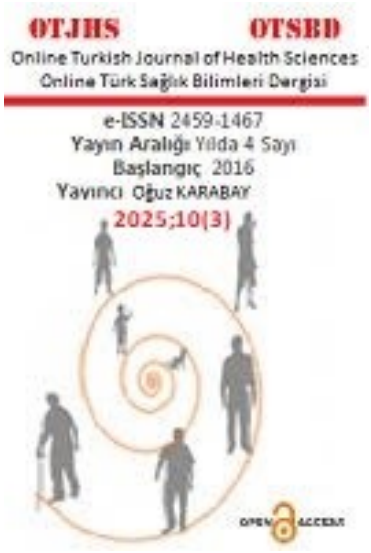

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# Determining the Risk Factors for Nosocomial Multidrug-Resistant Acinetobacter Infections in Patients in Intensive Care Units and Genotyping of Isolates

# Yoğun Bakım Ünitesinde Nosokomiyal Çoklu İlaç Dirençli Acinetobacter Enfeksiyonları için Risk Faktörlerinin Belirlenmesi ve İzolatların Genotiplendirilmesi

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**ABSTRACT**

**Objective:** This study aimed to identify the risk factors for hospital-acquired *Acinetobacter baumannii* infections in an intensive care unit (ICU), delineate the antibiotic resistance profiles of isolates, and elucidate the clonal relationships among strains through genotypic analysis.

**Materials and Methods:** This prospective case-control study was conducted between April 2011 and March 2012 and included 213 patients. The antibiotic susceptibility of *Acinetobacter* strains was evaluated using the Kirby–Bauer disk diffusion method. The DiversiLab system was used to determine the clonal relationships among *A. baumannii* strains.

**Results:** The key independent risk factors for hospital-acquired *A. baumannii* infections included age, mechanical ventilator use, tracheotomy, percutaneous endoscopic gastrostomy (PEG), carbapenem administration, and non-use of cephalosporins. High multi-antibiotic resistance was observed in 94% of the isolates. Furthermore, a substantial clonal closeness with an 86% clustering rate was observed among the isolates, with the largest cluster (P5) comprising 24 isolates persisting for approximately 14 months in the hospital setting.

**Conclusions:** The findings indicate the need for targeted preventive measures against specific risk factors for *A. baumannii* infections in ICUs. The genotypic analysis revealed significant clonal spread, necessitating enhanced infection control strategies.

**Keywords:** *Acinetobacter* infections, genotype, intensive care units

**ÖZ**

**Amaç:** Bu çalışma, Yoğun Bakım Ünitesi 'nde (YBÜ) hastane kaynaklı *Acinetobacter baumannii* enfeksiyonları ile ilişkili risk faktörlerini belirlemeyi, izolatların antibiyotik direnç profillerini çizmeyi ve genotipik analiz yoluyla suşlar arasındaki klonal ilişkileri aydınlatmayı amaçlamaktadır.

**Materyal ve Metot:** Bu çalışma Nisan 2011 ile Mart 2012 tarihleri arasında prospektif vaka-kontrol çalışması olarak yürütülmüş olup 213 hastayı kapsamaktadır. *Acinetobacter* suşlarının antibiyotik duyarlılıkları, Kirby–Bauer disk difüzyon yöntemi kullanılarak değerlendirilmiştir. *A. baumannii* suşları arasındaki klonal ilişkilerin belirlenmesi için DiversiLab sistemi kullanılmıştır.

**Bulgular:** Hastane kaynaklı *Acinetobacter* enfeksiyonu için bağımsız anahtar risk faktörleri yaş, mekanik ventilatör kullanımı, trakeotomi, perkütan endoskopik gastrostomi (PEG) uygulaması, karbapenem verilmesi ve sefalosporin kullanılmamasıdır. İzolatların %94'ünde yüksek çoklu antibiyotik direnci gözlemlenmiştir. Ayrıca izolatlar arasında %86 oranında belirgin bir klonal yakınlık gözlenmiş, en büyük kümeyi (P5) yaklaşık 14 ay boyunca hastane ortamında süregelen 24 izolat oluşturmuştur.

**Sonuç:** Bulgular, YBÜ'lerinde *A. baumannii* enfeksiyonları için belirli risk faktörlerine karşı hedeflenmiş önleyici tedbirlerin gerekliliğini vurgulamaktadır. Genotipik inceleme, artırılmış enfeksiyon kontrol stratejilerini gerektiren önemli bir klonal yayılımı ortaya koymaktadır.

**Anahtar Kelimeler:** *Acinetobacter* enfeksiyonları, genotip, yoğun bakım üniteleri

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## INTRODUCTION

*Acinetobacter baumannii*, recognized for its swift emergence of antibiotic resistance, frequently results in difficult-to-manage outbreaks.[1] This bacterium primarily occurs as a causative agent in bacteremia and respiratory tract diseases. According to the Centers for Disease Control and Prevention's Antibiotic Resistance Threats in the United States 2019 report, carbapenem-resistant *A. baumannii* has been reported as an urgent pathogenic threat.[2] The invasive procedures such as endotracheal mechanical ventilation and implanted invasive devices, admission to intensive care, recent surgery, use of broad-spectrum antibiotics, ineffective treatment, and septic shock at diagnosis are reported as risk factors for multidrug-resistant *A. baumannii* colonization or infection and higher mortality.[3,4] In addition, molecular techniques such as polymerase chain reaction are very useful in identifying *A. baumannii* and examining the genetic affiliation of clinical isolates of *A. baumannii* in hospitals.[5]

This study aimed to explore the risk factors for *A. baumannii* infections in intensive care units (ICUs). Furthermore, it aimed to provide insights and recommendations to reduce infection rates, formulate treatment procedures via culture antibiogram evaluations, and determine the clonal relationships of strains through genotypic analysis.

## MATERIALS AND METHODS

**Ethics Committee Approval:** This study was approved by the ethics committee of XX University (Date: 01.03.2011, decision no: 2011/14) and was conducted in accordance with the principles of the Declaration of Helsinki.

**Study Design:** This prospective case-control study was conducted at XX Medical Center in the adult ICU from April 2011 to March 2012 to identify the risk factors for hospital-acquired *A. baumannii* infections. It included 213 patients who were categorized into 108 cases and 105 controls. During the study period, the patients who were followed up in the adult ICU and developed a hospital-acquired *Acinetobacter* infection attack were included as the case group, and the patients who did not develop an infection attack were included as the control group. Each participant completed an "Epidemiological Patient Study Form" and the "Apache II Form."[6] The diagnostic criteria established by the Centers for Disease Control and Prevention in the United States[7] were used for hospital infection identification.

Clinical specimens from hospitalized patients were grown on blood and eosin–methylene blue agar. Traditional techniques were employed for the gram staining of colonies classified as *Acinