, and Doppler spectral analysis with a 40-60 Doppler spectrum angle. After the carotid system CD examination, transorbital sONSD measurements were performed on subjects with no significant carotid artery narrowing.

sONSD measurement Technique

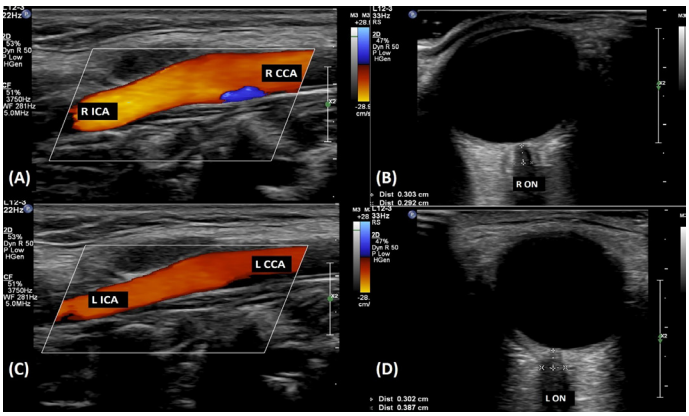
For the sONSD measurement, the subjects were positioned supine with the head and neck elevated 20°-30°, so as not to make any pressure change in the eyes. Before starting the examination, the subjects were instructed to hold this position for at least 1 minute and then close their eyes. Ultrasonic contact gel was applied to the eyelids. The probe was placed on the eyelids and the subjects were instructed to look straight ahead in this position. When the lens, globe, and optic nerve became visible, the brightness and contrast settings were optimized to obtain accurate sONSD measurements. As reported in the literature, the ONSD was measured transversely, perpendicular to the optic nerve, and 3 mm proximal to the optic disc to include hypoechoic lines (Figure I) (1, 20, 21).

Carotid system CD examination and transorbital sONSD measurements were performed by a radiology specialist with 15 years of neuroradiology experience using an Affiniti 70 US device (Philips Healthcare, Amsterdam, Netherlands) with L12-3 and L18-5 high-frequency linear probes.

Statistical Analysis

The data obtained in this study were statistically analyzed using SPSS version 22.0 software (SPSS Inc., Chicago, IL, USA). The conformity of numerical data to a normal distribution was examined using the Shapiro-Wilk and Kolmogorov-Smirnov tests. Descriptive statistics were reported using mean ± standard deviation values for numerical data when normally distributed, and median (min-max) values when the distribution was not normal. Descriptive statistics of categorical variables are reported using numbers (n) and percentages (%). Relationship studies and ratio comparisons between categorical variables were performed using either the chi-square test or Fisher's exact test, depending on the sample sizes in the crosstab cells. The Homogeneity of variances was eva-

**Figure I.** A, The right CD image in the sagittal plane of a 35-year-old female patient; with a history of COVID-19 positivity confirmed by PCR testing, without significant stenosis in the right CCA and ICA. B, Right ONSD is measured 2.9 mm. C, The CD image in the sagittal plane shows that the same patient has no significant stenosis in the left CCA and ICA. D, Left ONSD is measured 3.8 mm. (CCA, common carotid artery; ICA, internal carotid artery; L, left; ON, optic nerve; R, right)




luated using Levene's test. Comparisons of numerical data between two independent groups were performed with the Student's t-test for independent groups when parametric test assumptions were met, and with the Mann-Whitney U test when parametric test assumptions were not met. A value of $p<0.05$ was accepted as statistically significant. Differences were considered statistically significant at $p<0.05$.

## Results

The Evaluation was made of the data of a total of 123 subjects, comprising 70 (56.9%) females and 53 (43.1%) males with a mean age of 35.1±8.25 years (range, 22-60 years). No additional disease was present in 111 (90.2%) subjects, DM was determined in 5 (4.1%), CAD in 5 (4.1%), and HT in 2 (1.6%). Of the total group, 59 were smokers (48%). 83 (67.5%) of the patients included in the study were in group 1 and 40 (32.5%) were in group 2.

The clinical characteristics of the subjects with and without a history of COVID-19 and the statistical findings of the comparisons of the right- and left-eye sONSD values are presented in Table I. No statistically significant difference was found between the groups with and without a history of COVID-19 with respect to age, sex, comorbidities, and smoking status (*p=0.246, p=0.064, p=0.749, and p=0.943*, respectively) (Table I).

The differences in the right-left eye sONSD values were determined to be statistically significantly higher in the group with a history of COVID-19 than in the group without COVID-19 (*p=0.026*) (Table I). The distribution of sONSD differences between the groups is shown as a boxplot in Figure II. No significant difference was found between the groups with respect to the right eye sONSD measurements, left eye sONSD measurements, and the mean sONSD value for the right and left eyes (*p=0.226, p=0.628, p=0.360*, respectively) (Table I).

Subjects who had experienced COVID-19 infection at least once were separated into subgroups of those with and without neurological symptoms. The statistical results of comparisons of the absolute values of the sONSD differences between these two subgroups are shown in Table II. No statistically significant difference was found between the sONSD differences of subjects who had and had not lost a sense of smell, and between those who had and did not have confusion (*p=0.236* and *p=0.099*, respectively).

The sONSD differences of the subjects with visual impairment were determined to be statistically significantly higher than those of the subjects without visual impairment (*p=0.012*). The sONSD differences of the subjects with vertigo were determined to be statistically significantly higher than

**Table I.** Statistical findings regarding the comparison of socio-demographic characteristics and Optic Nerve Sheath Diameter (ONSD) differences of patients between groups

| | | COVID-19 negative (n=40) | COVID-19 positive (n=83) | *P values* |
|---|---|---|---|---|
| **Gender** | **Male**<br>**Female** | 22 (55%)<br>18 (45%) | 31 (37.3%)<br>52 (62.7%) | 0.064* |
| **Additional disease** | **No**<br>**Yes** | 37 (92.5%)<br>3 (7.5%) | 74 (89.2%)<br>9 (10.8%) | 0.749† |
| **Smoking** | **No**<br>**Yes** | 21 (52.5%)<br>19 (47.5%) | 43 (51.8%)<br>40 (48.2%) | 0.943* |
| **Age** | | 33.85±8.09 | 35.70±8.3 | 0.246‡ |
| **ONSD difference (mm)** | | 0.203±0.139 | 0.282±0.2 | 0.026‡ |
| **ONSD right (mm)** | | 3.43±0.41 | 3.54±0.48 | 0.226‡ |
| **ONSD left (mm)** | | 3.49±0.44 | 3.53±0.43 | 0.628‡ |
| **ONSD mean (mm)** | | 3.46±0.41 | 3.53±0.42 | 0.360‡ |

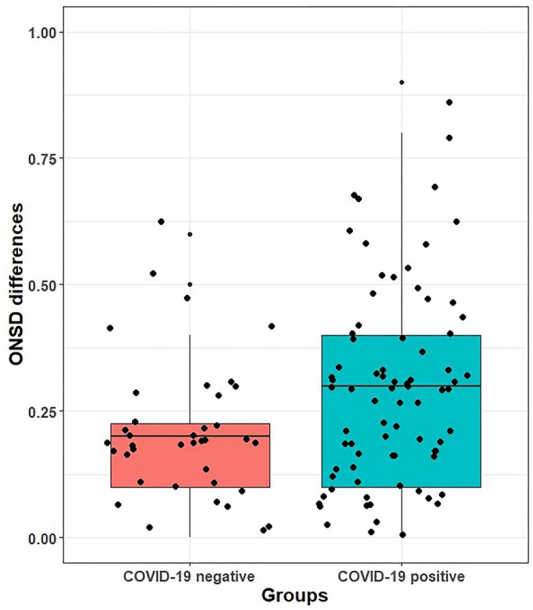
*Chi-square test
†Fisher exact test
‡Student's t-test with mean±standard deviation
ONSD: Optic Nerve Sheath Diameter

**Table II.** Statistical findings for the comparison of Optic Nerve Sheath Diameter (ONSD) differences between groups formed according to neurological symptoms

| | | ONSD difference | *P values* |
|---|---|---|---|
| **Loss of smell** | **No (n=53)** | 0.262 ± 0.199 | *0.236‡* |
| | **Yes (n=30)** | 0.316 ± 0.2 | |
| **Defect of vision** | **No (n=79)** | 0.269 ± 0.193<br>0.3 (0 - 0.9) | ***0.012§*** |
| | **Yes (n=4)** | 0.525 ± 0.189<br>0.45 (0.4 - 0.8) | |
| **Vertigo** | **No (n=78)** | 0.262 ± 0.186<br>0.25 (0 - 0.9) | ***0.001§*** |
| | **Yes (n=5)** | 0.58 ± 0.178<br>0.6 (0.4 - 0.8) | |
| **Confusion** | **No (n=73)** | 0.268 ± 0.193 | *0.099‡* |
| | **Yes (n=10)** | 0.38 ± 0.229 | |
| **Headache** | **No (n=61)** | 0.255 ± 0.16 | ***0.046‡*** |
| | **Yes (n=22)** | 0.354 ± 0.273 | |
| **At least one neurological symptom** | **No (n=37)** | 0.218 ± 0.144 | ***0.009‡*** |
| | **Yes (n=46)** | 0.332 ± 0.224 | |

‡Student's t-test with mean±standard deviation
§Mann Whitney U test with mean±standard deviation and median (min-max)
ONSD: Optic Nerve Sheath Diameter

**Figure II.** Boxplot showing the distribution of ONSD differences between COVID-19 positive and negative patient groups

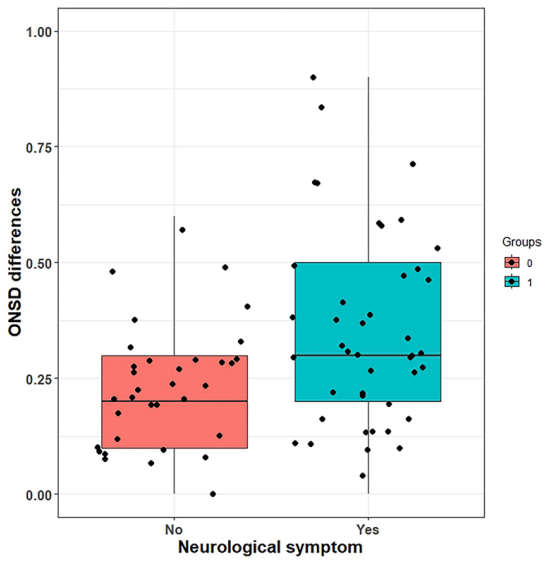



those of the subjects with no vertigo (*p=0.001*). The sONSD differences in the subjects with headaches were determined to be statistically significantly higher than those in the subjects without headaches (*p=0.046*). The sONSD differences of the subjects with at least one neurological symptom were determined to be statistically significantly higher than those of the subjects with no neurological symptoms (*p=0.009*). The distribution of the right-left eye sONSD differences between the subjects with at least one neurological symptom and those with no neurological symptoms is shown as a boxplot in Figure III.

## Discussion

Since the onset of the destructive effects of COVID-19 worldwide, neurological symptoms throughout the course of the disease indicate that SARS-CoV-2 creates potential CNS involvement in patients (14, 15). The SARS-CoV-2 virus binds to cells on angiotensin-converting enzyme (ACE)-2 receptors (22). Therefore, it can be said that cells with ACE-2 receptors are more sensitive to the virus and a priority target. In addition to neuronal and glial cells, ACE-2 receptors are also located in Müller, ganglion, retinovascular endothelial, and photoreceptor cells (15, 23). The widespread presence of ACE-2 receptors in both neural and non-neural tissues in the CNS has been shown to be a basic cause of the neuroinvasive behavior of the SARS-CoV-2 virus (14). This reveals that the retina and optic nerve are extremely likely to be affected in patients with COVID-19. However, it has also been reported that in addition to endothelial cell dysfunction, SARS-CoV-2 infection creates hypercoagulability due to intense thrombin production (24, 25). Associated with this, cerebrovascular events (CVE) and various neurological symptoms have been reported to be caused by hypercoagulability status, hypoxemia, ischemia, and severe inflammation (26-28). This strengthens the hypothesis that COVID-19 triggers non-arteritic anterior optic neuropathy (29). Blood flow to the optic nerve is provided by the ophthalmic artery, which includes common arterial variations (30). Therefore, when it is considered that the optic nerve is directly affected by significant stenoses or occlusions in the CCA or ICA, there is a high probability that this sensitive structure fed by the terminal branches of the ICA is exposed to microembolic ischemia caused by SARS-CoV-2 (12).

**Figure III.** Boxplot showing the distribution of ONSD differences among COVID-19 positive patients with at least one neurological symptom and those without any neurological symptoms




Spectral-domain (SD)-Optical Coherence Tomography (OCT) is a non-invasive, high-resolution imaging method, that provides cross-sectional evaluation of the retina and optic disc. It plays an important role in the quantitative evaluation of the optic nerve head (ONH) and the thickness of the peripapillary retinal nerve fiber layer (pRNFL) (31, 32). The retina and optic nerve are accepted as intraorbital extensions of the CNS. Therefore, quantitative changes determined with OCT in the retina, ONH, and RNFL can be evaluated as being associated with CNS pathologies. It has been shown in the literature that when ICA narrowing occurs, morphological changes can occur in the retina depending on the severity of the narrowing, and data obtained with OCT have shown that the macula and RNFL thicknesses are reduced in these cases (33-35).

In studies that have examined OCT data of patients who have contracted COVID-19, changes in RNFL thickness have drawn attention, and ONH involvement has been indicated in COVID-19 (14, 18, 36, 37). SARS-CoV-2 causes hypercoagulability and micro embolic processes, which show neurotropic and neuroinvasive behavior and can undoubtedly show similar morphological effects created in the RNFL on the optic nerve. This can give rise to misleading results in sonographic transorbital ONSD measurements, which have become more important in recent years in emergency departments and in the monitoring of critical patients in intensive care units. Therefore, as false positive or false negative results in this method can lead to irreversible clinical errors, its reliability must be investigated to be able to continue effective use after the COVID-19 pandemic.

In the current study, no significant difference was found between ONSD values measured by transorbital sonography in cases with a history of PCR-confirmed COVID-19 infection and those with no history of COVID-19 infection. There is no clear consensus on the subject of normal sONSD values in healthy adults. In the current study, the mean sONSD valu-

es for the groups who had or had not experienced COVID-19 were 3.53 mm and 3.46 mm, respectively. Although these values were consistent with the normal sONSD range in healthy volunteers and studies conducted in a European population, they were lower than the results of some studies in different populations (20, 38-42). There are no studies in the literature that have examined sONSD values in COVID-19 patients or those who have recovered. Studies conducted with OCT have reported different results, such as thickening, thinning, or no significant change in the RNFL in COVID-19 patients compared to those with PCR-negativity (36, 37, 43). In the current study, although not statistically significant, the fact that the sONSD values were higher in the group with a history of COVID-19 compared to the other group, supports the variable effects of SARS-CoV-2 on the optic nerve, similar to the results of OCT-based studies.

The basis for the use of transorbital sONSD measurement in the early diagnosis of unilateral intracranial pathologies is the difference that emerges between the right-left eye sONSD measurements associated with ICP increase on the side of the pathology, creating expansion on the ipsilateral optic nerve sheath. Studies in the literature have revealed the reliability of this method and although differences are seen in the studies, it has been attempted to determine cut-off values in healthy individuals taking sONSD asymmetry into consideration (1). In a study of 129 patients that examined the relationship between carotid system narrowing and sONSD thickness, the sONSD difference was reported to be 0.05±0.05 mm for both eyes in the group with no difference in respect to carotid pathology (12). Another study examined sONSD differences in ischemic stroke patients and reported the mean sONSD difference in healthy individuals to be 0.07±0.06 mm (10). The sONSD thickness was determined in elderly volunteers in another study, and the sONSD difference between both eyes was determined to be 0.15±0.17 mm in females and 0.18±0.19 mm in males, and it was emphasized that the sONSD difference was independent of age (11, 20). Other studies that have performed sONSD measurements in healthy volunteers of different ethnic populations have reported no significant differences between the right and left eye sONSD values (39, 44, 45).

In the current study, the sONSD difference between the two eyes was determined to be 0.203±0.139 mm in the group with a history of PCR-confirmed COVID-19 infection and 0.282±0.2 mm in the group with no history of COVID-19. These differences were larger than the sONSD differences reported in the literature for healthy individuals, and this can cause false-positive results in ICP monitoring related to sONSD measurement in patients with COVID-19.

Cut-off values for a unilateral ICP increase show a difference in the literature, and in one of these studies, a cutoff value of 0.45 mm was reported to have 80% sensitivity and 60% specificity (1). Another study that investigated the diagnostic efficacy of sONSD in patients with acute ischemic stroke reported a cutoff value of 0.29±0.06 mm (10). Although the right-left eye sONSD difference determined in the current study subjects with a history of COVID-19 exceeded these cutoff values, it is highly likely that it could cause false-positive or false-negative results even in critical patient management. Therefore, this value could be used to determine the corrected sONSD. However, in cases of suspected unilateral intracranial pathology, the question of which side-corrected sONSD should be used must be answered.

Symptoms such as dizziness, headache, loss of taste or smell, vertigo, and visual loss or impairment have been reported in COVID-19 patients (13). There are studies in the literature that have used OCT to examine the relationship between the presence and frequency of neurological symptoms in the course of COVID-19 with the optic nerve (13). However, no study has investigated the relationship between sONSD and neurological symptoms after disease onset. In the current study, the right-left eye sONSD differences in cases with at least one neurological symptom during COVID-19 infection were found to be significantly higher than those in cases with no neurological symptoms. The sONSD differences in the cases with visual impairment, vertigo, and/or headache during COVID-19 infection were higher than those in the cases with other symptoms. Studies have reported that the frequency of neurological symptoms in COVID-19 patients with have is 40% (46). From this result, it is clear that the right-left eye sONSD difference determined in cases with a history of COVID-19 will make ICP monitoring more difficult in cases with visual impairment, vertigo, and headache symptoms during the disease.

The relationship between the range of COVID-19 symptoms and the neurotropic behavior characteristics of SARS-CoV-2 is not yet clearly understood. However, the data obtained in this study demonstrated the effect of COVID-19 on sONSD measurements. To continue to safely use transorbital sONSD measurements in critical patient care units and emergency departments, there is a need for further studies with larger cohorts to present quantitative data and standardize this effect.

The statements of the current study participants that they had not had COVID-19 were confirmed by checking their health records, the hospital information system, and the healthcare network. Although the other demographic variables were similar in both groups, it is possible that there were some cases of asymptomatic disease or that SARS-CoV-2 positivity was not proven by PCR, which constitutes the most important limitation of this study.

Although the data obtained in this study opens up a discussion of the utility of sONSD in ICP monitoring and the best use of this method which has been standardized in many recent studies, there remains a need for further studies with larger patient groups. Histopathological studies that reveal the neuroinvasive character of SARS-CoV-2 will undoubtedly make a great contribution in this respect.

Limitations

Optic nerve diameter can be affected by age, gender, and previous chronic diseases. Studying in homogeneous groups may be beneficial in eliminating these effects. However, Coronavirus disease 2019 patients admitted to the emergency department do not consist of a certain age and gender. In order to create an accurate sample, patients of all age groups presenting with Coronavirus disease 2019 were included in the study (47).

## Conclusion

Transorbital sONSD measurement has become the preferred method for non-invasive ICP monitoring. However, this study was the first to examine the effect of COVID-19 on the reliability of this method. The data obtained in this study sup-

port the findings of previous OCT-based studies and have revealed varying effects of SARS-CoV-2 infection on sONSD. Certainly; future studies in which US and OCT will be used simultaneously will provide more effective results. This demonstrates that the existing standards for the use of this method, which has proven efficacy in critical patient management, could lead to false-positive or false-negative results. As this study has made the reliability of this method debatable, further studies with larger patient groups and different populations are needed to test the reliability of this method after COVID-19.

Acknowledgements: We thank Dr. Erdal KOMUT for editing of the manuscript.

## References

1. Komut E, Kozacı N, Sönmez BM, et al. Bedside sonographic measurement of optic nerve sheath diameter as a predictor of intracranial pressure in ED. The American journal of emergency medicine 2016;34:963-967.

2. Hirzallah MI, Lochner P, Hafeez MU, et al. Quality assessment of optic nerve sheath diameter ultrasonography: Scoping literature review and Delphi protocol. Journal of Neuroimaging 2022;32:808-824.

3. Hansen H, Helmke K. The subarachnoid space surrounding the optic nerves. An ultrasound study of the optic nerve sheath. Surgical and radiologic anatomy: SRA 1996;18:323-328.

4. Maissan IM, Dirven PJ, Haitsma IK, et al. Ultrasonographic measured optic nerve sheath diameter as an accurate and quick monitor for changes in intracranial pressure. Journal of neurosurgery 2015;123:743-747.

5. Geeraerts T, Launey Y, Martin L, et al. Ultrasonography of the optic nerve sheath may be useful for detecting raised intracranial pressure after severe brain injury. Intensive care medicine 2007;33:1704-1711.

6. Robba C, Santori G, Czosnyka M, et al. Optic nerve sheath diameter measured sonographically as non-invasive estimator of intracranial pressure: a systematic review and meta-analysis. Intensive care medicine 2018;44:1284-1294.

7. Dubourg J, Javouhey E, Geeraerts T, Messerer M, Kassai B. Ultrasonography of optic nerve sheath diameter for detection of raised intracranial pressure: a systematic review and meta-analysis. Intensive care medicine 2011;37:1059-1068.

8. Yılmaz F, Sonmez BM, Kavalci C, Arslan ED, Caliskan G, Beydilli I. Efficacy of bedside optic nerve sheath diameter measurement in differentiating provoked seizure from unprovoked seizure in the emergency department. Annals of Saudi Medicine 2023;43:42-49.

9. Bekerman I, Sigal T, Kimiagar I, Almer ZE, Vaiman M. Diagnostic value of the optic nerve sheath diameter in pseudotumor cerebri. Journal of Clinical Neuroscience 2016;30:106-109.

10. Kozaci N, Avci M, Caliskan G, Yuksel S. Variability of optic nerve sheath diameter in acute ischemic stroke. Hong Kong Journal of Emergency Medicine 2020;27:223-228.

11. Yagar A, Kozaci N, Avci M, Yildiz S, Karaman, Y. Determination of optic nerve sheath diameter variability with age in pediatric groups and comparison of increased intracranial pressure and optic nerve sheath diameter in pediatric patients with head trauma. Ann Med Res 2018;25:460.

12. Komut E, Murat M, Büyükşireci M, Komut S, Kozaci N. Relationship between internal carotid artery stenosis grade and optic nerve sheath diameter measured by transorbital ultrasonography. Journal of Clinical Ultrasound 2021;49:724-730.

13. Burgos-Blasco B, Güemes-Villahoz N, Vidal-Villegas B, et al. Optic nerve and macular optical coherence tomography in recovered COVID-19 patients. European Journal of Ophthalmology 2022;32:628-636.

14. Abrishami M, Daneshvar R, Emamverdian Z, Tohidinezhad F, Eslami S. Optic nerve head parameters and peripapillary retinal nerve fiber layer thickness in patients with coronavirus disease 2019. Ocular Immunology and Inflammation 2022;30:1035-1038.

15. Zhou Z, Kang H, Li S, Zhao X. Understanding the neurotropic characteristics of SARS-CoV-2: from neurological manifestations of COVID-19 to potential neurotropic mechanisms. Journal of neurology 2020;267:2179-2184.

16. Jossy A, Jacob N, Sarkar S, Gokhale T, Kaliaperumal S, Deb AK. COVID-19-associated optic neuritis–A case series and review of literature. Indian Journal of Ophthalmology 2022;70:310.

17. Pansell J, Rudberg PC, Bell M, Friman O, Cooray C. Optic nerve sheath diameter is associated with outcome in severe Covid-19. Scientific Reports 2022;12:17255.

18. Burgos-Blasco B, Güemes-Villahoz N, Donate-Lopez J, Vidal-Villegas B, García-Feijóo J. Optic nerve analysis in COVID-19 patients. Journal of Medical Virology 2021;93:190.

19. Demir TA, Yılmaz F, Sönmez BM, Karadaş MA, Okudan RN, Keskin O. Association of optic nerve sheath diameter measurement with hyponatremia in emergency department. The American Journal of Emergency Medicine 2019;37:1876-1879.

20. Avci M, Kozaci N, Komut E, Komut S, Caliskan G, Tulubas G. The measurement of elderly volunteers' optic nerve sheath diameters by ocular ultrasonography. Medicina.2019;55:413.

21. Akça E, Yılmaz F, Baltacıoğlu B, Tiftikçi İ, Arslan ED, Kavalcı C, et al. Bedside Ultrasonographic Assessment of the Optic Nerve Sheath Diameter to Assess Intracranial Pressure in Patients Given Ketamine in Emergency Department. Albanian Journal of Trauma and Emergency Surgery 2023;7:1273-1278.

22. Liu M-Y, Zheng B, Zhang Y, Li J-P. Role and mechanism of angiotensin-converting enzyme 2 in acute lung injury in coronavirus disease 2019. Chronic Diseases and Translational Medicine 2020;6:98-105.

23. Choudhary R, Kapoor MS, Singh A, Bodakhe SH. Therapeutic targets of renin-angiotensin system in ocular disorders. Journal of current ophthalmology 2017;29:7-16.

24. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. Journal of thrombosis and haemostasis 2020;18:1094-1099.

25. Schmitt FCF, Manolov V, Morgenstern J, et al. Acute fibrinolysis shutdown occurs early in septic shock and is associated with increased morbidity and mortality: results of an

observational pilot study. Annals of intensive care 2019;9:1-15.

26. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The lancet 2020;395:507-513.

27. Zhang Y, Cao W, Xiao M, et al. Clinical and coagulation characteristics in 7 patients with critical COVID-2019 pneumonia and acro-ischemia. Zhonghua xue ye xue za zhi 2020:302-307.

28. Nunes NDSM, Nascimento JSFD, Nascimento JKFD, et al. Brain and Covid-19: an integrative review. E-CRONICON NEUROLOGY 2020;12.

29. Catharino A, Neves M, Nunes N, Nascimento, JS, Nascimento JK. COVID-19 related optic neuritis: Case report. J Clin Neurol Neurosci 2020;1.

30. Prasad S, Galetta SL. Anatomy and physiology of the afferent visual system. Handbook of clinical neurology 2011;102:3-19.

31. Holló G, Zhou Q. Evaluation of retinal nerve fiber layer thickness and ganglion cell complex progression rates in healthy, ocular hypertensive, and glaucoma eyes with the Avanti RTVue-XR optical coherence tomography based on 5-year follow-up. Journal of Glaucoma 2016;25:e905-e909.

32. Cabrera DeBuc D, Gaca-Wysocka M, Grzybowski A, Kanclerz P. Identification of retinal biomarkers in Alzheimer's disease using optical coherence tomography: recent insights, challenges, and opportunities. Journal of clinical medicine 2019;8:996.

33. Çakır A, Düzgün E, Demir S, Çakır Y., Ünal MH. Spectral-domain optical coherence tomography findings in carotid artery disease. Turkish Journal of Ophthalmology 2017;47:326.

34. Sayin N, Kara N, Uzun F, Akturk IF. A quantitative evaluation of the posterior segment of the eye using spectral-domain optical coherence tomography in carotid artery stenosis: a pilot study. Ophthalmic Surgery, Lasers and Imaging Retina 2015;46:180-185.

35. Utsugi N, Takahashi K, Kishi S. Choroidal vascular occlusion in internal carotid artery obstruction. Retina 2004;24:915-919.

36. Dag Seker E, Erbahceci Timur IE. COVID-19: more than a respiratory virus, an optical coherence tomography study. International Ophthalmology 2021;41:3815-3824.

37. Örnek K, Temel E, Aşıkgarip N, Kocamış Ö. Localized retinal nerve fiber layer defect in patients with COVID-19. Arquivos Brasileiros de Oftalmologia 2021;83:562-563.

38. Chan P, Mok K. Transorbital sonographic evaluation of optic nerve sheath diameter in normal Hong Kong Chinese adults. Hong Kong Journal of Emergency Medicine 2008;15:197-204.

39. Asghar A, Hashmi M, Hussain A. Optic nerve sheath diameter evaluated by transorbital sonography in healthy volunteers from Pakistan. Anesthesia, Pain & Intensive Care 2019:282-286.

40. Bäuerle J, Lochner P, Kaps M, Nedelmann M. Intra-and interobsever reliability of sonographic assessment of the optic nerve sheath diameter in healthy adults. Journal of Neuroimaging 2012;22:42-45.

41. Goeres P, Zeiler FA, Unger B, Karakitsos D, Gillman LM. Ultrasound assessment of optic nerve sheath diameter in healthy volunteers. Journal of critical care 2016;31:168-171.

42. Ballantyne S, O'neill G, Hamilton R, Hollman AS. Observer variation in the sonographic measurement of optic nerve sheath diameter in normal adults. European journal of ultrasound 2002;15:145-149.

43. Aydin N, Çapraz M. Optic Nerve and Retinal Layer Measurements with Optical Coherence Tomography in PCR Positive and Negative COVID-19 Patients. Journal of Contemporary Medicine 2022;12:1-.

44. Kim DH, Jun J-S, Kim R. Ultrasonographic measurement of the optic nerve sheath diameter and its association with eyeball transverse diameter in 585 healthy volunteers. Scientific reports 2017;7:15906.

45. Maude RR, Amir Hossain M, Hassan MU, et al. Transorbital sonographic evaluation of normal optic nerve sheath diameter in healthy volunteers in Bangladesh. PloS one 2013;8:e81013.

46. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA neurology 2020;77:683-690.

47. Biondino D, Costigliola R, Mottola F, Graziano M, Yılmaz F. Comment on: Optic nerve sheath diameter measurement by ultrasound and age group. Annals of Saudi Medicine 2023;43:196-197.

# Effects of Standard Treatment Alone versus Standard Treatment Plus Plasmapheresis on the Levels of Serum Pseudocholinesterase and Erythrocyte Acetyl Cholinesterase in Critically Patients with Organophosphate Poisoning: Randomized Controlled, Open-Label, ClinicalTrial

**Gulten Can Sezgin[1], Hilal Sipahioglu[2], Kursat Gundogan[2], Ramazan Coskun[2], Sahin Temel[2], Cevat Yazici[3], Okhan Akdur[4], Murat Sungur[2], Muhammet Guven[5]**

[1] Erciyes University, Faculty of Medicine, Department of Internal Medicine, Division of Gastroenterology, Kayseri, Türkiye
[2] Erciyes University, Faculty of Medicine, Department of Internal Medicine, Division of Intensive Care, Kayseri, Türkiye
[3] Erciyes University, Faculty of Medicine, Department of Biochemistry, Kayseri, Türkiye
[4] Canakkale Onsekiz Mart University, Faculty of Medicine, Department of Emergency, Canakkale, Türkiye
[5] Lokman Hekim University, Faculty of Medicine, Department of Internal Medicine, Division of Intensive Care, Ankara, Türkiye

**Adres for Correspodence:** Lokman Hekim University, 06510, Cankaya, Ankara, Türkiye e-mail: muhammet.guven@lokmanhekim.edu.tr

**Orcid ID:** GCS: 0000-0001-5537-7882 KG: 0000-0002-8433-3480 ST: 0000-0002-2766-4312 OA: 0000-0003-3099-6876 MG: 0000-0001-9874-7185
HS: 0000-0002-7884-2094 RC: 0000-0002-5755-523X CY: 0000-0003-0625-9542 MS: 0000-0002-0011-3166

**Cite As:** Sezgin Can G, Sipahioglu H, Gundogan K, et al. Effects of standard treatment alone versus standard treatment plus plasmapheresis on the levels of serum pseudocholinesterase and erythrocyte acetyl cholinesterase in critically patients with organophosphate poisoning: Randomized controlled, open-label, clinical trial. Hitit Med J 2023;5(3): 209-215 https://doi.org/10.52827/hititmedj.1326182

## Abstract

**Objective:** Organophosphates are the insecticides commonly used worldwide. Inadequate treatment for organophosphates poisoning increases morbidity, and mortality. Purpose of the work was to determine the effect of standard treatment alone versus standard treatment plus plasmapheresis on the levels of serum pseudo-cholinesterase, and erythrocyte acetyl cholinesterase in severe patients with organophosphates poisoning.

**Material and Method:** This research is a prospective study. Patients diagnosed with organophosphates poisoning were included in the work. The patients were divided into two groups as the intervention group, and the standard group. The intervention group, plasmapheresis was performed in addition to the standard treatment.

**Results:** The research was conducted with forty cases. (Intervention group n=21, standard group n=19). Serum pseudo-cholinesterase values were 482.5 u/L at baseline, 3723 u/L after plasmapheresis. Erythrocyte acetyl cholinesterase values were 1.91 u/mL on admission, 2.53 u/mL after plasmapheresis. Erythrocyte acetyl cholinesterase and serum pseudo-cholinesterase values were compared between the two groups daily from the admission of patients to intensive care units during the first 5 days, and on the last day in the intensive care units. There was no statistical difference between two groups ($p> 0.05$), except for the second day. It was observed that there was a statistically significant difference between the pseudo-cholinesterase values in the second day comparison of both groups ($p=0.028$).

**Conclusion:** In conclusion, plasmapheresis treatment may contribute positively to pseudo-cholinesterase level. This treatment may have provided additional time for the organophosphates to be eliminated from the body. Although acetyl cholinesterase reactivation is achieved with oxime treatment, the clinical effect of this treatment is not clear.

**Keywords:** Erythrocyte acetyl cholinesterase, Intensive care units, Organophosphate poisoning, Plasmapheresis, Pseudo-cholinesterase.

## Özet

**Amaç:** Organofosfatlar dünya çapında yaygın olarak kullanılan insektisitlerdir. Organofosfat zehirlenmelerinde yetersiz tedavi morbidite ve mortaliteyi artırmaktadır. Çalışmanın amacı, organofosfat zehirlenmesi olan ciddi hastalarda serum psödo-kolinesteraz ve eritrosit asetil kolinesteraz düzeyleri üzerinde standart tedaviye karşı, standart tedavi artı plazmaferezin etkinliğini araştırmaktır.

Gereç ve Yöntem: Bu araştırma prospektif bir çalışmadır. Çalışmaya organofosfat zehirlenmesi tanısı alan hastalar dahil edildi. Hastalar müdahale grubu ve standart grup olarak iki gruba ayrıldı. Müdahale grubuna standart tedaviye ek olarak plazmaferez tedavisi uygulandı.

**Bulgular:** Çalışmaya kırk hasta alınmıştır (müdahale grubu n:21, standart grup n:19). Başlangıçta serum psödo-kolinesteraz değerleri 482,5 u/L, plazmaferez sonrası 3723 u/L idi. Eritrosit asetil kolinesteraz değerleri başvuruda 1,91 u/mL, plazmaferez sonrası 2,53 u/mL idi. Eritrosit asetil kolinesteraz ve serum psödo-kolinesteraz değerleri hastaların yoğun bakıma kabulünden itibaren ilk 5 gün ve yoğun bakımdaki son gün değerleri iki grup arasında karşılaştırıldı. İki grup arasında 2. gün dışında istatistiksel fark yoktu ($p> 0,05$). Her iki grubun ikinci gün karşılaştırmasında psödo-kolinesteraz değerleri arasında istatistiksel olarak anlamlı fark olduğu görüldü ($p=0,028$).

**Sonuç:** Sonuç olarak, plazmaferez tedavisi psödo-kolinesteraz düzeyine olumlu katkı sağlayabilir. Bu tedavi organofosfatların vücuttan atılması için ek süre sağlamış olabilir. Asetil kolinesteraz reaktivasyonu oksim tedavisi ile sağlansa da bu tedavinin klinik etkisi net değildir.

**Anahtar Sözcükler:** Eritrosit asetil kolinesteraz, Organofosfat zehirlenmesi, Plazmaferez, Psödo-kolinesteraz, YBÜ.

**Date of Submission:** 14.07.2023
**Date of Acceptance:** 23.09.2023
**Date of Publication:** 10.10.2023

Orally presented the date and the place: 32nd Annual Congress, ESICM LIVES, 28 September – 2 October 2019, Berlin, Germany.

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** A certificate was obtained from Erciyes University Faculty of Medicine Ethics Committee fort he study (Ethics Committee Decision no: 01/32).
**Plagiarism Checks:** Yes - iThenticate
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: MG, GCS Design: MG, GCS Data Collection/Data Processing: RC, HS, CY, KG, ST Data Analysis: OA, KG, MG, GCS Article Preparation: GCS, HS, KG, ST, CY, OA, MS, MG
**Informed Consent:** Consent has been obtained personally for the conscious patients, and from their legal guardians for the unconscious patients.
**Financial Disclosure:** This study was supported by Erciyes University Scientific Research Committee (Project no: TT-07-27, Gulten Can Sezgin)

## Introduction

Organophosphate (OP) compounds are among the most widely used insecticides around the world due to their low cost, and rapid effects (1, 2). These OP groups are also widely used in our country, and have an important place among the causes of poisoning (3, 4). When the causes of poisoning are examined, it is seen that they are caused by use in the field of agriculture, accidental exposure to the compounds, or suicide attempts (2, 4, 5). Delayed diagnosis, and inadequate treatment in patients with OP poisoning are factors that increase morbidity, and mortality (2, 6, 7). For this reason, early diagnosis, and appropriate treatment of OP poisoning is lifesaving. Patients diagnosed with OP poisoning should be followed up, and treated by multidisciplinary intensive care units (ICU), and their teams (3). New treatment modalities have recently been applied in addition to standard treatment in OP poisoning (8-11). Plasmapheresis is a therapeutic procedure used in many medical conditions that ensures the removal of plasma compounds such as antibodies, immunocomplexes, endogenous, and exogenous toxins from the body. In plasmapheresis, fresh frozen plasma (FFP), human albumin, and colloidal fluids may be used as replacement fluid. FFP is the most important source of pseudocholinesterase (PChE). In some previous studies, it has been determined that fresh frozen plasma has cholinesterase activity at adequate levels, and its use in patients with OP poisoning may reduce mortality, and morbidity, and it has been concluded that plasma cholinesterase functions as a reserve, and back-up for erythrocyte acetyl cholinesterase (AChE) (8, 11).

OP insecticides inhibit AChE, and cholinesterase enzymes, resulting in a clinical situation with overstimulation of cholinergic synapses. Today, in cases with OP poisoning, the serum PChE values are measured, and the diagnosis, and treatment management of the patients are performed (12). The serum cholinesterase enzyme can be highly variable due to hereditary deficiency. This situation reduces the diagnostic value of serum cholinesterase enzyme in OP poisoning cases. Some studies have shown that erythrocyte AChE activity serves as a key biomarker for synaptic AChE (13).

We hypothesize that if the patients with OP poisoning are subjected to standard treatment plus plasmapheresis with fresh frozen plasma, the PChE, and erythrocyte AChE levels return to normal in a shorter time. Rapid elevation of these enzymes may decrease morbidity, and mortality associated with OP poisoning.

Primary purpose of this study was to compare the levels of serum PChE, and erythrocyte AChE daily between the patients diagnosed with OP poisoning that are subjected to standard treatment plus a single plasmapheresis, and those subjected to standard treatment alone during the hospitalization in the ICU.

Secondary purpose was to compare clinical data, such as ventilator-associated pneumonia incidence, number of days on mechanical ventilation, and length of ICU stay between two groups above.

## Material and Methods

*Research design and setting*

The work has been carried out prospectively in Medical ICU. A certificate was obtained from the Ethics Committee for the study (Ethics Committee Decision no: 01/32). Consent has been obtained personally for the conscious patients, and from their legal guardians for the unconscious patients.

*Selection of participants*

Patients above 16 years old that were diagnosed with OP poisoning in emergency department, have PChE levels below normal value, and were indicated for hospitalization in the intensive care were enrolled in the study. The patient's relatives were requested to bring the causing OP compound from home, and OP compound was demonstrated to cause the poisoning. Among the patients visiting the emergency department with pre-diagnosis of OP poisoning, those with normal PChE level, without evidence of OP compound or rejecting to give consent have not been enrolled in the study. Standard treatment was applied to patients who applied to the emergency department with OP poisoning, plasmapheresis treatment was also recommended, and patients who accepted plasmapheresis treatment were included in the plasmapheresis intervention group. Although the cases included in the research were randomized, those who were in worse condition generally accepted the plasmapheresis procedure.

*Randomization*

-Patients admitted to the intensive care unit were then randomized. One session of plasmapheresis was performed to the patients in study group (intervention group) on the first day in addition to the standard treatment in the ICU for OP poisoning, and standard treatment alone was administered to the standard group (control group).

*Outcome measures*

Primary outcome was to compare serum PChE, and erythrocyte AChE levels of the patients in the intervention group, and the control group for the first 5 days from admission to the ICU, and on the discharge day in order to evaluate efficacy of plasmapheresis.

Secondary outcome was to compare clinical data, such as ventilator-associated pneumonia incidence rates, number of days on mechanical ventilation, number of days stayed in the intensive care unit, between the group treated with plasmapheresis, and the group administered standard treatment.

After admission of the patients to the ICU, demographic data, OP compound causing poisoning, way of poisoning, cause of poisoning were noted. Acute Physiology and Chronic Health Evaluation II (APACHE II) score and Glasgow Coma Score (GCS) were calculated. Patients were also followed up daily for mechanical ventilation need, new infections, and rhythm disorders on electrocardiogram (ECG), and the findings were noted. Atropine and pralidoxime (PAM) usage durations, and amounts were noted. Intermediate syndrome (IMS) incidence, number of days on intensive care, and intensive care mortality were also noted. IMS occurs approximately 24-96 hours after toxicity. The clinical situation is after resolution of the acute cholinergic crisis, and before the onset of delayed neuropathy, some patients develop muscle paralysis (12,14).

Once the patients were diagnosed, standard treatment for OP poisoning was initiated. Standard treatment included administration of general care, and supportive therapy, providing respiratory support to the patient as well as administration of activated carbon, and gastric lavage in the conscious patients. The patients with respiratory failure were intubated and monitored on mechanical ventilation. Patients whose breathing became shallow, who could not protect the airway

due to excessive secretions or impaired consciousness, and whose GCS was <8 were intubated.

Atropine, and PAM treatment initiated in emergency department was continued in the ICU. Atropine was started in the diagnosed patients at the initial dose of 1-2 mg intravenously, and it was repeated every 5-10 minutes with dose adjustment based on their individual clinical status. Treatment was continued with infusion at 0.5-2 mg/hour based on the clinical status of the patient. Dose of atropine infusion was adjusted based on the cholinergic findings. It was administered until hypersecretion is controlled, and discontinued 24 hours after appearance of atropinization signs. In case of that the symptoms reoccurred atropine infusion was reinitiated. Intravenous bolus dose of PAM was 1000 mg. Thereafter, treatment was continued with infusion at 4 mg/kg/hour. PAM treatment was continued for 72 hours. Total doses of atropine, and PAM given to each patient were calculated.

*Laboratory*

In order to check PChE levels, 2 cc blood was taken into the biochemistry tubes with gel from intervention group patients before and after plasmapheresis, during the first 5 days in the ICU, and on the discharge day, and from control group patients during the first 5 days in the ICU and on the discharge day. Serum PChE levels were measured by OLYMPUS 2700 device using the original kit (reference range 3930-10800 u/L). PChE value of fresh frozen plasma used in plasmapheresis was 7069.81±305.18 u/L.

Similarly, blood was taken into CBC tube from the intervention group patients before and after plasmapheresis for erythrocyte cholinesterase testing. The blood samples were kept in the fridge at +4°C. Erythrocyte cholinesterase was measured by spectrophotometry kits. Erythrocyte cholinesterase was tested with Test-mate ChE Cholinesterase Test System Model 400 (EQM Research brand) device using AChE Erythrocyte Cholinesterase Assay Kit (Model 460) original kit. The procedure of this test uses the Elman method. Carboxylic acid, and thiocholine are formed upon hydrolysis of AchE, and Acetylcholine. Thiocholine Ellman reagent (DTNB, dithionitrobenzoic acid) reacts, the formed yellow color is measured with spectrophotometry at 450 nm wavelength.

Plasma corresponding to total plasma volume was used in one session of plasmapheresis. One session of plasmapheresis was performed on the first day. All side effects observed during the procedure were noted.

*Statistical Analysis*

SPSS 22.00 (Statistical Packages for Social Sciences; SPSS Inc. Chicago, Illinois, USA) and Sigma stat 3.5 133 programs were used for statistical analyses in the study. Qualitative variables were presented using percentages, and frequencies. Mean and standard deviation were used for normally distributed quantitative variables, median, and ranges were used for non-normally distributed quantitative variables. Normality of data was tested by 'Shapiro-Wilk' test. Comparisons between qualitative variables were done with using Chi-square test. Comparison of continuous variables was done with using Student's t test for normally distributed independent variables, and Mann Whitney U test for non-normally distributed independent variables. The statistical significance was set at $p<0.05$.

## Results

A total of 40 cases were included in this study. Twenty-one patients were assigned to the plasmapheresis group (intervention group), and 19 patients were assigned to the standard group (control group). Detailed demographic data, and clinical results of the patients are presented in Table I. OP poisoning was mostly caused by dichlorvos (20%), malathion (12.5%), and monocrotophos 12.5% (Table II).

Based on the evaluation of the patients by the cause of poisoning, intervention group included 15 (71.4%) patients poisoned due to suicide attempt, and 6 (28.6%) patients accidentally poisoned. Control group included 14 (73.7%) patients poisoned due to suicide attempt, and 5 (26.3%) patients accidentally poisoned.

**Table I.** Patient demographic and clinical characteristics

| Variables | General (n=40) | Intervention group (n=21) | Control group (n=19) | *P value* |
|---|---|---|---|---|
| Age± SD, years | 37±16 | 41 ± 16 | 33 ± 15 | *0.114* |
| Gender, n (%) | | | | |
| Male | 24(60) | 14(35) | 10(25) | |
| Female | 16(40) | 7(17.5) | 9(22.5) | *0.520* |
| APACHE II score, ± SD | 9±5 | 11.38 ± 4.33 | 9 ± 3.85 | *0.037* |
| Length of ICU stay (range), day | 6 (3-26) | 7 (5-26) | 6 (3-10) | *0.153* |
| Duration of MV stay (range), day | 4 (2-17) | 5 (2-17) | 4 (3-7) | *1.000* |
| Need for MV, n (%) | 11 (%27) | 7 (%33) | 4 (%21) | *0.607* |
| VAP, n (%) | 6 (15) | 4 (60) | 2 (40) | *0.550* |

APACHE II: Acute Physiology, Age, Chronic Health Evaluation II, ICU: Intensive Care Unit, MV: Mechanical Ventilation, VAP: Ventilator Associated Pneumonia

**Table II.** OP compounds that cause of intoxication

| OP compound | Number (%) (n = 40) |
|---|---|
| Dichlorvos | 8 (20) |
| Monocrotophos | 5 (12.5) |
| Malathion | 5 (12.5) |
| Chlorpyrifos | 4 (10) |
| Diazinon | 4 (10) |
| Clofenvinfos | 3 (7.5) |
| Methidathion | 3 (7.5) |
| Coumaphos | 2 (5) |
| Parathionmetil | 2 (5) |
| Triklorfon | 2 (5) |
| Azinphosmetil | 1 (2.5) |
| Methamidophos | 1 (2.5) |

Based on the patient's history data, 20 (95.2%) patients were poisoned orally, and 1 (4.8%) patient was poisoned by respiratory route in the intervention group, while 19 (100%) patients were poisoned orally in the control group. Patients in both groups continued to live.

IMS occurred in 2 (9.5%) patients in the intervention group. IMS did not occur in control group. Morbidity was present 8 (38.1%) patients in the intervention group and 7 (36.8%) patients in the control group. Causes of morbidity are given in Table III. There was no significant difference between the two groups in terms of atropine administration time and atropine amount ($p = 0.454$, $p = 0.735$, respectively). Additionally, when both groups were compared, no statistically significant difference was observed in terms of PAM administration time and amount ($p=0.714$, $p=0.518$, respectively) (Table IV).

After admission to the ICU, serum PChE values of the pa-

**Table III.** Causes of morbidity in patient with OP poisinin

| Causes of morbidity | Intervention group (n) | Control group (n) | Total (n) |
|---|---|---|---|
| VAP | 4 | 2 | 6 |
| UTI | 1 | 1 | 2 |
| GIB | 0 | 1 | 1 |
| Aspiration pneumonia | 1 | 2 | 3 |
| Catheter infection | 1 | 0 | 1 |
| Thrombosis | 1 | 0 | 1 |
| Candida esophagitis | 0 | 1 | 1 |
| Total | 8 | 7 | 15 |
| *p=0.550* | | | |

VAP:Ventilator associated pneumonia, UTI:Urinary tract infection, GIB:Gastrointestinal bleeding

**Table IV.** Comparison of atropine and PAM treatment, duration and dose amount between two groups

| | Intervention group (n:21) | Control group (n:19) | *P value* |
|---|---|---|---|
| Atropin duration, SD (day) | 4.31±2.11 | 3.84±1.76 | *p=0.454* |
| Atropin total dose,SD (mg) | 83.33 ±49.34 | 88.79±75.41 | *p=0.735* |
| PAM duration, SD (day) | 2.76±0.90 | 2.79±0.95 | *p=0.714* |
| PAM total dose, SD (mg) | 16641.14±5084.32 | 15497.68±5996.58 | *p=0.518* |

PAM: Pralidoxime

tients of intervention group, and control group were compared daily during the first 5 days, and on last day of intensive care. There was no statistical difference between two groups, except for the 2nd day. It was observed that there was a statistically significant difference between the PChE values in the second day comparison of both groups (*p=0.028*). (Table V) (Figure I).

The mean PChE value of the intervention group at the first admission to the hospital was found to be 388 (range: 218- 2092) u/L, but after plasmapheresis treatment, mean PChE value was found to be 3723 (range:541.50-5422.25) u/L. There was a significant difference when PChE hospitalization value, and post-plasmapheresis value were compared (*p<0.050*). There was also a significant difference, when PChE admission value was compared with the 3rd day, 5th day, and discharge value (*p <0.001*) (Table V).

Intervention group AChE values were compared between days, there was no significant difference (*p>0.05*). After admission to the ICU, erythrocyte AChE values of the patients of intervention group, and control group were compared daily during the first 5 days, and on last day of intensive care. There was no statistically significant difference between two groups (Table IV) (Figure II).

Complication occurred in 5 patients (23.8%) during plasmapheresis procedures. The most frequent complication was hypocalcaemia (3 patients, 14.2%). Urticaria was observed in 2 patients (9.5%). No patient died due to the complications of plasmapheresis.

**Figure I.** Median serum PChE levels over time between intervention and control treatment groups

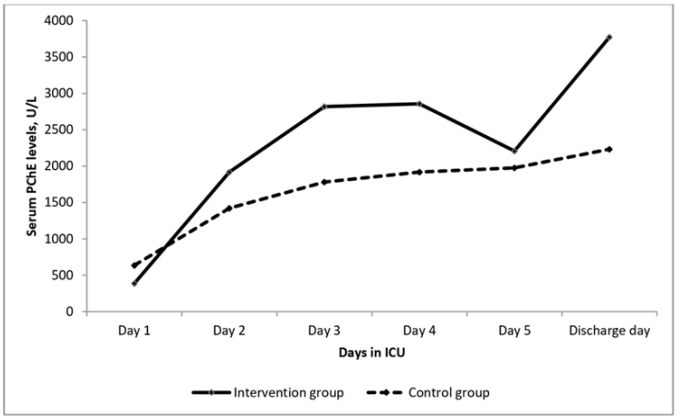



Figure 1 legend: On day 1, serum PChE level of the patients was 388 (218- 2092) u/L in plasmapheresis group, and 637 (177-3883) u/L in control group (*p=0.155*). On day 2, serum PChE level of the patients was 4112 (174-7078) u/L in plasmapheresis group, and 1423 (194-4800) u/L in control group (p=0.028). On day 3, serum PChE level of the patients was 2819 (181-1918) u/L in plasmapheresis group, and 1781 (231-4764) u/L in control group (*p=0.250*). On day 4, serum PChE level of the patients was 2857 (161-9993) u/L in plasmapheresis group, and 1920 (263-4029) u/L in control group (p=0.323). On day 5, serum PChE level of the patients was 1175 (178- 8464) u/L in plasmapheresis group, and 1477 (181-3439) u/L in control group (*p=0.514*). Serum PChE level of the patients was 3773 (121-10597) u/L in plasmapheresis group, and 2233 (239-4454) u/L in control group (*p=0.261*) on the discharge day.

**Table V.** Serum PChE levels over time between intervention and control treatment groups

| PChE level | Intervention, u/L | Control, u/L | *P-value* |
|---|---|---|---|
| Day 1 | 388 (251.50-643.75)* | 637 (351.50-1966.25) | *0.155* |
| Day 2 | 4112 (174-7078) | 1423 (194-4800) | *0.028* |
| Day 3 | 2819 (181-1918)* | 1781 (231-4764) | *0.250* |
| Day 4 | 2857 (161-9993) | 1920 (263-4029) | *0.323* |
| Day 5 | 1175 (178-8464)* | 1477 (181-3439) | *0.514* |
| Discharge day | 3773 (121-10597)* | 2233 (239-4454) | *0.261* |

PChE: Pseudo-cholinesterase , *P*=<0.001*

## Discussion

**Figure II.** Median plasma erythrocyte AChE levels over time between intervention and control treatment groups

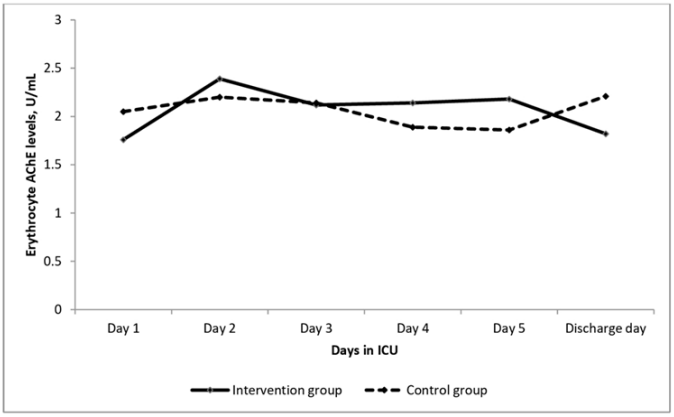



Figure 2 legend: On day 1, plasma erythrocyte AChE level of the patients was 1.76 (0.12- 4.85) um/L in plasmapheresis group, and 2.05 (0.19-4.84) u/mL in control group (*p=0.871*). On day 2, plasma erythrocyte AChE level of the patients was 2.39 (0.01-3.90) u/mL in plasmapheresis group, and 2.20 (0.19-4.27) u/mL in control group (p=0.914). On day 3, plasma erythrocyte AChE level of the patients was 2.12(0.07-4.30) u/mL in plasmapheresis group, and 2.14 (0.27-4.20) u/mL in control group (*p=0.705*). On day 4, plasma erythrocyte AChE level of the patients was 2.14(0.07-3.58) u/mL in plasmapheresis group, and 1.89 (0.27-4.24) u/mL in control group (*p=0.645*). On day 5, plasma erythrocyte AChE level of the patients was 2.27 (0.12-4.19) u/mL in plasmapheresis group, and 1.45 (0.19-4.01) u/mL in control group (*p=0.581*). Plasma erythrocyte AChE level of the patients was 1.81 (0.09-3.92) u/mL in plasmapheresis group, and 2.21 (0.41-4.37) u/mL in control group (*p=0.250*) on the discharge day

**Table VI.** Erythrocyte AChE levels over time between intervention and control treatment groups

| AChE level | Intervention, u/mL | Control, u/mL | *P-value* |
|---|---|---|---|
| Day 1 | 1.76 (0.12-4.85) | 2.05 (0.19-4.84) | *0.871* |
| Day 2 | 2.39(0.01-3.90) | 2.20 (0.19-4.27) | *0.914* |
| Day 3 | 2.12(0.07-4.30) | 2.14 (0.27-4.20) | *0.705* |
| Day 4 | 2.14(0.07-3.58) | 1.89 (0.27-4.24) | *0.645* |
| Day 5 | 2.27 (0.12-4.19) | 1.45 (0.19-4.01) | *0.581* |
| Discharge day | 1.81 (0.09-3.92) | 2.21 (0.41-4.37) | *0.250* |

AChE: Acetyl cholinesterase

In this study, serum PChE and erythrocyte AChE levels of the patients hospitalized due to OP poisoning that were subjected to standard treatment, and standard treatment plus plasmapheresis were compared daily during their treatment in the ICU. The main treatment for OP poisoning is administration of atropine, and PAM (15). Atropine is a muscarinic antagonist (16,17). The oximes provide reactivation of the AChE by removing the phosphoryl group attached to the active site of AChE as a result of OP toxicity in its region (18). Oximes are supportive agents in treatment, and some studies have shown that they may have some adverse effects (19). PAM increases AChE reactivation, however, does not lead to improved survival, or decreased intubation need (20). In a study, duration and amount of atropine administration were not associated with prognosis (21). In our study, there was no significant difference between the two groups in terms of the duration, and amount of both drugs.

Plasmapheresis is not a new treatment method for toxic conditions and has been clearly shown to play an effective role in many conditions (22). Under such difficult circumstances, it may elevate cholinesterase levels and may be an effective alternative (23). Guven et al. reported that plasmapheresis was successfully used in the sepsis associated with organophosphate poisoning. It was shown that the patient who developed sepsis with OP intoxication, after performing plasmapheresis with FFP for sepsis treatment, the PChE level increased to normal levels, plasmapheresis increased the PChE level, and contributed to the recovery of the patient (8).

Qiu et al. published a meta-analysis on 433 severe, and acute OP poisoning cases. 211 patients were administered standard treatment plus plasmapheresis, while 222 patients were administered standard treatment alone. Meta-analysis showed that mortality was lower in the plasmapheresis group (24). In addition, in the case report presented in the literature, it was shown that an effective treatment was performed with plasmapheresis in a patient diagnosed with Guillain-Barre Syndrome due to OP poisoning (25).

Measuring both plasma cholinesterase, and erythrocyte cholinesterase levels are methods used to diagnose. The results of these are important in terms of evaluating the treatment (26, 27). In the study carried out by Liu et al., PChE level elevated to 3823 IU/l from 200 IU/l within 21 days (28). In our study, PChE level was 344 u/L during the first five visit and on the discharge day. When the two groups were compared in each other, there was no difference, except for the second day. It was observed that there was a significant difference between the second day values of the two groups (p=0.028). AChE levels were not different between control, and intervention groups. When the enzyme values of the patients after plasmapheresis were compared with their admission values, there was a significant increase in PChE value. The positive effects of plasmapheresis may be in the form of AChE increase, and / or PChE loading its role in the absence of AChE. Possible mechanisms for AChE increase; the affinity of PChE to OP may be greater than AChE. In this way, AChE may be leaving the OP, and increasing in level, or the PChE may act as a reserve for AchE, and be transforming. The exact function of the PChE enzyme measured in OP toxicity is unknown. AChE levels may be more important. It is generally accepted that PChE normally has no physiological function in the body. Before the physiologically important AChE enzyme is inhibited by OP compounds in the target areas, it is thought that replacement of PChE to the patient may be a useful therapy by binding the circulating OP. PChE has natural physiological functions in certain regions, and functions by accompanying AChE in the regulation, and support of cholinergic transmission (29). This supportive role seems to become important, when AChE activity for some reason is reduced, or lost (9). PChE in plasma binds to OP, and inactivates them, thus protecting AChE. One PChE enzyme can inactivate one OP compound (30). Brahmi et al. showed that the decrease in erythrocyte AChE activity is a very important prognostic factor in patients with OP poisoning. Levels below 23.5 mmol/mL is associated hypoxemia, hypotension, and bradycardia (13).

Ashani et al. claimed that early administration of PChE with good timing could prevent the crises that develop with OP poisoning, the development of IMS, and the delayed toxic effects of OP (30). FFP can be an important source of PChE. Guven et al. showed that because FFP is an important source of cholinesterase, it has sufficient enzyme activity, and may play an important role in increasing the low PChE level seen in OP poisoning (8). Increased PChE levels were seen to be effective in preventing the development of IMS, and associated mortality. In this study, it is thought that the early application of FFP together with the initial antidote treatment is more beneficial especially in the development of IMS and the prevention of mortality (9). Yilmaz et al. applied plasmapheresis treatment to 17 patients who developed IMS as a result of OP poisoning, and a significant decrease in plasma OP level, and a very significant increase in PChE enzyme level in the early period were observed in patients due to this treatment (31).

IMS may develop because of insufficient administration of oximes used in medical therapy, and/or paralysis of neuromuscular transmission because of long-term nicotinic receptor stimulation. The administration of PChE, which is not dependent on OP, with plasmapheresis can play an important role in these cases. PChE administered to the patient may also prevent the long-term adverse effects seen because of AChE inactivation by the OP. In the presented study, IMS developed in 2 patients in the plasmapheresis group, but the patients continued to live. Plasmapheresis may have contributed positively to the recovery of these patients.

The incidence of complications during plasmapheresis varies from 4.6% to 36%. The most frequent complications are chills, rigors, urticaria, and paresthesia and muscle cramps associated with hypocalcaemia caused by citrate (32-34). In our study, mild hypocalcaemia symptoms in 3 patients, and urticaria in 2 patients were observed. No severe complication

occurred. In the light of these data, when we evaluate the plasmapheresis procedure in terms of risk, and incidence of complications, it can be concluded that it is a safe method.

Studies have shown that APACHE II values have high prognostic importance in OP poisoning (35, 36). In our study, absence of mortality in the patients group treated with plasmapheresis with high APACHE II values indicates that plasmapheresis treatment is an important treatment method in OP poisoning. Acute respiratory distress syndrome (ARDS) has been reported after OP poisoning. It is not clear whether ARDS in people with OP poisoning occurs after aspiration or due to the direct effect of OP. Perhaps the cause of post-aspiration deaths is related to ARDS. Differential diagnosis of aspiration pneumonia and ARDS is very important for effective treatment in these patients (37). In our study, aspiration pneumonia was observed in a total of 3 patients in both groups (intervention group: 1 patient, control group: 2 patients). There were no patients diagnosed with ARDS in both groups.

Studies show that PChE has natural physiological functions, accompanies AChE in regulating, and supporting cholinergic transmission, and this back-up role becomes more important, when AChE is suppressed, or absent. Although AChE enzyme values did not differ between groups in our study, the increase in AChE values after the procedure in the patient group who underwent plasmapheresis supports that PChE has a reserve, or back-up role for AChE. The idea that the PChE enzyme given externally plays the role of this enzyme in OP poisoning, in which AChE is inhibited, prevents mortality, and morbidity that may develop, strengthened with this study. PChE enzyme administered by plasmapheresis binds to OP by competing with endogenous AChE, thus it is thought to prevent, or reduce the toxic effect of OP.

The limitations of the study were that we did not perform a power analysis according to the number of patients, single session plasmapheresis, and open-label design. Another limitation of our study was that it consisted of patients poisoned by different physical characteristics OP that may affect the benefit of plasmapheresis.

## Conclusion

As a result, plasmapheresis treatment increases PChE levels. Even if the APACHE II score is high, individual death may be prevented with PChE administered externally to the patient. However, the effectiveness of these records is not yet clear. This is a broad research area and new research needs to be done.

## References

1.Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. Lancet (London, England). 2008; 371(9612): 597-607.

2.Sungur M, Guven M. Intensive care management of organophosphate insecticide poisoning. Critical care (London, England) 2001; 5(4): 211-215.

3.Coskun R, Gundogan K, Sezgin GC, et al. A retrospective review of intensive care management of organophosphate insecticide poisoning: Single center experience. Nigerian journal of clinical practice 2015; 18(5): 644-650.

4.Ozturk MA, Kelestimur F, Kurtoglu S, Guven K, Arslan D. Anticholinesterase poisoning in Turkey--clinical, laboratory and radiologic evaluation of 269 cases. Human & experimental toxicology 1990; 9(5): 273-279.

5.Guven M, Unluhizarci K, Goktas Z, Kurtoglu S. Intravenous organophosphate injection: an unusual way of intoxication. Human & experimental toxicology 1997; 16(5): 279-280.

6.Simsek ZO, Simsek Y, Sungur M, Gundogan K, Guven M. Effects of Organophosphate Poisoning on Endocrine System in Long-Term: A Pilot Study. Erciyes Med J 2019.

7.Selim K. Acute and Long-term Effects of Organophosphate Poisoning. Erciyes Medical Journal 2019; 41(1): 3-4.

8.Guven M, Sungur M, Eser B. The effect of plasmapheresis on plasma cholinesterase levels in a patient with organophosphate poisoning. Human & experimental toxicology 2004; 23(7): 365-368.

9.Guven M, Sungur M, Eser B, Sari I, Altuntas F. The effects of fresh frozen plasma on cholinesterase levels and outcomes in patients with organophosphate poisoning. Journal of toxicology Clinical toxicology. 2004; 42(5): 617-23.

10.Disel NR, Acikalin A, Kekec Z, Sebe A. Utilization of plasmapheresis for organophosphate intoxication: A case report. Turkish journal of emergency medicine 2016; 16(2): 69-71.

11.Yukselmis U, Ozcetin M, Cag Y, Yildizdas D, Yilmaz HL. The role of plasmapheresis in organophosphate poisoning: Case reports of three pediatric patients. The Turkish journal of pediatrics 2017; 59(4): 491-496.

12.Dayananda VP, Bhaskara B, Pateel GN. A study of effectiveness of fresh frozen plasma in organophosphorous compound poisoning in reducing length of Intensive Care Unit stay and in reducing need for tracheostomy. Anesthesia, essays and researches 2016; 10(2): 268-272.

13.Brahmi N, Mokline A, Kouraichi N, et al. Prognostic value of human erythrocyte acetyl cholinesterase in acute organophosphate poisoning. The American journal of emergency medicine 2006; 24(7): 822-827.

14.Senanayake N KL. Neurotoxic effects of organophosphorus insecticides: An intermediate syndrome. N Engl J Med 1987; 316: 761–763.

15.Choi P T-L, Quınonez LG, Cook DJ. Acute Organophosphate insecticide poisoning. Clinical Intensive Care 1995; 6:5.

16. Johnson MK, Jacobsen D, Meredith TJ. Evaluation of antidotes for poisoning by organophosphorus pesticides. Emerg Med 2000; 12:22–37.

17. Connors NJ, Harnett ZH, Hoffman RS. Comparison of current recommended regimens of atropinization in organophosphate poisoning. J Med Toxicol 2014; 10: 143–147.

18. Eyer P. The role of oximes in the management of organophosphorus pesticide poisoning. Toxicol Rev. 2003; 22:165–190.

19. Samuel J, Thomas K, Jeyaseelan L, Peter JV, Cherian AM. Incidence of intermediate syndrome in organophosphorous poisoning. The Journal of the Association of Physicians of India 1995; 43(5): 321-323.

20. Eddleston M, Eyer P, Worek F, et al. Pralidoxime in acute organophosphorus insecticide poisoning a randomised controlled trial. PLoS medicine 2009; 6(6): e1000104.

21.Lin TJ, Jiang DD, Chan HM, Hung DZ, Li HP. Prognostic factors of organophosphate poisoning between the death and survival groups. The Kaohsiung journal of medical scien-

ces 2007; 23(4): 176-182.

22. Schwartz J, Padmanabhan A, Aqui N, et al. Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue J Clin Apher 2016; 31:149-162.

23. Zhong P, Wang Q, Sheng H. Alteration of banked blood cholinesterase level and its significance in emergency treatment of acute organophosphorus pesticide poisoning. Zhonghua Nei Ke Za Zhi 2000; 39(10):658-659.

24. Qiu HM, Zheng SC, Wan WG, Zou HJ. Meta-analysis of the effectiveness of plasma exchange in treatment of severe and acute organophosphate poisoning. Zhonghua lao dong wei sheng zhi ye bing za zhi = Zhonghua laodong weisheng zhiyebing zazhi = Chinese journal of industrial hygiene and occupational diseases 2011; 29(10): 779-781.

25. Bibi S, Kauser S, Ahsan I. Guillain-Barre Syndrome: A Rare Complication of Organophosphate Poisoning. J Coll Physicians Surg Pak 2022; 32(4): 52-54.

26. Lotti M. Clinical toxicology of anticholinesterase agents in humans. In: Krieger R, editor. Handbook of pesticide toxicology. Volume 2. Agents. 2 edn. Academic Press; San Diego: 2001.p.1043–1085.

27. Li B, Sedlacek M, Manoharan I. Butyrylcholinesterase, paraoxonase, and albumin esterase, but not carboxylesterase, are present in human plasma. Biochem Pharmacol 2005;70:1673–1684.

28. Liu H, Kan B, Jian X, Zhang W, Zhou Q, Wang J. Parasuicidal poisoning by intramuscular injection of insecticide: A case report. Experimental and therapeutic medicine 2013; 6(3): 696-698.

29. Li B, Stribley JA, Ticu A, et al. Abundant tissue butyrylcholinesterase and its possible function in the acetylcholinesterase knockout mouse. J Neurochem. 2000; 75:1320-1331.

30. Ashani Y. Prospective of human butyrilcholinesterase as a detoxifying antidote and potential regulator of controlled-release drugs. Drug Dev Res 2000; 50:298-308.

31. Yilmaz M, Sebe A, Ay MO, et al. Effectiveness of therapeutic plasma exchange in patients with intermediate syndrome due to organophosphate intoxication. The American journal of emergency medicine 2013; 31(6): 953-957.

32. Korach JM, Guillevin L, Petitpas D, Berger P, Chillet P. Apheresis registry in France: indications, techniques, and complications. French Registry Study Group. Therapeutic apheresis: official journal of the International Society for Apheresis and the Japanese Society for Apheresis 2000; 4(3): 207-210.

33. Ring A, Sieber WA, Studt JD, et al. Indications and Outcomes of Patients Receiving Therapeutic Plasma Exchange under Critical Care Conditions: A Retrospective Eleven-Year Single-Center Study at a Tertiary Care Center. J Clin Med 2023; 12(8): 2876.

34. Norda R, Stegmayr BG. Therapeutic apheresis in Sweden: update of epidemiology and adverse events. Transfusion and apheresis science: official journal of the World Apheresis Association : official journal of the European Society for Haemapheresis 2003; 29(2): 159-66.

35. Lee P, Tai DY. Clinical features of patients with acute organophosphate poisoning requiring intensive care. Intensive Care Med 2001; 27: 694-699.

36. Tsai JR, Sheu CC, Cheng MH, et al. Organophosphate poisoning: 10 years of experience in southern Taiwan. Kaohsiung J Med Sci 2007; 23:112-119.

37. Eddleston M. The pathophysiology of organophosphorus pesticide self-poisoning is. Fundam Appl Toxicol.1991;17:177-185. Neth J Med 2008; 66:146-148.

# Radial Arter Yoluyla Yapılan Elektif Koroner Anjografi Sırasında Radial Sheat İçerisinden Yapılan Nitrogliserin Dozu ile Radial Arter Spazmının İlişkisi

**Yücel Kanal[1], Hatice Eftal Şeyda Kanal[2]**

[1] Sivas Cumhuriyet Üniversitesi Tıp Fakültesi, Kardiyoloji Bölümü, Sivas, Türkiye
[2] Tokat İl Sağlık Müdürlüğü, Tokat, Türkiye

**Yazışma Adresi:** : Sivas Cumhuriyet Üniversitesi Tıp Fakültesi Kardiyoloji Kliniği, Sivas, Türkiye
e-posta: yucel_kanal@hotmail.com

**Orcid NO:** YK: 0000-0003-0934-0266
HEŞK: 0000-0002-0311-050X

**Atıf:** Kanal Y, Kanal HEŞ. Radial Arter Yoluyla Yapılan Elektif Koroner Anjografi Sırasında Radial Sheat İçerisinden Yapılan Nitrogliserin Dozu ile Radial Arter Spazmının İlişkisi. Hitit Med J 2023;5(3): 216-220. https://doi.org/10.52827/hititmedj.1334133

## Özet

**Amaç:** Koroner girişimlerde transradial yaklaşım, daha düşük vasküler komplikasyon oranları, azalan işlem maliyetleri ve daha erken hasta mobilizasyonu nedeniyle giderek daha popüler hale gelmektedir. Transradial yaklaşımda radial arter spazmı çözülmesi gereken önemli problemlerin başında gelmektedir. Radial arter spazmın azaltılmasında kalsiyum kanal blokerleri, nitratlar ve moksidosin gibi çeşitli vazodilatörlerin damar içine uygulamasıyla azaltılabileceği gösterilmiştir. Transradial yaklaşımda kullanılan nitrogliserin dozu ile ilgili net bir veri olmamakla birlikte, çalışmalarda damar içine doz olarak 100 mcg- 500 mcg dozlar kullanılmıştır. Biz çalışmamızda elektif koroner anjiografi yapılan hastalarda farklı nitrat dozları ile radial arter spazmı ve işlem sırasında gelişen hipotansiyon ilişkisini değerlendirdik.

**Gereç ve Yöntem:** Bu retrospektif araştırmaya hastanemiz katater laboratuarında transradial yaklaşım ile koroner anjografi yapılan ve medikal takip kararı verilen hastalar dahil edilmiştir. Belirlenen hastalar radial sheat yerleştirildikten sonra 200 mcg ve 300 mcg nitrogliserin verilenler olarak iki gruba ayrıldı. Sonuç olarak iki grup arası radial arter spazm oranları değerlendirilerek, verilen nitrogliserin dozu ile radial arter spazmı arasında ilişki incelendi.

**Bulgular:** Çalışmamıza dahil edilen, 133 hastanın yaş ortalaması 61 ± 10,8 yıl olarak saptanmıştır ve çalışmaya dahil edilen hastaların %43'ü kadın olarak izlenmiştir. Radial arter spazmı, 200 mcg nitrogliserin yapılan hastalarda 300 mcg nitrogliserin yapılanlara göre anlamlı düzeyde yüksek bulundu (%16,1-%4,2; $p= 0.03$). Bu iki grup arasında hipotansiyon gelişmesi açısından anlamlı fark yoktu. Çok değişkenli lojistik regresyon analizinde nitrogliserin dozunun ve açlık glukozunun radial arter spazmın bağımsız belirleyicileri olduğunu gösterildi ($p<0,05$).

**Sonuç:** Çalışmamızda transradial yaklaşım öncesi sheat içinden damar içine 200 mcg nitrogliserin yerine 300 mcg nitrogliserin verilerek, radial arter spazm etkin bir şekilde azaltılmıştır. Bu hastalarda işlem esnasında anlamlı bir hipotansiyon da gelişmemiştir.

**Anahtar Sözcükler:** Koroner anjiografi, Radial arter spazmı, Transradial yol

**Geliş Tarihi:** 30.07.2023
**Kabul Tarihi:** 19.09.2023
**Yayım Tarihi:** 10.10.2023

**Hakem Değerlendirmesi:** Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
**Etik Beyanı:** Tokat Gaziosmanpaşa Üniversitesi Etik Kurulundan,19.01.2023 tarihinde, 23-KAEK-010 no ile onay alınmıştır.
**İntihal Kontrolleri:** Evet - intihal.net
**Çıkar Çatışması:** Yazarlar arasında çıkar çatışması belirtilmemiştir.
**Şikayetler:** hmj@hitit.edu.tr
**Katkı Beyanı:** Fikir/Hipotez: YK, HEŞK Tasarım: YK, HEŞK Veri Toplama/Veri İşleme: YK, HEŞK Veri Analizi: YK, HEŞK Makalenin Hazırlanması: YK, HEŞK
**Hasta Onamı:** Onama gerek yoktur.
**Finansal Destek:** Finansal destek alınmamıştır.

# The Relationship Between the Dose of Nitroglycerin Administered through the Radial Sheath and Radial Artery Spasm During Elective Coronary Angiography via the Radial Artery

**Yucel Kanal[1], Hatice Eftal Seyda Kanal[2]**

[1]Sivas Cumhuriyet University Faculty of Medicine, Department of Cardiology, Sivas, Türkiye
[2]Tokat Provincial Health Directorate, Tokat, Türkiye

**Adres for Correspodence:** Sivas Cumhuriyet University Faculty of Medicine Cardiology Clinic, Sivas, Türkiye
e-mail: yucel_kanal@hotmail.com

**Orcid ID:** YK: 0000-0003-0934-0266
HESK: 0000-0002-0311-050X

**Cite As:** Kanal Y, Kanal HES. The Relationship Between the Dose of Nitroglycerin Administered through the Radial Sheath and Radial Artery Spasm During Elective Coronary Angiography via the Radial Artery Hitit Med J 2023;5(3): 216-220. https://doi.org/10.52827/hititmedj.1334133

## Abstract

**Objective:** Transradial approach in coronary interventions is becoming increasingly popular due to its lower rates of vascular complications, reduced procedural costs, and earlier patient mobilization. Radial artery spasm is a significant issue that needs to be addressed during transradial approach. Various vasodilators such as calcium channel blockers, nitrates, and moxisylyte have been shown to reduce radial artery spasm when administered intra-arterially. While no clear data exists on the nitroglycerin dosage used in transradial approach, studies have utilized doses ranging from 100 mcg to 500 mcg. This study evaluated the relationship between different nitrate dosages and radial artery spasm and procedural hypotension in patients undergoing elective coronary angiography.

**Material and Method:** This retrospective study included patients who underwent coronary angiography with transradial approach in our hospital's catheter laboratory and were discharged with medical follow-up. The selected patients were divided into two groups based on the dose of nitroglycerin administered: 200 mcg and 300 mcg after radial sheath placement. The incidence of radial artery spasm between the two groups was compared, and the relationship between the administered nitroglycerin dose and radial artery spasm was analyzed.

**Results:** The study included 133 patients with an average age of 61 ± 10.8 years, and 43% of the patients were female. Radial artery spasm was significantly higher in patients receiving 200 mcg of nitroglycerin than those receiving 300 mcg (16.1% vs. 4.2%, *p= 0.03*) . There was no significant difference in the occurrence of hypotension between the two groups. Multivariate logistic regression analysis indicated that the nitroglycerin dose and fasting glucose were independent predictors of radial artery spasm ($p<0.05$).

**Conclusion:** In our study, the intra-arterial administration of 300 mcg nitroglycerin, as opposed to 200 mcg, effectively reduced radial artery spasm before transradial approach. Moreover, significant hypotension did not occur during the procedure in these patients.

**Keywords:** Coronary angiography, Radial artery spasm, Transradial access

**Date of Submission:** 30.07.2023
**Date of Acceptance:** 19.09.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** Approval was received from Tokat Gaziosmanpaşa University Ethics Committee on 19.01.2023, number 23-KAEK-010
**Plagiarism Checks:** Yes - intihal.net
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: YK, HESK Design: YK, HESK Data Collection/Data Processing: YK, HESK Data Analysis: YK, HESK Article Preparation: YK, HESK
**Informed Consent:** Not applicable.
**Financial Disclosure:** There is no financial support used in the study.

## Giriş

Koroner girişimlerde transradial yaklaşım (TRA), daha düşük vasküler komplikasyon oranları, azalan işlem maliyetleri ve daha erken hasta mobilizasyonu nedeniyle giderek daha popüler hale gelmektedir (1,2). Transfemoral yaklaşımda lokal vaskuler komplikasyon oranı %2,8 iken; TRA yaklaşımda lokal vaskuler komplikasyonlar %0,3 oranında izlenmiştir (3,4). TRA'nın ana komplikasyonları %4-20 oranında meydana gelen radial arter spazmı (RAS) ve %2-30'a varan bir sıklıkla giriş yerinde oluşan tromboz sonucunda gelişen radial arter tıkanıklığı (RAO) olmakla beraber, daha az görülen komplikasyonları arasında lokal kanama, hematom, psödoanevrizma oluşumu ve nadiren vasküler perforasyon yer alır (5,6). Radial arter çapının küçük olması, kadın cinsiyet, sık kateter değişimi, işlem süresinin uzun olması, kullanılan sheat boyutunun büyümesi, operatörün deneyimsizliği gibi faktörlerle RAS oranının arttığı gösterilmiştir (7). RAS'ın kalsiyum kanal blokerleri, nitratlar ve moksidosin gibi çeşitli vazodilatörlerin damar içine uygulanmasıyla azaltılabileceği gösterilmiştir. Bu vazodilatörlerin monoterapi veya kombinasyon ile kullanıldığı çeşitli çalışmalar yapılmıştır. Birçok çalışmada kombinasyon tedavilerinin ek fayda getirmediği saptanmıştır (8). TRA'da kullanılan nitrogliserin dozu ile ilgili net bir veri olmamakla birlikte, çalışmalarda damar içine doz olarak 100 mcg- 500 mcg dozlar kullanılmıştır (9). TRA'da kullanılan ideal nitrogliserin dozunu belirlemek için yapılan çalışmalar yetersizdir. Bu çalışmada elektif koroner anjiografi yapılan hastalarda farklı nitrat dozları ile RAS ve işlem sırasında gelişen hipotansiyon ilişkisi değerlendirilmiştir.

## Gereç ve Yöntemler

Bu retrospektif araştırmaya hastanemiz kateter laboratuvarında 1 Mart 2020 - 1 Aralık 2022 tarihleri arasında TRA yoluyla koroner anjiografi (KAG) yapılan ve medikal takip kararı verilen hastalar dahil edilmiştir. Bu hastalar içinden, daha önce radial arter kateterizasyonu öyküsü olan, radial iğnesi ile birden fazla giriş denenmesi yapılan, aynı seansta veya 1 ay içinde radial koroner girişim geçiren, işlem öncesinde oral kalsiyum kanal blokeri veya oral nitrat kullanan, işlem öncesi sistolik kan basıncı < 90 mmhg olan, malignite öyküsü olan, son dönem böbrek ya da karaciğer hastalığı olan, atrial fibrilasyon (AF) veya başka bir sebepten antikoagülan tedavi altında olan, 1 ay sonra poliklinik kontrolüne gelmeyen ve işlem sonrası verilerine ulaşılamayan hastalar dışlandı. Kalan 133 hasta final çalışma grubu olarak belirlendi. Çalışmamız, Tokat Gaziosmanpaşa Üniversitesi Etik Kurulundan, 19.01.2023 tarihinde, 23-KAEK-010 no ile onay almıştır.

Değerlendirmeye alınacak veriler hastanemizin kardiyoloji kliniği kateter laboratuvarı arşivinden, hasta dosyalarından ve hastane bilgisayar kayıt sisteminden elde edildi. TRA yoluyla KAG yapılan ve medikal takip kararı verilen hastaların verileri incelenerek işlem esnasında RAS gelişen hastalar RAS (+) grubu olarak belirlendi. Belirlenen hastalar radial sheat yerleştirildikten sonra 200 mcg ve 300 mcg nitrogliserin verilenler olarak iki gruba ayrıldı. Sonuç olarak iki grup arası RAS oranları değerlendirilerek, verilen nitrogliserin dozu ile RAS arasında ilişki incelendi. Ayrıca bu hastalarda nitrogliserin dozu sonrası hipotansiyon gelişenler de kaydedildi.

KAG, operatör tercihine göre sağ ya da sol radial yolla yapıldı. Tüm hastaların işlem yerine radial ponksiyon öncesi, insülin enjektör iğnesi kullanılarak 2 ml %2 prilokain subkutan enjekte edildi. Ardından 20 gauce radial iğne ile ponksiyon yapıldıktan sonra 0.021 inçlik 45 cm kılavuz tel yerleştirildi. Daha sonra bu telin üzerinde 6F 7 cm uzunluğunda REPA marka sheat yerleştirildi ve bu sheat içerisinden 5000 U heparin yapıldı. Ayrıca tüm hastalara sheat içinden operatör tercihine göre 200 ya da 300 mcg nitrogliserin verildi. Takibinde sheat içinden 10 cc serum fizyolojik verildi. KAG öncesi ve nitrogliserin yapıldıktan 5 dk içindeki en düşük sistolik kan basıncı kayıt edildi. İki kan basıncı arasındaki fark 20 mmhg nin üzerindeki hastalar, hipotansiyon gelişen hastalar olarak belirtildi.

Koroner anjiografi işlemi için ilk tercih olarak sağ ve sol 6F Judkins 3,5 diagnostik kateterler kullanıldı. Bu kateterler 0,035 normal guide tel ile gönderildi. İşlem sürecinde RAS hastaları belirlendi. RAS, hastaların işlem sırasında ağrı hissetmesi ve operatörler tarafından saptanan kateter veya kılavuz telleri ilerletme veya geri çekme zorluğu ile tespit edildi. Ardından radial arterde gözlenen diffüz spazmın, nitrogliserin infüzyonu ve beklemeyle düzelmesi ile spazm belgelendi.

RAS saptanan hastaların demografik ve klinik verileri, kan parametreleri, KAG sonuçları da kaydedildi. KAG sonucunda, koroner arter darlığı olmayan hastalar normal, koroner arter darlığı <% 50 olan minimal KAH, >% 50 darlık olan ciddi KAH olarak belirlenmiştir.

*Statistical Analysis*

Elde edilen veriler Windows Statistical Package For Social Sciences (SPSS) 23.0 kullanılarak araştırmacı tarafından bilgisayar ortamında analiz edildi. Sürekli değişkenler ortalama ± standart sapma veya ortanca (minimum-maksimum) olarak tanımlandı ve kategorik değişkenler yüzde olarak ifade edildi. Kolmogorov-Smirnov ve Shapiro-Wilk testleri ile dağılımın normalliği saptandıktan sonra sürekli değişkenler Mann-Whitney U testi veya Student t-testi ile, kategorik değişkenler ise Ki-kare testi veya Fisher's Exact testi ile karşılaştırıldı. Çok değişkenli lojistik regresyon analizi kullanılarak RAS'ın bağımsız öngörücüleri bulundu. Çok değişkenli model, tek değişkenli regresyon analizindeki p değerini temel alarak, anlamlı ölçüde ilişkili olan (p<0,20) tüm değişkenleri içeriyordu. RAS'ın bağımsız öngörücüleri için ROC (Receiver operating characteristic) analizi yapıldı. *p değeri 0,05*'ten küçük hesaplandığında istatistiksel olarak anlamlı kabul edildi.

## Bulgular

Çalışmamıza dahil edilen 133 hastanın yaş ortalaması 61 ± 10,8 yıldır ve %43'ü kadındır. Hastaların demografik, klinik ve anjiyografik özellikler Tablo 1'de listelenmiş olup, spazm (+) ve spazm (-) grupları karşılaştırılmıştır. RAS, 200 mcg nitrogliserin yapılan hastalarda 300 mcg nitrogliserin yapılanlara göre anlamlı düzeyde yüksek bulunmuştur (% 16,2 - % 4,6; *p= 0,03*) (Tablo I). Yalnızca bir hastada (300 mcg nitrogliserin) işlem esnasında hipotansiyon gelişmiştir. İki grup arasında demografik, klinik ve diğer anjiografik parametreler açısından anlamlı fark yoktur.

Laboratuvar verilerine bakıldığında RAS (+) hastalarda açlık glukozu anlamlı olarak daha yüksek saptanmıştır (*p= 0,011*) (Tablo II). Diğer parametrelerde iki grup arasında anlamlı fark belirlenmemiştir.

Tek değişkenli lojistik regresyon analizinde, nitrogliserin dozu ve açlık glukozu, RAS ile anlamlı şekilde ilişkilidir. Çok değişkenli lojistik regresyon analizinde, nitrogliserin dozunun

**Tablo I.** Hastaların Demografik, Klinik ve Anjiyografik Özellikleri

| Değişkenler | Spazm (+) (n=14) | Spazm (-) (n=119) | *p* |
|---|---|---|---|
| Yaş, yıl | 59,6 ± 10,8 | 61,4 ± 10,8 | *0,567* |
| Kadın, n (%) | 8 (57,1) | 49 (41,2) | *0,253* |
| Hipertansiyon (%) | 6 (42,9) | 69 (58,0) | *0,280* |
| DM, n (%) | 6 (42,9) | 40 (33,6) | *0,557* |
| VKİ, kg/m² | 28,5 (23,4-39,5) | 28,2 (20,2-44,9) | *0,758* |
| Sigara, n (%) | 3 (21,4) | 46 (38,7) | *0,206* |
| KAG sonuç, n (%) | | | *0,720* |
| Normal | 5 (35,7) | 38 (31,9) | |
| Minimum KAH | 6 (42,9) | 43 (36,1) | |
| Ciddi KAH | 3 (21,4) | 38 (31,9) | |
| Kullanılan radial arter, n (%) | | | *0,432* |
| Sağ radial arter | 13 (92,9) | 115 (96,6) | |
| Sol radial arter | 1 (7,1) | 4 (3,4) | |
| İşlem süresi, dakika | 5,5 (2,0-17,0) | 5,0 (2,0-28,0) | *0,994* |
| Nitrogliserin dozu, n (%) | | | *0,030* |
| 200 ug | 11 (78,6) | 57 (47,9) | |
| 300 ug | 3 (21,4) | 67 (52,1) | |
| Hipotansiyon, n (%) | 0 (0,0) | 1 (0,8) | *1,000* |

DM, Diabetes mellitus; VKİ, vücut kitle indeksi; KAG, Koroner anjiografi; KAH, Koroner arter hastalığı; *p <0,05* istatistiksel önemi gösterir.

**Tablo II.** Hastaların Laboratuvar Bulguları

| Değişken | Spazm (+) (n=14) | Spazm (-) (n=119) | *p* |
|---|---|---|---|
| WBC, x10⁹/L | 7,5 (5,1-14,0) | 7,9 (4,1-16,0) | *0,714* |
| Hemoglobin, g/dl | 14,5 (12,0-17,6) | 14.2 (9,2-38,0) | *0,670* |
| Hemotokrit, % | 43,0 (37,0-52,7) | 43,0 (31,0-55,9) | *0,852* |
| MCV, fL | 85,0 (81,0-97,0) | 87,0 (10,0- 96,9) | *0,933* |
| Platelet sayısı x10⁹/L | 241,0 (172,0-440,0) | 242,0 (140,0-400,0) | *0,747* |
| Kan üre nitrojeni, mg/dl | 36,0 (27,0-89,0) | 33,0 (17,0-81,0) | *0,070* |
| Kreatinin, mg/dl | 0,8 (0,6-1,4) | 0,8 (0,5-1,9) | *0,635* |
| Açlık kan şekeri, mg/dl | 125,5 (83,0-320,0) | 102,0 (11,0-326,0) | *0,011* |
| AST, u/l | 19,0 (11,0-50,0) | 22,0 (8,0-75,0) | *0,139* |
| ALT, u/l | 16,0 (7,0-37,0) | 20,0 (9,0-72,0) | *0,081* |
| GGT, u/l | 34,5 (10,0-137,0) | 28,0 (6,0-82,0) | *0,259* |
| HDL-C, mg/dl | 42,0 (30,0-65,0) | 45,0 (21,0-97,0) | *0,200* |
| LDL-C, mg/dl | 110,0 (83,0-163,0) | 110,5 (26,0-192,0) | *0,462* |
| Trigliserit, mg/dl | 169,5 (77,0-590,0) | 129,5 (49,0-521,0) | *0,091* |
| Total kolesterol, mg/dl | 182,5 (145,0-274,0) | 190,0 (93,0-298,0) | *0,652* |
| Albumin, g/L | 43,0 (31,0-45,0) | 42,0 (33,0-52,0) | *0,671* |
| C-reactive protein, mg/L | 2,0 (0,6-15,0) | 3,0 (0,2-45,0) | *0,634* |

WBC, Beyaz kan hücresi sayımı; MCV, Ortalama eritrosit hacmi; AST, Aspartat transaminaz; ALT, Alanin transaminaz; GGT, Gama glutamil transferaz; HDL-C, Yüksek dansiteli lipoprotein kolesterol; LDL-C, Düşük dansiteli lipoprotein kolesterol; *p <0,05* istatistiksel önemi gösterir.

ve açlık glukozunun RAS'ın bağımsız öngörücüleri olduğu gösterilmiştir (*p<0,05*) (Tablo III).

ROC eğrisinin altında kalan alan (AUC) açlık kan şekeri için oluşturuldu (AUC: 0,709, %95 güven aralığı [CI]: 0,565-0,853, *p= 0,011*), çünkü bu parametre RAS'ın bağımsız bir öngörücüsüydü. Açlık kan glukozu 104,5 mg/dl kesme noktası ile RAS'ı %85 duyarlılık ve %55 seçicilik ile öngörmüştür (Şekil I).

## Tartışma

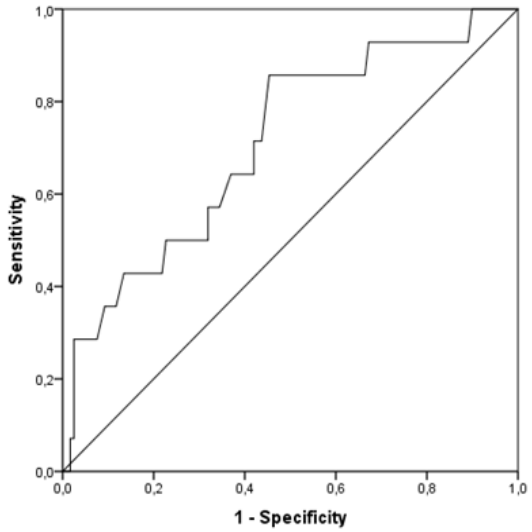
TRA, son zamanlarda kılavuzlarda önerilen etkin ve güvenli girişim yoludur (3). Yapılan çalışmalarda TRA'nın transfemoral yaklaşıma göre mortalitede azalma, hastanede yatış

**Tablo III.** Radyal Arter Spazmı Öngörücüleri İçin Tek Değişkenli ve Çok Değişkenli Regresyon Analizi

| Değişken | Univariate Analiz | | | Multivariate Analiz | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | p | OR | 95% CI | p |
| Nitrogliserin dozu | 3,988 | 1,059-15,024 | 0,041 | 4,331 | 1,071-17,512 | 0,040 |
| Açlık kan glukozu | 1,012 | 1,003-1,021 | 0,008 | 1,013 | 1,003-1,022 | 0,008 |

OR, Odds oranı; CI, Güven aralığı; *p <0,05* istatistiksel önemi gösterir.

**Şekil I.** Radial arter spazmında açlık kan glukozu için Receiver Operating Characteristics (ROC). AUC, eğri altında kalan alan; *p <0,05* istatistiksel önemi gösterir.




süresinin azalması, maliyet azalması ve hasta konforu ile ilişkili olduğu gösterilmiştir (3,8,10). RAS, TRA'da hala önemli bir sorundur ve bu yöntemi kullanan operatörler bu komplikasyondan kaçınmanın en iyi yolunu bulmaya çalışmaktadır. Biz de bu nedenle çalışmamızda, radial anjiografi öncesi radial sheat içinden yapılan nitrogliserin dozu ile RAS arasında anlamlı ilişki olup olmadığını değerlendirdik. Çalışmamızda RAS oranını %10,5 olarak saptadık. Daha önce yapılan birçok farklı çalışmayı içeren derlemede ortalama RAS oranı % 14,7 olarak gösterilmiştir (6).

TRA'da kullanılan nitrogliserin dozu ile ilgili net bir veri olmamakla birlikte, çalışmalarda damar içine doz olarak 100 mcg- 500 mcg dozlar kullanılmıştır (9). Çalışmamızda 200 mcg nitrogliserin verilen grupta RAS oranı %16,2 iken, 300 mcg nitrogliserin verilen grupta %4,6 izlenmiştir. İki grup karşılaştırıldığında düşük doz (200 mcg) nitrogliserin yapılan hastalarda anlamlı olarak daha fazla RAS gelişmiştir (p= 0,03). Yüksek ve düşük doz nitrogliserin yapılan gruplar arasında işlem esnasında gelişen hipotansiyon arasında anlamlı fark yoktur. Monoterapiler ile ilgili daha önce yapılan çalışmaları analiz eden bir metaanalizde 200 mcg nitrogliserin ile %2 RAS geliştiği izlenirken; 100 mcg nitrogliserin ile %4 RAS izlenmiştir (11). Nitrogliserin monoterapi dozlarını karşılaştıran bu çalışma ve bizim çalışmamız dışında başka literatür izlenmemiştir. Kombinasyon tedavisinin RAS üzerine etkisini değerlendiren bir çalışmada diltizem ve nitrogliserin kombinasyonunun sadece nitrogliserin verilen hastalarla kıyaslandığında, RAS üzerine ek fayda göstermediği belirlenmiştir. Tüm bu çalışmalar da bizim çalışmamızın sonucunu destekler niteliktedir. Bizim çalışmamızın ve önceki çalışmaların sonu-

cuna dayanarak, TRA'da 300 mcg nitrogliserin kullanılarak güvenle RAS azaltılabilir.

Daha önce yapılan çalışmalarda TRA'da diyabetes mellitus (DM), kadın cinsiyet, genç yaş ve daha düşük vücut kitle indeksinin (9) RAS oranını arttırdığı gözlenmişse de bizim çalışmamızda bu parametrelerde iki grup arasında anlamlı fark izlenmemiştir. Ayrıca RAS gelişen grup ile diğer grup arasında işlem süresi açısından da anlamlı fark izlenmemiştir.

Bizim çalışmamızda açlık kan glukozu yüksek olan hastalarda RAS daha fazla izlenmiştir. Daha önceki çalışmalarda açlık glukozu ile RAS ilişkisiyle ilgili bir veri bulunmamaktadır. DM ile RAS ilişkili olsa da bizim çalışmamızda DM ile RAS arasında ilişki saptanmamıştır. Bunun öncelikli sebebinin çalışmamızdaki hasta sayısının az olmasına bağlıyoruz. Bu çalışmada DM olsun ya da olmasın açlık glukozu yüksek olan hastalarda RAS anlamlı düzeyde daha fazla izlenmiştir. Hipergliseminin arterler üzerine direk ve indirek etkileriyle, vaskuler endotel hasarı sonucu ateroskleroza zemin hazırlaması ve vaskuler düz kaslardaki etkileri nedeniyşe bu durumun olabileceğini düşünmekteyiz (12,13).

Çalışma retrospektif olarak tasarlanmıştır. Operatöre veya hastaya kör değildir. RAS tanımı, operatörün kateter manipülasyonunda zorluk hissetmesine, hastanın ağrı farkındalığı ve bildirimine bağlı olduğu için objektif değildir ve bir dereceye kadar yanlılığa açıktır. Çalışmanın örneklem büyüklüğü sınırlıdır ve tek bir merkezde yapılmıştır. Bu durum, sonuçların genelleştirilebilirliğini kısıtlayabilir. Gelecekte, çok merkezli daha büyük ölçekli çalışmaların yapılması, sonuçların daha geniş bir hasta grubuna uygulanabilirliğini doğrulamak açısından faydalı olacaktır.

## Sonuç

Çalışmamızda TRA öncesi sheat içinden radial arter içine 200 mcg nitrogliserin yerine 300 mcg nitrogliserin verilerek, RAS etkin bir şekilde azaltılmıştır. Bu hastalarda işlem esnasında anlamlı bir hipotansiyon da gelişmemiştir. Bu nedenle biz TRA'da 200 mcg nitrogliserin yerine 300 mcg nitrogliserin kullanımını öneriyoruz.

## Kaynaklar

1. Kiemeneij F, Laarman GJ, Slagboom T, van der Wieken R. Outpatient coronary stent implantation. J Am Coll Cardiol 1997;29(2):323-327.

2. Mann T, Cubeddu G, Bowen J, et al. Stenting in acute coronary syndromes: a comparison of radial versus femoral access sites. J Am Coll Cardiol 1998;32(3):572-576.

3. Mehta SR, Jolly SS, Cairns J, et al. Effects of radial versus femoral artery access in patients with acute coronary syndromes with or without ST-segment elevation. J Am Coll Cardiol 2012;60(24):2490-2499.

4. Varenne O. How to prevent & to manage radial artery spasm during coronary interventions? Indian Heart J 2010;62(3):230-233.

5. Wagener JF, Rao SV. Radial artery occlusion after transradial approach to cardiac catheterization. Curr Atheroscler Rep 2015;17(3):489.

6. Kristic I, Lukenda J. Radial artery spasm during transradial coronary procedures. J Invasive Cardiol 2011;23(12):527-531.

7. Lo TS, Nolan J, Fountzopoulos E, et al. Radial artery anomaly and its influence on transradial coronary procedural outcome. Heart 2009;95(5):410-415.

8. Curtis E, Fernandez R, Lee A. The effect of vasodilatory medications on radial artery spasm in patients undergoing transradial coronary artery procedures: a systematic review. JBI Database System Rev Implement Rep 2017;15(7):1952-1967.

9. Abdelazeem B, Abuelazm MT, Swed S, et al. The efficacy of nitroglycerin to prevent radial artery spasm and occlusion during and after transradial catheterization: A systematic review and meta-analysis of randomized controlled trials. Clin Cardiol 2022;45(12):1171-1183.

10. De Luca G, Schaffer A, Wirianta J, Suryapranata H. Comprehensive meta-analysis of radial vs femoral approach in primary angioplasty for STEMI. Int J Cardiol 2013;168(3):2070-2081.

11. Kwok CS, Rashid M, Fraser D, Nolan J, Mamas M. Intra-arterial vasodilators to prevent radial artery spasm: a systematic review and pooled analysis of clinical studies. Cardiovasc Revasc Med 2015;16(8):484-490.

12.Brownlee,M. Biochemistry and molecular cell biology of diabetic complications. Nature 2001;414(6865):813-820.

13. Kofler S, Nickel T, Weis M. Role of cytokines in cardiovascular diseases: a focus on endothelial responses to inflammation. Clin Sci (Lond) 2005;108(3):205-213.

# Türkiye'nin Çorum İlinde Yaşam Bölgelerine Göre Tamamlayıcı-Alternatif Tıp Bilgi ve Tutumları

**Hülya Yılmaz Başer[1,2], Coşkun Öztekin[3]**

[1]Bandırma Onyedi Eylül Üniversitesi Tıp Fakültesi, Acil Tıp Anabilim Dalı, Balıkesir, Türkiye
[2]Aile Hekimi Uzmanı, Balıkesir, Türkiye
[3]Hitit Üniversitesi Tıp Fakültesi, Aile Hekimliği Anabilim Dalı, Çorum, Türkiye

**Yazışma Adresi:** Bandırma Onyedi Eylül Üniversitesi Tıp Fakültesi, Acil Tıp Anabilim Dalı, Balıkesir, Türkiye
e-posta: ylmz_hly_35@yahoo.com

**Orcid NO:** HYB: 0000-0002-1416-1521
CÖ: 0000-0002-4490-7136

**Atıf:** Başer HY, Öztekin C. Türkiye'nin Çorum İlinde Yaşam Bölgelerine Göre Tamamlayıcı-Alternatif Tıp Bilgi ve Tutumları. Hitit Med J 2023;5(3): 221-226. https://doi.org/10.52827/hititmedj.1323358

## Özet

**Amaç:** Tüm dünyada Tamamlayıcı ve Alternatif Tıp farkındalığı ve kullanımı giderek artmaktadır. Bu çalışmada, Türkiye'de kentsel ve kırsal kesimde yaşayan insanların Tamamlayıcı ve Alternatif Tıp yöntemleri ve etkileyen faktörler hakkındaki bilgi ve tutumlarını araştırmayı amaçladık.

**Gereç ve Yöntem:** Yüz yüze anket yöntemiyle gerçekleştirilen kesitsel-tanımlayıcı tipteki bu çalışmada, 3. basamak bir eğitim ve araştırma hastanesinin aile hekimliği polikliniğine 10 ve 31 Mart 2021 tarihleri arasında başvuran 18-65 yaş arası hastalar çalışmaya dâhil edilmiştir.

**Bulgular:** Araştırmaya kentte 277 (%71,9) ve kırsalda 108 (%28,1) olmak üzere toplam 385 kişi katılmıştır. En az bir Tamamlayıcı ve Alternatif Tıp yöntemi uygulama oranı kentsel kesimde %51, kırsal kesimde %43,4 olarak bulundu. Yaşam alanlarına göre istatistiksel olarak anlamlı fark yoktu (*p=0,229*). Her iki bölgede de eğitim düzeyleri ile Tamamlayıcı ve Alternatif Tıp yönteminin uygulanması arasında istatistiksel olarak anlamlı bir ilişki bulunmuştur (kentsel *p=0,017*, kırsal *p=0,020*). Eğitim düzeyine paralel olarak sosyal medya, internet ve arkadaşlar Tamamlayıcı ve Alternatif Tıp'ın yayılmasında rol oynamaktadır.

**Sonuç:** Tamamlayıcı ve Alternatif Tıp uygulamaları hakkında farkındalık artmaktadır. Sağlığın korunması ve sürdürülmesine yönelik Tamamlayıcı ve Alternatif Tıp uygulamalarındaki farklılıkları ortaya çıkaracak çalışmalara ihtiyaç vardır.

**Anahtar Sözcükler:** Bilgi, Sosyodemografi, Tamamlayıcı-Alternatif Tıp, Tamamlayıcı tıp, Tutumlar

**Geliş Tarihi:** 05.07.2023
**Kabul Tarihi:** 02.10.2023
**Yayım Tarihi:** 10.10.2023

**Hakem Değerlendirmesi:** Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
**Etik Beyanı:** Çalışma Hitit Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulu tarafından 10.03.2021 tarih ve 428 karar numarası ile onaylandı.
**İntihal Kontrolleri:** Evet - iThenticate
**Çıkar Çatışması:** Yazarlar arasında çıkar çatışması belirtilmemiştir.
**Şikayetler:** hmj@hitit.edu.tr
**Katkı Beyanı:** Fikir/Hipotez: HYB, CÖ Tasarım: HYB, CÖ Veri Toplama/Veri İşleme: HYB, CÖ Veri Analizi: HYB, CÖ Makalenin Hazırlanması: HYB, CÖ
**Hasta Onamı:** Katilimcilardan bilgilendirilmis onam formu alinmistir.
**Finansal Destek:** Finansal destek alınmamıştır.

Bu yayından elde edilen bazı sonuçlar, 20-23 Mayıs 2021 tarihlerinde Adana'da düzenlenen 20. Uluslararası Doğu Akdeniz Aile Hekimliği Kongresi'nde sunuldu.

# Complementary-Alternative Medicine Knowledge and Attitudes According to Living Regions in Corum, Türkiye

**Hulya Yılmaz Baser[1,2], Coskun Oztekin[3]**

[1]Bandırma Onyedi Eylul University Faculty of Medicine, Department of Emergency Medicine, Balıkesir, Türkiye
[2]Family Physician Specialist, Balıkesir, Türkiye
[3]Hitit University Faculty of Medicine, Department of Family Medicine, Corum, Türkiye

**Adres for Correspodence:** Bandırma Onyedi Eylul University Faculty of Medicine, Department of Emergency Medicine, Balıkesir, Türkiye
e-mail: ylmz_hly_35@yahoo.com

**Orcid ID:** HYB: 0000-0002-1416-1521
CÖ: 0000-0002-4490-7136

**Cite As:** Baser HY, Oztekin C. Complementary-Alternative Medicine Knowledge and Attitudes According to Living Regions in Corum, Türkiye. Hitit Med J 2023;5(3): 221-226. https://doi.org/10.52827/hititmedj.1323358

## Abstract

**Objective:** The awareness and use of Complementary and Alternative Medicine is increasing all over the world. In this study, we aimed to investigate the knowledge and attitudes of people living in urban and rural areas in Türkiye about Complementary and Alternative Medicine methods and influencing factors.

**Material and Method:** In this cross-sectional-descriptive study, which was conducted with the face-to-face survey method, Patients between the ages of 18-65 who applied to the family medicine outpatient clinic of a 3rd level training and research hospital between 10 and 31 March 2021 were included in the study.

**Results:** A total of 385 people, 277 (71.9%) from urban and 108 (28.1%) from rural areas, participated in the research. The rate of application of at least one Complementary and Alternative Medicine method was 51 % in urban areas and 43.4% in rural areas. There was no statistically significant difference according to living areas ($p=0.229$). A statistically significant relationship was found between education levels and the application of Complementary and Alternative Medicine methods in both regions (urban $p=0.017$, rural $p=0.020$). In parallel with the level of education, social media, internet and friends play a role in the spread of Complementary and Alternative Medicine.

**Conclusion:** Awareness about Complementary and Alternative Medicine applications is increasing. There is a need for studies that will reveal the differences in Complementary and Alternative Medicine applications for the protection and maintenance of health.

**Keywords:** Attitudes, Complementary-Alternative Medicine, Complementary medicine, Knowledge, Sociodemographics

**Date of Submission:** 05.07.2023
**Date of Acceptance:** 02.10.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** The study was approved by the Hitit University Faculty of Medicine Clinical Research Ethics Committee with the date 10.03.2021 and decision number 428.
**Plagiarism Checks:** Yes - iThenticate
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: HYB, CO Design: HYB, CO Data Collection/Data Processing: HYB, CO Data Analysis: HYB, CO Article Preparation: HYB, CO
**Informed Consent:** Informed consent forms were obtained from the participants.
**Financial Disclosure:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

## Giriş

İnsanlık tarihi boyunca değişmeyen öncelikli hedeflerden biri sağlıklı olmaktır. Dünya Sağlık Örgütü (WHO) sağlığı "sadece hastalık veya sakatlığın olmayışı değil, fiziksel, ruhsal ve sosyal yönden tam bir iyilik hali" olarak tanımlamaktadır (1). Modern tıptaki gelişmelerden önce toplumların sağlık için uyguladıkları yöntemleri yaşadıkları coğrafyaya, kültürlerine veya inançlarına göre şekillendirdikleri görülmektedir. 19. yüzyıldan itibaren modern tıptaki gelişmelerle birlikte bu uygulamalar yerini modern tıp yöntemlerine bırakmaya başlamıştır. Konvansiyonel Tıp: Eğitimli profesyoneller tarafından uygulanan kanıtlara dayalı olarak geliştirilen, okullarda okutulan dünya çapında tanınan tıptır. Modern tıp, ortodoks tıp, batı tıbbı, bilimsel tıp olarak da adlandırılır (2). Ortalama yaşam süresinin uzaması, buna bağlı kronik hastalıklara yakalanan yıllar içinde artması, sağlıklı ve genç kalmanın popülerleşmesiyle birlikte sağlığa verilen önem artmış ve bu arayışta modern tıp dışı yöntemler de bir seçenek haline gelmiştir. Dünyada ve ülkemizde geleneksel olmayan tıbbi yöntemlere talep artmıştır.

Literatüre bakıldığında Geleneksel ve tamamlayıcı tıp (GETAT) konusunda yapılan bilimsel araştırmaların sayısı her geçen gün artmaktadır. Ancak, kentsel ve kırsal bölgelerde yaşayan insanların bilgi ve tutumlarını inceleyen araştırmaların sayısı sınırlıdır. Çalışmamızın amacı, Çorum ilinde kentsel ve kırsal bölgede yaşayan insanların geleneksel ve tamamlayıcı tıp yöntemleri hakkındaki bilgi ve tutumlarını karşılaştırmak, bunu etkileyen faktörleri ortaya koymak ve Türkiye'den elde edilen verilerle ulusal ve uluslararası literatüre katkıda bulunmaktır.

## Gereç ve Yöntemler

Çalışmamız, 10 Mart–31 Mart 2021 tarihleri arasında Hitit Üniversitesi Çorum Erol Olçok Eğitim ve Araştırma Hastanesi aile hekimliği polikliniğine başvuran 18-65 yaş arası bireylerin katılımı ile gerçekleştirilmiştir.

Bu araştırma, kesitsel-tanımlayıcı bir çalışma olarak planlanmıştır. Çalışma Hitit Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulu tarafından 10.03.2021 tarih ve 428 karar numarası ile onaylandı.

Bilgilendirilmiş onam formunu okuyup onaylayan ve dışlama kriterlerini karşılamayan 18-65 yaş arası katılımcılar çalışmaya dâhil edildi. Çalışmamızın dışlama kriterleri; Fiziksel, zihinsel ve bilişsel engelleri olan GETAT uygulayıcıları ve sağlık çalışanları olarak tanımlanmıştır.

Araştırmada veri kaynağı olarak araştırmacılar tarafından benzer özelliklere sahip literatür taranarak belirlenen sorulardan oluşan anket formu kullanılmıştır. Anket formu; Sosyo-demografik özellikler, tamamlayıcı ve alternatif tıp ile ilgili bilgi ve tutumları sorgulayan 2 bölümden oluşmaktadır.

*İstatistik Yöntemler*

Araştırma verileri SPSS 22.0 (IBM Co., Armonk, NY, USA) istatistik paket programı ile değerlendirilmiştir. Tanımlayıcı istatistikler nicel veriler aritmetik ortalama, standart sapma, kategorize veriler frekans, yüzde ve sayı olarak sunuluştur. İstatistiksel yöntem olarak kentsel ve kırsal bölgede yaşayanlar arasında, sürekli nicel veriler normal dağılımı Kolmagorov-Smirnow / Shapiro-Wilks testleri ile test edildikten sonra dağılım şekline göre; normal dağılım gösteriyor ise Stutend t test, normal dağılım göstermiyorsa Mann Whitney-U testleri kullanılarak değerlendirildi. Yaşam bölgelerine göre Kategorize verilerin karşılaştırılmasında Ki-kare / Fisher exact test kullanıldı. Yaşam bölgelerine göre en az bir veya daha fazla GETAT uygulaması yöntemi duyulmasına etki eden sosyo-demografik özelliklerin değerlendirilmesinde, yaşam bölgelerine göre en az bir GETAT yöntemi uygulatılmasına etki eden sosyo-demografik özelliklerin değerlendirilmesinde ve yaşam bölgelerine göre GETAT isminin duyulmasına etki eden sosyo-demografik özelliklerin değerlendirilmesinde spearman korelasyon analizi (rho) kullanıldı. İstatistiksel anlamlılık için $p<0,05$ kabul edildi.

## Bulgular

Çalışmamıza 385 kişi katıldı. Katılımcıların yaş ortalaması 40,71±12,73 yıl idi. Katılımcıların 277'si (%71,9) kentsel bölgede, 108'i (%28,1) kırsal bölgede yaşamaktadır. Kentsel ve kırsal kesimde yaşayan katılımcıların temel sosyo-demografik özellikleri Tablo I'de gösterilmiştir.

**Tablo I.** Kentsel ve kırsal bölgede yaşayan katılımcıların temel sosyo-demografik özellikleri

| | Kentsel n=277 | Kırsal n=108 | *p* |
|---|---|---|---|
| Yaş Grupları n (%) | | | |
| 18 – 29 Yaş | 58 (20,9) | 30 (27,8) | *0,004* |
| 30 – 39 Yaş | 76 (24,4) | 23 (21,3) | |
| 40 – 49 Yaş | 79 (28,5) | 16 (14,8) | |
| 50 – 65 Yaş | 64 (23,1) | 39 (36,1) | |
| VKİ Grupları n (%) | | | |
| Zayıf (< 18,5 Kg/m$^2$) | 8 (2,9) | 2 (1,2) | *0,891* |
| Normal (18,5 – 24,9 Kg/m$^2$) | 117 (42,2) | 44 (40,7) | |
| Kilolu (25,0 – 29,9 Kg/m$^2$) | 88 (31,8) | 34 (31,5) | |
| Obez / Morbid Obez (≥30,0 Kg/m$^2$) | 64 (23,1) | 28 (25,9) | |
| Cinsiyet n (%) | | | |
| Kadın | 155 (56) | 47 (43,5) | *0,028* |
| Erkek | 122 (44) | 61 (56,5) | |
| Medeni Durum n (%) | | | |
| Evli | 213 (76,9) | 72 (66,7) | *0,109* |
| Bekar | 53 (19,1) | 31 (28,7) | |
| Dul / Boşanmış | 11 (4,0) | 5 (4,6) | |
| Eğitim Durumu n (%) | | | |
| Okur/yazar | 6 (2,2) | 9 (8,3) | *<0,001* |
| İlk Okul | 61 (22,0) | 36 (33,3) | |
| Orta Okul | 31 (11,2) | 26 (24,1) | |
| Lise | 74 (26,7) | 29 (26,9) | |
| Üniversite | 105 (37,9) | 8 (7,4) | |
| Aylık Gelir Seviyesi n (%) | | | |
| Az | 47 (17,2) | 31 (28,7) | *0,036* |
| Orta | 218 (79,6) | 75 (69,4) | |
| Yüksek | 9 (3,3) | 2 (1,9) | |
| Sigara Kullanımı n (%) | | | |
| Evet | 78 (28,2) | 26 (24,1) | *0,417* |
| Hayır | 199 (71,8) | 82 (75,9) | |
| Kronik Hastalık Varlığı n (%) | | | |
| Evet | 84 (30,3) | 29 (26,9) | *0,501* |
| Hayır | 193 (69,7) | 79 (73,1) | |

VKİ; Vücut kitle indeksi

GETAT yöntemlerinden en az birini kentsel bölgede uygulama oranı %51 (255 kişiden 130'u), kırsal kesimde %43,4 (83 kişiden 36) idi. Uygulanan GETAT yöntemlerinden en az birine sahip olduğunu belirten katılımcıların yaşadıkları bölgeye göre istatistiksel olarak anlamlı fark yoktu ($p=0,229$). Her iki bölgede de eğitim düzeyleri ile GETAT yöntemlerinin uygulanması arasında istatistiksel olarak anlamlı bir ilişki bulunmuştur (kentsel $p=0,017$, kırsal $p=0,020$).

Ankette sorulan GETAT uygulamalarından bağımsız olarak katılımcılara "Geleneksel ve tamamlayıcı tıp (GETAT)" kelimesini duyup duymadıkları sorulduğunda; kentsel bölgede yaşayan 277 katılımcıdan 128'i (%46,2), kırsal bölgede yaşayan 108 katılımcıdan 41'i (%38) daha önce geleneksel ve

tamamlayıcı tıp kelimesini duyduğunu bildirdi. GETAT adının daha önce duyulmasının yaşanılan bölgelere göre farklılık göstermediği görüldü (*p=0,143*). Kentsel bölgede daha önce GETAT adını duyan katılımcıların yaş ortalaması 38,38±11,0 yıl iken, kırsal bölgede 39,22±13,55 yıl idi. Kentte ve kırsalda yaşayanlar arasında yaş farkı yoktu (*p=0,687*). Kentsel ve kırsal yaşam bölgelerine göre GETAT ismini daha önce duymaya etki eden faktörlerin korelasyon analizinde; kentsel bölgede yaşayanlarda genç yaşta olmanın, eğitim düzeyinin artmasının, aylık gelir durumunun artması ile GETAT ismini daha önce duyulması arasında pozitif korelasyon saptandı (Sırasıyla *rho=0,160, p=0,007, rho=0,447, p<0,001, rho=0,224, <0,001, rho=0,138, =0,021 ve rho=0,224, <0,001*). Kırsal bölgede yaşayanlarda ise yaş ile anlamlı bir korelasyon saptanmadı (*rho=0,098, p=0,312*). Eğitim düzeyinin artması, aylık gelir durumunun artması ile GETAT ismini daha önce duyulması ile pozitif korelasyon saptandı (Sırasıyla *rho=0,306, p=0,001, rho=0,230, p=0,017*).

Katılımcıların GETAT yöntemlerini nereden duydukları sorusuna verdikleri cevaplar Tablo 2'de gösterilmiştir. Kentsel bölgede yaşayanlar sırasıyla; %62,5'i internetten, %54,3'ü televizyondan, %50,8'i arkadaşlarından duyduğunu belirtti. Kırsal kesimde yaşayanlar %63,4 ile televizyondan, %48,8 ile internetten ve %47,5 ile arkadaşlarından duyduklarını belirtmişlerdir. GETAT yöntemlerinin işitme kaynağı açısından kentsel ve kırsal yaşam alanları arasında istatistiksel olarak anlamlı fark yoktu (Tablo II).

**Tablo II.** Katılımcıların yaşadıkları bölgeye göre GETAT yöntemlerini nereden duydukları sorusuna verdikleri cevaplar.

| GETAT yöntemlerini nereden duydunuz? * | | Kentsel n (%) | Kırsal n (%) | *p* |
|---|---|---|---|---|
| Arkadaşlar | Evet | 65 (50,8) | 19 (47,5) | 0,717 |
| | Hayır | 63 (49,2) | 21 (52,5) | |
| Sosyal medya platformları (Facebook, Instagram, vb.) | Evet | 63 (49,2) | 17 (41,5) | 0,387 |
| | Hayır | 65 (50,8) | 24 (48,5) | |
| İnternet siteleri | Evet | 80 (62,5) | 20 (48,8) | 0,120 |
| | Hayır | 48 (37,5) | 21 (51,2) | |
| Televizyon | Evet | 69 (54,3) | 26 (63,4) | 0,308 |
| | Hayır | 58 (45,7) | 15 (36,6) | |
| Hastane | Evet | 30 (23,4) | 10 (24,4) | 0,901 |
| | Hayır | 98 (76,6) | 31 (75,6) | |
| Aile hekimi | Evet | 26 (20,3) | 5 (12,2) | 0,242 |
| | Hayır | 102 (79,7) | 36 (87,8) | |
| Gazete ve benzeri yazılı materyaller | Evet | 21 (16,4) | 6 (14,6) | 0,788 |
| | Hayır | 107 (83,6) | 35 (85,4) | |

* İlgili soruya birden fazla cevap verilmiş olup, cevaplayan sayısına göre yüzde hesaplanmıştır.

## Tartışma

Modern tıptaki gelişmelerden önce toplumların sağlık için uyguladıkları yöntemleri yaşadıkları coğrafya, kültür ya da inançlara göre şekillendirdikleri görülmektedir. 19. yüzyıldan itibaren modern tıptaki gelişmelerle birlikte bu uygulamalar terk edilmeye başlanmıştır, yerini modern tıbbi yöntemlere bırakmıştır. Geleneksel Tıp: Okullarda öğretilen ve eğitimli profesyoneller tarafından uygulanan kanıtlara dayalı olarak geliştirilen dünyaca ünlü tıp. Modern tıp, ortodoks tıp, batı tıbbı ve bilimsel tıp olarak da adlandırılır (2). Yaşam süresinin uzaması, yaşlanmayla birlikte kronik hastalıkların artması, sağlıklı ve genç kalmanın yaygınlaşmasıyla birlikte sağlığa verilen önem artmış ve bu arayışta modern tıp dışı yöntemler de bir seçenek haline gelmiştir. Dünyada ve ülkemizde geleneksel olmayan tıbbi yöntemlere talep artmıştır. Literatüre bakıldığında geleneksel ve tamamlayıcı tıp alanında yapılan bilimsel araştırmaların sayısı her geçen gün artmaktadır. Ancak, kentsel ve kırsal bölgelerde yaşayan insanların bilgi ve tutumlarını inceleyen araştırmaların sayısı sınırlıdır. Türkiye kaynaklı literatürde GETAT yöntemlerinin uygulanmasının %12,2 ile %70 arasında olduğu belirtilmektedir (3-7). Uluslararası literatürde GETAT yöntemlerinin uygulanma oranı %31 ile %70 arasında değişmektedir (8-12). Fox ve ark. 2010 yılındaki çalışmasında yıllar içinde GETAT kullanımı için doktor ziyaretlerde artma eğilimi olduğunu, benzer şekilde Meier-Girard ve ark. 2017'deki çalışmalarında GETAT kullanım yaygınlığını 2012 ile 2017 arasında %24,7'den %28,9'a arttığını belirtmişlerdir (13,14). Çalışmamızda ise son güncel bilgi olarak en az bir veya daha fazla GETAT yöntemi uygulatılması kentsel bölgede %51, kırsal bölgede %43,4 saptanmıştır. Sonuçlarımız ülkemizden yapılan çalışmalar ile karşılaştırıldığında literatürde belirtilen artma eğilimin ülkemizde de devam ettiğini gösterdiği söylenebilmektedir. En sık uygulatılan GETAT yöntemleri ise Türkiye kaynaklı çalışmalarda bölgesel farklılıklar olmakla birlikte; Ak ve ark. Ankara merkezli çalışmalarında en sık hacamat (%39,7) uygulandığını, bunu sırasıyla sülük (%17,7) ve akupunktur (%16,1) uygulamalarının izlediğini belirtmişlerdir (5). Türkiye kaynaklı diğer merkezlerden yapılan çalışmalarda ise fitoterapi en sık uygulanan GETAT yöntemi (%38,2-70,1) olarak bulunmuştur (15-17). Diğer uluslararası çalışmalarda ise ABD'de %37 ile fitoterapinin en sık kullanılan yöntem olduğu saptanmıştır (18). Bir başka uluslararası çalışmada ise fitoterapinin en çok Doğu ülkelerinde uygulandığı belirtilmektedir (19). Boccolini ve ark. en çok kullanılan uygulamanın fitoterapi olduğunu, ardından akupunktur, homeopati, meditasyon ve yoga olduğunu ifade etmişlerdir (20). Brezilya'da yapılan bir çalışmada ise GETAT kullanımında önemli coğrafi farklılıklar olduğuna dikkat çekilmiştir (20). Reid ve ark. çalışmalarında bölgesel farklılıklar olduğunu ve masaj terapisi veya kayropraktik tedavi gibi manuel terapilerin kullanımının kırsal nüfus arasında daha yaygın olduğu belirtilmiştir (21). Benzer şekilde, Adams ve ark. Avustralya'da 10.638 kadınla yaptıkları çalışmada, yaşanılan yere göre (kent, kır ve uzak olmak üzere 3 grupta incelenmiş) GETAT kullanımında anlamlı farklılık olduğunu bildirmişlerdir (22). Literatürde kentsel ve kırsal kesimde yaşayanlar arasında fark olmadığını belirten çelişkili çalışmalarda mevcuttur. Bu çalışmalarda kadınlarda ve eğitim düzeyi yüksek kişilerde GETAT kullanımının daha sık olduğu, aradaki farkın bundan kaynaklandığı belirtilmektedir (23). ABD kaynaklı çalışmalarda eğitim düzeyi ve gelir arttıkça GETAT kullanımının arttığı belirtilmektedir (24,25). Çalışmamızda kentsel ve kırsal alanlar arasında GETAT uygulanmasında fark bulunmadı. Ayrıca her iki bölgede en sık uygulanan yöntem olan masaj tedavisinde de bölgeler arasında fark bulunmadı. Ancak literatüre benzer şekilde çalışmamızda da eğitim seviyesinin artması ile GETAT yöntemlerinin uygulanması arasında pozitif yönde bir ilişki olduğu gözlenmiştir.

Literatürde GETAT yöntemleri ile ilgili bilgi kaynakları da farklılık göstermektedir. Bamidele ve ark. Nijerya'da GETAT yöntemleri ile ilgili bilgi kaynağının radyo (%70,9) ve televizyon (%59,1) gibi iletişim araçları olduğunu belirtmişlerdir (26). Elolemy ve ark. Suudi Arabistan'da en sık (%46,3) aile/akraba/arkadaşlardan bilgi aldığını saptamışlardır (27). Liem ve ark. Endonezya'da GETAT yöntemleri ile ilgili en yaygın bilgi kaynağının (%59) arkadaşlardan geldiğini belirtmişlerdir

(28). Türkiye'de GETAT yöntemleri ile ilgili bilgilerin kaynağı ile ilgili yayınlar değerlendirildiğinde; Oral ve ark. GETAT ile ilgili bilgilerin en sık (%79,5) akraba, arkadaş veya komşulardan alındığını saptamışlardır (16). Benzer şekilde Biçen ve ark. kronik böbrek yetmezliği olan hastalarda fitoterapi kullanımını araştırmışlar ve en fazla bilginin (%61,5) komşu/akraba/arkadaşlardan alındığını bulmuşlardır (29). Çalışmamızda kentsel alanlarda GETAT yöntemleri hakkında en yaygın bilgi kaynağının internet (%62,5) olduğu, bunu sırasıyla arkadaşların (%50,8) ve sosyal medya platformlarının (%49,2) izlediği gösterilmiştir. Kırsal kesimde GETAT yöntemleri ile ilgili en yaygın bilgi kaynağının televizyon (%63,4), bunu internet (%48,8) ve arkadaşların (%47,5) takip ettiği görüldü. Bulgularımızın literatür ile örtüşmesi bu yöntemlerin benzer kaynaklardan duyulduğunu göstermektedir.

Bu çalışma yorumlanırken sadece Orta Karadeniz'den bir bölge örneğinin sunulması dikkate alınması gereken bir sınırlılıktır. Ek olarak kırsal ve kentsel nüfusa uygun katılımcı çalışmaya alınmış olsa da; genel popülasyonda tamamlayıcı ve alternatif tıp kullanımına ilişkin daha geniş bir görüş elde etmek amacıyla genel popülasyonu temsil eden bir örnekleme yöntemi kullanılmamış olması da çalışmanın bir kısıtlılığıdır.

## Sonuç

GETAT uygulamaları hakkında farkındalık artmaya devam etmektedir. Eğitim düzeyine paralel olarak sosyal medya, internet ve arkadaşlar bu etkileşimde halen önemli bir yer tutmaktadır. Sağlığın korunması ve sürdürülmesi için GETAT uygulamalarına ilişkin mevcut bölgesel (kent-kırsal yerleşim bölgeleri) farklılıkları ortaya koyacak ve bilimsel yönetimini sağlayacak çalışmalara ihtiyaç vardır.

## Teşekkür

Yazarlar, bu çalışmanın uygulanmasına katkılarından dolayı katılımcılara teşekkür eder.

## Kaynaklar

1. WHO (World Health Organization). What is the WHO definition of health? Available from: https://www.who.int/about/who-we-are/frequently-asked-questions,
2. Dalen JE. "Conventional" and "unconventional" medicine: can they be integrated? Arch Intern Med 1998;158(20):2179-2181.
3. Yıldırım R. Aydın Adnan Menderes Üniversitesi Tıp Fakültesi Aile Hekimliği Polikliniğine Başvuran Hastalarda Geleneksel ve Tamamlayıcı Tıp Kullanma Durumları. Tıpta Uzmanlık Tezi, Adnan Menderes Üniversitesi Tıp Fakültesi, Aile Hekimliği Anabilim Dalı, Aydın; 2020. Available from: https://tez.yok.gov.tr/UlusalTezMerkezi/tezSorguSonucYeni.jsp,
4. Öztürk M, Uskun E, Özdemir R et al. Public Interest to Traditional Medicine in Isparta. Turkiye Klin J Med Ethics-Law Hist 2005;13(3):179-186.
5. Ak N, Aksakal F. Bazı Aile Sağlığı Merkezlerine Başvuranların Geleneksel ve Tamamlayıcı Tıp Uygulamaları ile İlgili Bazı Bilgi ve Tutumları. Geleneksel ve Tamamlayıcı Tıp Dergisi 2020;3(2):191-198.
6. Özaydın M. Trabzon Kalkınma Mahallesi Aile Sağlığı Merkezine Başvuran 18-65 Yaş Arası Bireylerin Geleneksel ve Tamamlayıcı Tıp Hakkındaki Tutum ve Davranışlarının Değerlendirilmesi. Tıpta Uzmanlık Tezi, Karadeniz Teknik Üniversitesi Tıp Fakültesi Aile Hekimliği Anabilim Dalı, Trabzon; 2020. Available from: https://tez.yok.gov.tr/UlusalTezMerkezi/tezSorguSonucYeni.jsp,
7. Tan M, Uzun O, Akçay F. Trends in complementary and alternative medicine in eastern Turkey. J Altern Complement Med 2004;10(5):861-865.
8. T.C. Ministry of Health. International Perspective on Traditional Complementary and Alternative Medicine Practices Conference Proceeding 2014. Pages 13–193. Available from: https://shgmgetatdb. saglik.gov.tr/Eklenti/5934/0/geleneksel-tip-kitabipdf.pdf,
9. World Health Organization (WHO). Traditional medicine: report by the Secretariat. 2003. Available from: https://apps.who.int/iris/handle/10665/78122
10. NCCIH (National Center for Complementary and Integrative Health). NCCIH 2016 Strategic Plan. 2016. Available from: https://www.nccih.nih.gov/about/nccih-2016-strategic-plan
11. Herron M, Glasser M. Use of and attitudes toward complementary and alternative medicine among family practice patients in small rural Illinois communities. J Rural Health 2003;19(3):279-284.
12. Harris PE, Cooper KL, Relton C, Thomas KJ. Prevalence of complementary and alternative medicine (CAM) use by the general population: a systematic review and update. Int J Clin Pract 2012;66(10):924-939.
13. Fox P, Coughlan B, Butler M, Kelleher C. Complementary alternative medicine (CAM) use in Ireland: a secondary analysis of SLAN data. Complement Ther Med. 2010;18(2):95-103.
14. Meier-Girard D, Lüthi E, Rodondi PY, Wolf U. Prevalence, specific and non-specific determinants of complementary medicine use in Switzerland: Data from the 2017 Swiss Health Survey. PLoS One 2022;17(9):e0274334.
15. Durmuş M, Çarlı A, Karapınar U, Keskin İ. Nadir Bir Geleneksel Tıp Uygulaması: Olgu Sunumu. TAF Prev Med Bull 2014;13(1):89-92.
16. Oral B, Öztürk A, Balcı E, Sevinç N. Aile sağlığı merkezine başvuranların geleneksel /alternatif tıpla ilgili görüşleri ve kullanım durumu. TAF Prev Med Bull 2016;15(1):75.
17. Güven ŞD, Muz G, Ertürk NE, Özcan A. Hipertansiyonlu Bireylerde Tamamlayıcı ve Alternatif Tedavi Kullanma Durumu. Balikesir Saglik Bil Derg 2013;2(3):160-166.
18. U.S. Department of Health and Human Services, National Institutes of Health. Complementary and Alternative Medicine: What People Aged 50 and Older Discuss With Their Health Care Providers. AARP and National Center for Complementary and Alternative Medicin; 2011. Available from: https://files.nccih.nih.gov/s3fs-public/news/camstats/2010/NCCAM_aarp_survey.pdf,
19. Dağtaş Gülgün PC, Kaya H. Complementary and Alternative Medicine Use in Lung Cancer Patients and Its Impact on the Quality of Life. Kafkas J Med Sci 2015;5(2):41-47.
20. Boccolini PMM, de Lima Sírio Boclin K, de Sousa IMC, Boccolini CS. Prevalence of complementary and alternative medicine use in Brazil: results of the National Health Survey, 2019. BMC Complement Med Ther 2022;22(1):205.
21. Reid R, Steel A, Wardle J, Trubody A, Adams J. Complementary medicine use by the Australian population: a critical mixed studies systematic review of utilisation, perceptions and factors associated with use. BMC complementary and alternative medicine 2016;16:176.

22. Adams J, Sibbritt D, Lui CW. The urban-rural divide in complementary and alternative medicine use: a longitudinal study of 10,638 women. BMC Complement Altern Med 2011;11:2.

23. von Conrady DM, Bonney A. Patterns of complementary and alternative medicine use and health literacy in general practice patients in urban and regional Australia. Aust Fam Physician 2017;46(5):316-320.

24. Bishop FL, Lewith GT. Who Uses CAM? A Narrative Review of Demographic Characteristics and Health Factors Associated with CAM Use. Evid Based Complement Alternat Med 2010;7(1):11-28.

25. Weizman AV, Ahn E, Thanabalan R, et al. Characterisation of complementary and alternative medicine use and its impact on medication adherence in inflammatory bowel disease. Aliment Pharmacol Ther 2012;35(3):342-349.

26. Bamidele JO, Adebimpe WO, Oladele EA. Knowledge, attitude and use of alternative medical therapy amongst urban residents of Osun State, southwestern Nigeria. Afr J Tradit Complement Altern Med 2009;6(3):281-288.

27. Elolemy AT, Albedah AM. Public knowledge, attitude and practice of complementary and alternative medicine in riyadh region, saudi arabia. Oman Med J 2012;27(1):20-26.

28. Liem A, Newcombe PA. Indonesian provisional clinical psychologists' knowledge, attitudes, and behaviours towards complementary-alternative medicine (CAM). Complement Ther Clin Pract 2017;28:204-211.

29. Biçen C, Erdem E, Kaya C, Karataş A, Elver Ö, Akpolat T. Herbal Product Use in Patients with Chronic Kidney Disease. Turk Neph Dial Transpl 2012;21(2):136-140.

# Kanser Hastalarında Kötü Haber Vermede Güncel Yaklaşım

**Yusuf Karakaş**

Acıbadem Bodrum Hastanesi Onkoloji Kliniği, Muğla,Türkiye

**Yazışma Adresi:** Acıbadem Bodrum Hastanesi Onkoloji Kliniği. Bodrum/Muğla
e-mail: dryusufkarakas@yahoo.com

**Orcid NO:** YK: 0000 0003 0205 4590

**Atıf:** Karakas Y. Kanser Hastalarında Kötü Haber Vermede Güncel Yaklaşım. Hitit Med J 2023;5(3): 227-231. https://doi.org/ 10.52827/hititmedj.1334284

## Özet

Kanser, ölüm nedeni olarak dünyada ve ülkemizde ikinci sırada bulunmaktadır. Ölüm oranının yüksek olması, tedavi esnasında yaşanan sorunlar ve gelecek hakkındaki belirsizlikler nedenli kanser hastaları diğer hastalardan farklı, oldukça zor ve sıkıntılı bir süreç yaşarlar. Onkoloji hastalarında tedavi planı nasıl multidisipliner yapılıyor ise, hasta bakımına da mutlidisipliner yaklaşılması gerekir. Hasta bakımı ekibinin içinde medikal onkoloji uzmanı, psikiyatrist, palyatif bakım hekimi ve hemşiresi olması önerilir.

Kanser gibi adı anıldığında hastayı ürküten, tanısı ve tedavisi hasta ve hasta yakınlarıyla paylaşıldığında korku, çaresizlik, üzüntü, kızgınlık ve panik gibi son derece doğal duyguların ortaya çıkmasına neden olan hastalığın yönetimi beklenildiği üzere zordur. Bu nedenle kanserle ilgilenen sağlık çalışanlarında, hasta iletişimi rahatsızlık hissi uyandırmakta ve kötü haber verme mesleki zorluklar arasında yer almaktadır. Tanı konulduktan sonra hastanın bilgi gereksinimi artar ve bu ihtiyacı karşılayacak en uygun kişi hekimlerdir. Hastalarını desteklemek, hastalıkla başa çıkmalarına yardımcı olabilmek için etkin iletişim kurmaya, yeterli klinik bilgiyi aktarmaya çalışmaktadırlar. Etkin iletişim kurabilmek için uyulması gereken kurallar ve yaklaşımlar bu yazıda özetlenmeye çalışılmıştır.

**Anahtar Sözcükler:** İletişim, Kanser, Kötü Haber Verme.

**Geliş Tarihi:** 28.07.2023
**Kabul Tarihi:** 25.09.2023
**Yayım Tarihi:** 10.10.2023

**Hakem Değerlendirmesi:** Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
**Etik Beyanı:** Çalışma Derleme türünde olduğundan etik kurul onayına gerek yoktur.
**İntihal Kontrolleri:** Evet - intihal.net
**Çıkar Çatışması:** Yazarlar arasında çıkar çatışması belirtilmemiştir.
**Şikayetler:** hmj@hitit.edu.tr
**Katkı Beyanı:** Fikir/Hipotez: YK Tasarım: YK Veri Toplama/Veri işleme: YK Veri Analizi: YK Makalenin Hazırlanması: YK
**Hasta Onamı:** Onama gerek yoktur.
**Finansal Destek:** Finansal destek alınmamıştır.

# Current Approach to Reporting Bad News in Cancer Patients

**Yusuf Karakaş**

Bodrum Acıbadem Hospital, Department of Oncology, Mugla, Türkiye

**Adres for Correspodence:** Bodrum Acıbadem Hospital, Department of Oncology, Mugla, Türkiye
e-mail: dryusufkarakas@yahoo.com

**Orcid ID:** YK: 0000 0003 0205 4590

**Cite As:** Karakas Y. Current Approach to Reporting Bad News in Cancer Patients. Hitit Med J 2023;5(3): 227-231. https://doi.org/ 10.52827/hititmedj.1334284

## Abstract

Cancer is the second cause of death in the world and in our country. Due to the high mortality rate, problems experienced during treatment and uncertainties about the future, cancer patients experience a very difficult and troublesome process, different from other patients. Just as the treatment plan in oncology patients is made multidisciplinary, patient care should be approached in a multidisciplinary manner.It is recommended that the patient care team includes a medical oncologist, psychiatrist, palliative care physician and nurse.

The management of a disease such as cancer, which scares the patient when its name is mentioned and causes fear, helplessness, sadness, anger and panic when the diagnosis and treatment is shared with the patient and their relatives, is difficult as expected. For this reason, patient communication creates a feeling of discomfort in healthcare professionals dealing with cancer, and reporting bad news is among the professional challenges.

After the diagnosis is made, the patient's need for information increases and physicians, who are the most suitable person to meet this need, are responsible for trying to communicate effectively and convey sufficient clinical information to support their patients and help them cope with the disease. The rules and approaches to be followed for effective communication are tried to be summarized in this article.

**Keywords:** Cancer, Diabetes, Thyroid.

**Date of Submission:** 28.07.2023
**Date of Acceptance:** 25.09.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** Not applicable.
**Plagiarism Checks:** Yes - intihal.net
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: YK Design: YK Data Collection/Data Processing: YK Data Analysis: YK Article Preparation: YK
**Informed Consent:** Not applicable.
**Financial Disclosure:** There is no person/organization that supports the study financially.

## Giriş

Hastalara ve yakınlarına kötü haber verme düzenli ve belirli bir program dahilinde sunulması gerekmektedir. Kanserin ilk tanısının paylaşılması, kanserin tekrarlanması ve aktif tedavi sürecinin tamamlanarak palyatif bakım sürecine geçilmesi gibi konuşulması zor konular yeterli bilgi ve deneyimle birlikte, adım adım bir çerçeve dahilinde sunulmalıdır. Sunum planının içinde olması gereken; temel iletişim becerileri, tedavi hedefleri ve prognozun paylaşılması, hastaya uygulanması planlanan tedavi seçenekleri, mevcut klinik çalışmalara katılım ve tedavi maliyetleri hakkında bilgilendirme, yaşam sonunun planlanması başlıklar halinde açıklanmaya çalışılmıştır. Derlememizde kötü haber vermek gibi son derece karmaşık ve zor iletişim görevini belirli bir çerçevede sunularak, hem haberi alan hastanın. Hem de haberi veren sağlık çalışanının hissettiği zorluk hafifletilmeye çalışılmıştır.

*Temel İletişim Becerileri*

Her görüşme öncesi hekim, hastanın tıbbi bilgilerini gözden geçirmeli, görüşme hedeflerini belirlemeli, hasta ve ailesinin ihtiyaçlarını tahmin etmelidir (1). İletişimin başında, hekim, hastanın hastalığı ile ilgili ne bildiğini keşfetmeli, hasta ve ailesinin neyi öğrenmek istediğini sorguladıktan sonra, genel durumun iyi bir resmini oluşturmalı sonra bilgilendirmeye başlamalıdır. Hastanın hastalığı ile ilgili ne bildiğini anlamak için "bugüne kadar sağlık durumunuz hakkında ne söylendi?" veya "bu tomografiyi neden yaptığımız konusunda bir fikriniz var mı?" gibi açık uçlu sorular sorulabilir. Hastanın öğrenmek istediklerine uygun bilgilendirme yaptıktan sonra, hastadan anlatılanları ne kadar anladığını kontrol etmeli ve buradan çıkacak sonuç hasta dosyasına yazılmalıdır. Bu bilgilendirme sürecinde hastalarımız duygulandıklarında, empatik bir şekilde yanıt verilmeli ve hastanın hekim tarafından anlaşıldığını hissetmesi sağlanmalıdır. Hastanın duygu yoğunluğu fazla ise bu durum geçene kadar beklenmeli veya bir sonraki kontrole görüşme ertelenmelidir. Hastalar genelde hekimlerinin en güçlü psikolojik destekçileri olduğuna inanırlar (2). Bundan dolayı hastayla etkin iletişim kurulmalıdır. Hasta-hekim ilişkisi iyi olan hastaların, hastalıklarıyla daha fazla başa çıkabildiği, tedaviye uyumlarının arttığı, depresyon, anksiyete gibi psikiyatrik rahatsızlıklara daha az rastlandığı çalışmalarla gösterilmiştir (3, 4). Hasta hekim iletişimine engel olabilecek başlıca faktörler ise; hastayı bilgilendirirken fazlaca tıbbi terimler kullanmak, ilgilenebileceğinden fazla sayıda hastanın olması, yeterli vakit ayrılamaması, hastanın hastalığıyla ilgili soru sormasına izin verilmemesi, hastanın yerine karar verilmesi ve son zamanlarda adından daha çok bahsettiren sağlık çalışanlarının tükenmişlik yaşamalarıdır (5).

*Tedavi Hedefleri ve Prognozu Konuşmak*

Hekim, hastayı yanıltmadan, hastanın ihtiyaçlarına uygun, umut ve güvence sağlayan tanı ve prognostik bilgiler sağlamalıdır. Bilgilendirmede en önemli noktalardan biri de hastanın umudunun korunmasına dikkat edilmesidir. Örneğin metastatik pankreas kanserinde bilindiği gibi prognoz oldukça kötüdür ve 5 yıllık sağ kalım %5'in altındadır. Yani bu evredeki hastaların %95'inden fazlası 5 yıl içinde vefat edecektir. Bu bilgiyi hasta yakınlarıyla paylaşmakta bir sakınca yok iken, hastanın kendisiyle konuşulduğunda hastada büyük bir umutsuzluğu neden olabilir. O nedenle hastaların umudunun korunması maksadıyla bu evrede olup 5 yıldan daha fazla yaşayan hastaların varlığını hatırlatarak, hastanın yaşama sevinci, yaşama arzusu ve direncini sağlamlaştırmak daha doğru olacaktır. Buna ek olarak tedavi süreci ve planlar hakkında hastaya bilgi verilmeli, böylelikle hastanın aklında oluşabilecek belirsizlikler ve gelecek kaygısı giderilmeye çalışılır. Ancak hastanın tıbbi durumu ile ilgili bilgi alma isteği farklılık gösterebilir. Kimi hasta tedavi süreci ve prognozu ile ilgili ayrıntılı bilgi almak isterken çoğu hasta tedavi sürecini hekimine bırakır. Hastanın durumuyla ilgili ne kadar bilgi almak istediği "mevcut durumla ilgili tüm detayları size anlatmamı ister misiniz, yoksa konuşmamı istediğiniz başka birisi var mı?" şeklinde sorulabilir (6). Hekim, hastanın tedavisinde önemli bir değişiklik düşündüğünde, hastanın hedefleri, önceliklerini tekrar değerlendirmeli ve basit, anlaşılır ve tıbbi terimlerden arındırılmış bilgi sağlamalıdır.

Kötü haber verme başlı başına bir iletişim yeteneğidir. "Kötü haber verme" tanım olarak umut duygusunu yok eden, kişinin ruhsal ve fiziksel iyilik haline tehdit oluşturan, yerleşik yaşam düzenini kökten bozacak anlamı taşıyan mesajlardır (7). İnsanoğlu genelde oluşabilecek tüm kötülüklerin başkasının başına geleceğini düşünür. "Bana bir şey olmaz, ben her zaman bir çaresini bulurum" mantığındadır (8). Yalom, bu durumu insanın biyolojik bir varlık oluşu gerçeğine ters düşen bir düşünce bozukluğu olarak değerlendirmiştir. İnsanların ölümlü olduğu gerçeğini en net hissettikleri anlardan birisi de kanser tanısıyla yüzleştikleri zamandır (9). Bireyler günlük hayatlarında unutmuş/bastırmış olduğu ölme, yok olma, planlanan veya arzulanan geleceğin hiç olmaması gibi bazı gerçeklerle yüzleşir. Hekimin görevi ise hastanın durumunu en doğru şekilde kabul etmesini sağlamak ve tedaviye uyumu için desteklemektir. Tanının söylenip söylenmemesi kültürden kültüre değişiklik göstermektedir. ABD'de konu kanunlar ve kişinin kendi hayatı üzerine karar verme hakkı olarak tanımlandığından, tanı söylenmektedir (10). Benzer eğilim Batı ve Kuzey Avrupa ülkelerinde de geçerlidir (11). Ülkemizin de içinde bulunduğu doğu ülkelerinde ise tanının ve prognozun söylenmemesi eğilimi vardır ancak son yıllarda bu eğilimin değiştiğini gösteren bilgiler gelmektedir (11, 12). Tanının söylenmesi tam olarak hekimin sorumluluğundadır. Zaten Eylül 1995 tarihinde Dünya Tabipler Birliği Uluslararası Hasta Hakları Bildirgesi 7.maddesi, Hasta Hakları Yönetmeliği 3.bölüm 15.maddesi, Türk Tıbbi Deontoloji Nizamnamesi ve İlaç Araştırmaları Yönetmeliği hastanın bilgilendirilme hakkını yasalara bağlamıştır (13, 14). Artık mevcut yasal koşullar ve modern yaklaşım ışığında hastaya tanıyı söylememek gibi bir durum söz konusu değildir. Artık bu bilginin uygun şekilde nasıl verileceği düşünülmelidir. Ülkemizde ne yazık ki hasta yakınları, hastanın tanısını öğrenmemesi için ciddi çaba harcadığı klinik pratiğimizde çok sık karşımıza çıkmaktadır. Hasta yakınları, hastanın psikolojik olarak çok fazla etkileneceği, hastayı koruma arzusu, nasıl davranacağı ve konuşacağını bilememe gibi nedenlerden tanıyı gizlemeye çalışmaktadır (5).

Günümüzde bilgi edinmenin bu kadar kolay ve ulaşılabilir olduğu düşünüldüğünde hastaya tanısının söylenmediği durumda hastanın sözel olmayan ipuçlarından hastalığını öğrenmesi, en azından sezmesi neredeyse kaçınılmazdır (15). Böyle bir durumda hasta, korkuları ve kaygılarıyla tek başına kalır. Duygularını paylaşacak kimseyi yakınında göremediğinden derin bir yalnızlığa mahkum olur (15, 16). Ayrıca bakımından sorumlu aile bireyleri ve özellikle tedavi ekibine karşı ciddi bir güvensizlik gelişir. O nedenle hasta yakınlarının anlamsız ikna çabaları yerine, uygun koşullarda, acele etmeden doğru bir bilgilendirme yapmak hastanın yararına olacaktır (16).

Hastayı takip eden hekim veya sağlık profesyonelinin bilgi vermekten kaçınması da üzerinde durulması gereken başka bir sorundur. Böyle bir durumda hasta sağlıklı bilgi alamadığından, durumunun çok kötü olduğunu, sonunun yaklaştığını, emek ve çabaya değmeyeceği gibi düşüncelere kapılır. Tanının ne zaman söyleneceği de ayrı bir tartışma konusudur. Ancak genel olarak kabul edilen görüş tanının kesinleşmediği durumda bilgilendirmenin yapılmaması yönündedir. Ancak tanı kesin ve ilerleyen klinik gidişin olduğu anda tanı hastayla paylaşılmalıdır.

Kötü haber verme esnasında uyulması gereken bazı kurallar vardır. Öncelikle görüşmenin yapılacağı yer özel olarak belirlenmelidir. Koridor, poliklinik önü, hastanın mahremiyetinin korunamayacağı kalabalık ortamlar bu görüşme için hiç uygun değildir. Bilgilendirmeyi hastayı uzun süredir takip eden hekim yapmalı ve bu esnada hastaya yeterli zamanı ayırması gerekir (17). Yapılan bir çalışmada, hastaların bakış açısına göre bir görüşmeyi başarısız kılan en önemli faktör, bilgilendirme için yeterli sürenin ayrılamamasıdır. Hekimlerin kısa sürede yeterli bilgilendirmeyi yapamadığı bu koşullarda, hastalar hekimini duyarsız, tedavide bir hedefi olmayan ve hastasını desteklemeyen olarak algılarlar (18). Aile bireyleri bilgilendirmeye dahil edilmeli, hastanın yanında eşlik edecek aile bireylerini hastanın seçmesi sağlanmalıdır. Hastayla temas kurulmalı, ön planda göz teması, mümkünse de kola dokunmak gibi hastanın yanında olduğunu hissettirecek davranışlar sergilenmelidir. Hastanın duygularını ifade etmesine fırsat tanınmalı ve onu yargılamadan konuşmasına izin verilmelidir. Bu özel görüşme esnasında görüşmenin (telefon veya kapıdan başka hastanın girmesi gibi) bölünmemesine çok dikkat edilmeli, bunun için uygun ortam hazırlanmalıdır.

Kötü haber karşısında verilen tepkileri Elizabeth Kubler Ross tarafından evrelere ayırmıştır.

1.) İnkar: Genellikle durum yok sayılır. Bir yanlışlık olduğu düşünülür." Ben kanser olamam, bu tanı doğru değil".

2.) Öfke/Kızgınlık: Hasta, hastalığına, yakınlarına, hekimlere öfke duyar. "Neden ben, neden o değil?"

3.) Pazarlık: Bu safhada hasta iş birliği yapmak ister. Durumunu kabul eder. "Bu hastalık varsa, çözümü de vardır. Bu hastalığa yakalanan tek ben değilim ki, bir çaresi bulunur"

4.) Depresyon: Durum tam olarak anlaşılmıştır. Bundan ötürü bir mutsuzluk hakim olmaya başlar. "Başıma neler gelecek?", "Tam olarak düzelebilecek miyim?"

5.) Kabullenme: Tanı kabul edilir ve yaşanılan sürece uyum sağlandığı dönemdir.

Bu evrelerin her biri hastada görülmeyebileceği veya sırasının değişebileceği de akılda tutulmalıdır. Hastada görülmesi son derece normal olan bu evrelerin uzaması veya tedaviyi aksatacak duruma gelmesi halinde psikiyatri konsültasyonu önem taşımaktadır (19).

Bu beş aşamada da varlığını koruyan duygu umuttur. Umut, hastanın günler, aylar süren acı ve sıkıntılara katlanmasının asıl nedenidir. Tüm hastalar bu zorlu süreç içerisinde umutlarını korumaktadır. Bu kaybedilmeyen umut, sağlık çalışanlarına güven duyulmasını ve tedaviye devam edilmesini sağlamaktadır (20).

*Tedavi Seçenekleri ve Klinik Çalışmalar Hakkında Bilgilendirme*

Hastayla tedavi seçenekleri konuşulmadan önce, hekim tedavinin hedeflerini (kür, sağ kalım süresini uzatmak, yaşam kalitesinin iyileştirilmesi) netleştirmelidir. Böylelikle hasta olası sonuçları anlayabilir ve tedavi hedefleri ile kendi beklentilerini ilişkilendirebilir. Hastanın tedavisinden sorumlu hekim, tedavi seçeneklerini hastanın umudunu koruyacak, kendi başına karar vermesini destekleyecek ve anlamasını kolaylaştıracak şekilde anlatmalıdır. Gelecek ile ilgili planı olan hastalar daha az endişe duygusu taşırlar. Mevcut durumu felaketleştirecek "derhal tedavi almazsanız öleceksiniz" gibi ifadelerden veya "başka bir şey yapılamaz" mesajından kaçınılmalıdır. Hekim, klinik çalışma ve palyatif bakım dahil tüm tedavi seçeneklerini hastayla paylaşmalı. Klinik çalışmaya uygun olsa bile standart tedavi hakkında bilgi vermelidir.

*Yaşam Sonunun Paylaşılması*

Hasta yakınları ve hasta, yaşam sonu hakkında ayrı ayrı olarak bilgilendirilmeli. Hastanın kültürünün, dininin veya manevi inanç sisteminin yaşamının son döneminde etkisinin farkında olunmalı, destek tedavisini mümkün olduğunca buna uyumlu hale getirilmeye çalışılmalıdır. Hekim, sadece hastanın değil. Hasta yakınlarının da keder, üzüntülerini takip etmeli, uygun gördüğünde hasta yakınlarını sosyal hizmetler uzmanı, psikolog veya psikiyatristlere yönlendirmelidir. Hastanın yaşam sonu bakımında, hastalara ve ailelerine daha etkin destek sağlamak için bölgesel destek üniteleri belirlenmeli ve gerekli görüldüğü durumlarda bu ünitelere (Palyatif bakım merkezleri) hastalar yönlendirilmelidir.

*Hasta Ailesinin Hasta Bakımına Dahil Edilmesi*

Tedavi hedeflerini ve hasta bakımını gerçekleştirmede – hastanın rızasını almak kaydıyla-, hasta yakınlarının da tedavi planlamasına dahil edilmeye çalışılmalıdır. Hasta ve ailelerinin farklı inançlara, deneyimlere, anlayışlara ve beklentilere sahip olabileceğinin farkında olarak iletişime geçilmelidir. Cinsel yönelim ve cinsiyet kimliği hakkında varsayımlardan kaçınılmalı. Cinsellik- cinsel davranışlar konuşulurken yargılayıcı olmayan bir dil kullanılmalıdır.

*İletişim Engeli Olan Hastalarda Etkili İletişim Kurulması*

Hekim ile aynı dili konuşmayan hastalar için, aile içi tercüman yerine tıbbi tercüman tercih edilmelidir. Düşük sağlık-okur yazarlığı olan hastalarda, iletişimde en önemli noktalara odaklanılmalı, sade bir dil kullanılmalı ve hastanın bilgilendirmelerden anlayıp-anlamadığı sık sık kontrol edilmelidir. Mümkünse benzer tanıyı alan hastalar ile grup toplantıları organize ederek, hastalığın sadece kendilerinde olmadığı hissettirilmeye çalışılmalıdır.

*Tedavi Maliyetleri Hakkında Bilgilendirme*

Günümüzde kanser hastalığı ile ilgili çok sayıda klinik çalışma yürütülmekte ve ilaç endüstrisinin önemli yatırımları söz konusudur. Ne yazık ki ölümle iç içe olan bu hastalığın iyileştirilmesinde harcanan çabalar yanında yüksek maliyetli tedavileri de getirmiştir. Ülkemizde hastalarımızın çoğunun hizmet aldığı sosyal güvenlik kurumunun bu tedavi maliyetlerini karşılaması mümkün değildir. Buna rağmen yeni tedavi seçeneklerinin hastayla paylaşılması etik ve yasal sorumluluk açısından hekimler için büyük önem taşımaktadır. Hasta mevcut koşullarda bu tedavilere ulaşamıyor bile olsa, böyle bir tedavinin varlığından haberdar olması gerekir. Aksi takdirde hastanın hastalığı ilerlediği veya ölüm gerçekleştikten sonra, hasta veya yakınları yeni tedavi alamadıklarından hastalığın ilerlediğini öne sürerek hekimden şikayetçi olma durumu söz konusu olabilir.

*İletişim Becerileri Konusunda Hekimlerin Eğitimi*

İletişim becerileri eğitimi, temel tıp eğitiminin bir parçası

kabul edilmeli, teorik uygulamalar ve doğrudan gözlem içeren bileşenleri olmalıdır. 2003 yılında ulusal kanser kongresinde yapılan bir anket çalışmasında katılımcıların %48'inin tanıyı ya hiç söylemediği yada nadir olarak söylediği tespit edilirken, iletişim eğitimi alan hekimlerde gerçeği söyleme oranının oldukça fazla olduğu görülmüş (21). Bu çalışma iletişim becerileri eğitiminin hastanın tedaviye uyumunu ve hekim-hasta iletişimini doğrudan etkilediğini göstermiştir. Çoğu sağlık profesyonelinin iyi niyetle söyledikleri "moralini iyi tutarsan daha iyi olursun", "daha ne kötüleri var sen yine iyisin", "kimin başına ne geleceği belli olmaz, bende trafik kazası geçirip ölebilirim" gibi sözler hastanın isteğini karşılamaktan çok, kaygıya ve moral bozukluğuna sebep olacağını bilmek gerekir. Ayrıca hastaların sıkça karşı karşıya kaldıkları yazılı ve görsel basında "kanseri yok eden yeni tedavi", "kanseri ikinci kez yendi" gibi haberler hastanın endişelerini arttırmakta ve günün sonunda hayal kırıklığına neden olabilecek ümitlenmelere neden olabilmektedir. Bu durum hekim hasta iletişimini olumsuz etkileyeceğinden hasta merak ettiği konularda hekiminin bilgisine başvurabileceği iletişim kanallarını açık tutmak gerekir.

Sonuç olarak, kanser hastalarıyla iletişim, belirli kurallar çerçevesinde, bilgi ve deneyimi harmanlayarak gerçekleştirilebilecek bir eylemdir. Hastaların hassasiyetlerini anlayarak, hekimin empati yeteneğiyle yapacağı iletişim, verilen tedaviler kadar önemlidir.

## Kaynaklar


1. Moore PM, Rivera S, Bravo-Soto GA, Olivares C, Lawrie TA. Communication skills training for healthcare professionals working with people who have cancer. Cochrane Database of Systematic Reviews 2018(7).
2. Buckman R. Breaking bad news: why is it still so difficult? British medical journal (Clinical research ed) 1984;288(6430):1597.
3. Mack JW, Block SD, Nilsson M, Wright A, Trice E, Friedlander R, et al. Measuring therapeutic alliance between oncologists and patients with advanced cancer: the Human Connection Scale. Cancer: Interdisciplinary International Journal of the American Cancer Society 2009;115:3302-3311.
4. Parker PA, Baile WF, de Moor C, Lenzi R, Kudelka AP, Cohen L. Breaking bad news about cancer: patients' preferences for communication. Journal of clinical oncology 2001;19:2049-2056.
5. Yılmaz M. Sağlık Profesyonelleri için İletişim. I.Basım. Ankara: Akademisyen Yayınevi, 2020; 235-262
6. Demirkol ME, Koç F. Kötü haber verme teknikleri. İnternet Erişim adresi: http://www. noroloji. org. tr/TNDData/Uploads/files/K% C3 (Erişim tarihi:24.9.2023)
7. Ptacek JT, Eberhardt TL. Breaking bad news: a review of the literature. Jama 1996;276:496-502.
8. Özkan S. Psikiyatrik tip: konsültasyon-liyazon psikiyatri. Bull Clin Psychopharmacol 1990;1:10-17.
9. Dülgerler Ş, Çam O. Kanser Tanısı Konan Hastalarda Tanıyı Söyleme Süreci ve Hemşirelik Yaklaşımları. Kocaeli Üniversitesi Sağlık Bilimleri Dergisi 2016;2:15-19.
10. Burton M, Watson M. Counselling people with cancer. Chichester: John Wiley & Sons Ltd, 1998;197 pp
11. Grassi L, Gritti P, Rigatelli M, Gala C. for the Italian Consultation-Liaison Group. Psychosocial problems secondary to the cancer: an Italian multicentre survey of consultation-liaison psychiatry in oncology. European Journal of Cancer 2000;36:579-585.
12. Khalil RB. Attitudes, beliefs and perceptions regarding truth disclosure of cancer-related information in the Middle East: a review. Palliative & supportive care 2013;11:69-78.
13. Ayan M. Tıbbi müdahalelerden doğan hukuki sorumluluk. Kitap, Kazancı Yayınevi, Ankara,1991; 195.sayfa.
14. TC Sağlık Bakanlığı Hasta hakları yönetmeliği. Resmi Gazete. 1998;1:23420. İnternet Erişim adresi :https://www.mevzuat.gov.tr/mevzuat?MevzuatNo=4847& MevzuatTur=7&MevzuatTertip=5 (Erişim tarihi 24.09.2023).
15. Gautam S, Nijhawan M. Communicating with cancer patients. The British Journal of Psychiatry. 1987;150:760-4.
16. Slevin ML. Talking about cancer: how much is too much? British journal of hospital medicine. 1987;38:56, 8-9.
17. Marcelle Kaplan R. SPIKES: a framework for breaking bad news to patients with cancer. Clinical journal of oncology nursing. 2010;14:514.
18. Back AL, Arnold RM, Tulsky JA, Baile WF, Fryer-Edwards KA. Teaching communication skills to medical oncology fellows. Journal of clinical oncology. 2003;21:2433-6.
19. Okyavuz U.H. Ölümcül Hastalık Tanısı Almak: Bir Yaşam Krizi Kötü Haber Verilmeli Mi? Kriz Dergisi. 2003;11:29-35.
20. Bahadir M. An Assessment of the Position of Death in Modern Human Life. Beytulhikme An International Journal of Philosophy. 2018:535-52.
21. Ozdogan M, Samur M, Artac M, Yildiz M, Savas B, Bozcuk HS. Factors related to truth-telling practice of physicians treating patients with cancer in Turkey. Journal of palliative medicine. 2006;9:1114-9.

# Coexistence of Ipsilateral Sacroiliitis and Simple Cyst in the Iliac Bone: A Case Report

**Zeynep Kırac Unal[1], Methiye Kubra Sezer[1], Aynur Turan[2], Ajda Bal[1]**

[1]University of Health Sciences, Diskapi Yildirim Beyazit Education and Research Hospital, Department of Physical Medicine and Rehabilitation, Ankara, Türkiye
[2]Department of Radiology, University of Health Sciences Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Türkiye

**Address for Correspondence:** Physical Medicine and Rehabilitation Clinic, University of Health Sciences Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Türkiye
e-mail: zeynepkirac88@gmail.com

**Orcid ID:** KUZ: 0000-0002-8139-3971 TA: 0000-0001-6654-3129
SMK: 0000-0003-3453-2518 BA: 0000-0002-3910-2851

**Cite As:** Unal Kirac Z, Sezer Methiye K, Aynur T, et al. Coexistence of Ipsilateral Sacroiliitis and Simple Cyst in the Iliac Bone: A Case Report. Hitit Med J 2023;5(3): 232-234. https://doi.org/ 10.52827/hititmedj.1284873

## Abstract

Here, a 36-year-old female patient with inflammatory sacroiliitis and simple bone cyst of the ipsilateral iliac bone is presented. Simple bone cysts occur in the developing skeleton, usually asymptomatic; however, they are benign lytic bone lesions that can cause pathological fractures. The prevalence of simple bone cysts in the whole body has been reported as 0.30/100000. Only 2% of these rare cysts are found in the pelvis, and according to our knowledge, it is the first case in which iliac simple bone cyst is seen together with sacroiliitis on the same side.

**Keywords:** Low back pain, Sacroilitis, Simple bone cyst

## Özet

Burada, ipsilateral iliak kemiğinde inflamatuar sakroileit ve basit kemik kisti bulunan 36 yaşında bir kadın hasta sunulmaktadır. Basit kemik kistleri gelişmekte olan iskelette asemptomatik olarak ortaya çıkar; ancak patolojik kırıklara neden olabilen iyi huylu litik kemik lezyonlarıdır. Tüm vücutta basit kemik kisti prevelansı 0,30/100000 olarak bildirilmiştir. Bu nadir kistlerin sadece %2`lik kısmı pelviste bulunur ve bilgilerimize göre bu olgu, iliak basit kemik kistinin aynı tarafta sakroileit ile birlikte görüldüğü ilk vakadır.

**Anahtar Sözcükler:** Basit kemik kisti, Bel ağrısı, Sakroileit

**Date of Submission:** 17.04.2023
**Date of Acceptance:** 05.09.2023
**Date of Publication:** 10.10.2023

**Peer Review:** Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
**Ethical Statement:** Not applicable.
**Plagiarism Checks:** Yes - intihal.net
**Conflict of Interest:** No conflict of interest has been declared by the authors.
**Complaints:** hmj@hitit.edu.tr
**Authorship Contribution:** Idea/Hypothesis: ZKU MKS, AT, AB Design: ZKU, AB Data Collection/Data Processing: ZKU, MKS, AT, AB Data Analysis: ZKU, AT, AB Article Preparation: ZKU, AB
**Informed Consent:** Informed consent was obtained from the patient.
**Financial Disclosure:** No financial support has been received.

## Introduction

Pain originating from the sacroiliac joint constitutes 13-30% of all low back pain (1). Sacroiliac joint dysfunction, rheumatological diseases causing inflammatory sacroiliitis, trauma, pregnancy, and sports-related pain are the causes of pain originating from the sacroiliac joint (2). Simple bone cysts (SBC) are seen in the developing skeleton, usually asymptomatic; however, they are benign lytic bone lesions that can cause pathological fractures (3). The prevalence of SBC in the whole body has been reported as 0.30/100000 (4). Only 2% of these rare cysts are located in the pelvis (5).

Here, a case with inflammatory sacroiliitis and SBC in the ipsilateral iliac bone is presented.

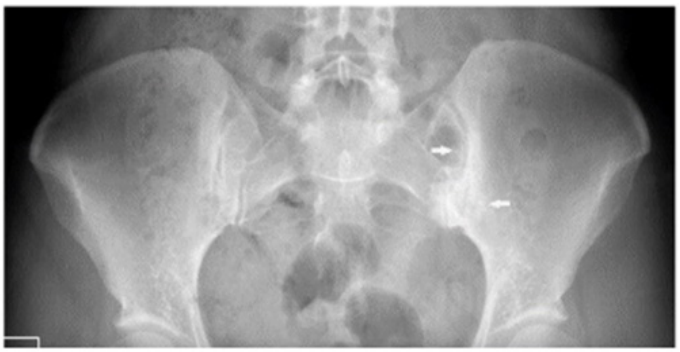
## Case Report

A 36-year-old female patient who applied to our polyclinic had low back and left hip pain for 8 years; but intensified in the last 3 months. Back and neck pain have been added to low back pain in the last year. Low back pain decreased with movement and increased with rest. The patient did not have night pain, but had morning stiffness lasting up to two hours. It was learned that she had hypothyroidism and used levothyroxine 25 mcg/day. The patient's family history was unremarkable. In the systemic examination, skin rash, peripheral arthritis, uveitis, oral and genital aphthae, diarrhea, constipation were not detected.

On physical examination, cervical spine movements were painful; but there was no limitation. Movements of the lumbar spine were painful and limited. Chest expansion was 2.5 cm. The fingertip-to-floor distance was 10 cm, the Modified Schober was 5 cm, the lumbar lateral flexion was 9 cm, and the intermalleolar distance was 104 cm. Gaenslen, Mennel, and compression tests were positive in the left sacroiliac joint. The FABER test was positive on the left. There were tenderness in the bilateral 1st and 7th costochondral joints, bilateral iliac crests, bilateral spina iliaca posterior superiors, and the 5th lumbar spinous process.

In laboratory examination, hemogram, biochemical tests and inflammatory markers were within normal limits. Brucella agglutination test was negative. In the pelvic anteroposterior radiograph, there were irregularities suggesting sacroiliitis in the left sacroiliac joint, sacral and iliac wings, and increased sclerosis (Figure 1).

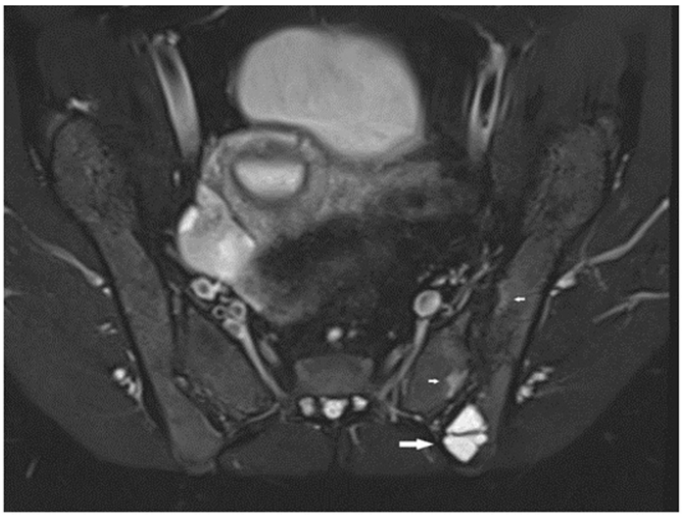
**Figure I.** Anteroposterior pelvis X-ray



**Arrows:** Left iliac and sacral wing irregularities suggesting sacroiliitis and increased sclerosis

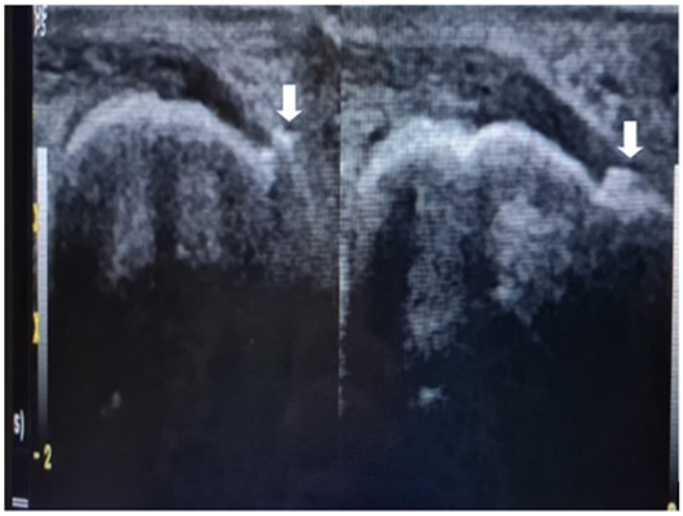
In the sacroiliac joint magnetic resonance imaging (MRI), hyperintense bone marrow edemas in the anterior of the iliac wing in the axial STIR sequence and in the posterior of the sacral ala in the left sacroiliac joint and areas of hyperintense fat accumulation evaluated in favor of structural changes on T1-weighted images were observed. These findings were evaluated as acute and chronic inflammatory sacroiliitis. In addition, MRI examination revealed a 25x18 mm lesion in the posteroinferior aspect of the left iliac bone, which was hyperintense on STIR (Figure 2) and hypointense on T1-weighted images, consistent with benign, naturally septated SBC. HLAB-27 was negative. In the ultrasonographic evaluation of both feet, bilateral Achilles enthesophyties were determined (Figure 3).

**Figure II.** Sacroiliac joint MRI STIR sequence axial plan view



**Thick arrow:** Bone cyst with hyperintense appearance in posterior iliac wing
**Thin arrows:** Bone marrow edema with subchondral hyperintense appearance in the sacral region and iliac wing

**Figure III.** Bilaterally foot ultrasonography



**Arrows:** Achilles enthesopathy

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was 5.6, and the Bath Ankylosing Spondylitis Functional Index (BASFI) was 1.8.

With the diagnosis of axial spondyloarthropathy and iliac bone cyst, the patient was started on a physical therapy program consisting of hot pack TENS, ultrasound, breathing, posture, flexors stretching, extensors strengthening exercises, and 3x50 mg/g indomethacin treatment.

In the follow-up two weeks later, BASDAI was 2.3 and BASFI was 0.6. The same medical treatment was continued. Written informed consent was obtained from the patient.

## Discussion

SBC are benign, usually asymptomatic lesions that are seen at the age of 5-15 years and slightly more frequently in men, although they can occur at any age (6). Two-thirds of SBC are located in long bones such as the proximal femur or proximal humerus (7). Rarely, cysts located in the calcaneus or pelvis are also encountered (8-10). Our case was female, and the cystic lesion adjacent to the sacroiliac joint was a very rare site of involvement (11).

In the differential diagnosis of sacroiliitis, causes such as inflammatory rheumatic diseases, acne and isoretinoic acid-related arthritis, specific and nonspecific infections, sarcoidosis, hyperparathyroidism, and paraplegia are included. Our case presented with inflammatory low back and hip pain. In accordance with the physical examination and laboratory findings, and in the imaging methods requested with a preliminary diagnosis of sacroiliitis, SBC was detected on the same side of the pelvis with sacroiliitis. Because SBC are usually painless, most cases have pathological fractures, while those found in the ileum and calcaneum are usually diagnosed incidentally.

Although SBC are mostly seen in childhood, in a study examining 16 cases located in the pelvis, it was shown that 5 patients had cysts in the posterior part of the ilium adjacent to the sacroiliac joint, and these posterior lesions occurred in the older patient group (8). In another study evaluating 75 SBC, it was argued that those with pelvic localization were seen in older patients, while another study reported four cases of simple pelvic cysts seen in the adolescent group (5, 12). It can be thought that pelvic lesions may remain asymptomatic for a longer period of time, since they usually occur in the non-weight-bearing parts of the ileum.

The presence of accompanying sacroiliitis on the same side was effective in detecting SBC at a relatively early age in our case.

In conclusion; SBC in the pelvis are an extremely rare condition. Our case is interesting because, to our knowledge, it is the first case in which sacroiliitis and SBC of the iliac bone were seen together with ipsilateral sacroiliitis. Diagnosis and follow-up of SBS are important because they carry a risk of bone fracture.

## References

1. Schwarzer AC, Aprill CN, Bogduk N. The sacroiliac joint in chronic low back pain. Spine 1995;20:31-37.

2. Kul A, Bağcıer F, Bayraktutan Ü. Sakroiliak Ağrının Nadir Bir Nedeni: iliak Kemik Kisti. Turk J Osteoporos 2017;23:119-120.

3. Zhang P, Zhu N, Du L, Zheng J, Hu S, Xu B. Treatment of simple bone cysts of the humerus by intramedullary nailing and steroid injection. BMC Musculoskeletal Disord 2020;21(1),70.

4. Zehetgruber H, Bittner B, Gruber D, et al. Prevalence of aneurysmal and solitary bone cysts in in young patients. Clin Orthop Relat Res 2005;439:136-143.

5. Abdelwahab IF, Hermann G, Norton KI, Kenan S, Lewis MM, Klein MJ. Simple bone cysts of the pelvis in adolescents. A report of four cases. J Bone Joint Surg Am 1991;73(7):1090-1094.

6. Hagmann S, Eichorn F, Moradi B, et al. Mid- and long-term results of surgical therapy in unicameral bone cysts. BMC Muscloskelet Disord 2011;12:281.

7. Boseker E, Bickel W, Dahlin D. A Clinicopathologic Study of Simple Unicameral Bone Cyst. Surg Gynec and Obstet 1968;127:550-560.

8. Hammoud S, Weber K, Mc Carthy EF. Unicameral bone cysts of the pelvis: a study of 16 cases. Iowa Orthop J 2005;25:69-74.

9. Moreau G, Letts M. Unicameral bone cyst of the calcaneus in children. J Pediatr Orthop 1994;14(1):101-104.

10. Polat O, Sağlik Y, Adıgüzel HE, Arikan M, Yildiz HY. Our experience on calcaneal bone cysts. 36 cysts in 33 patients. Arch Orthop Trauma Surg 2009;129(11):1489-1494.

11. Bloem JL, Reidsma II. Bone and soft tissue tumors of hip and pelvis. Eur J Radiol 2012;81:3793-3801.

12. Norman A, Schiffman M. Simple bone cysts: factors of age. Radiology 1977;124(3):779-782.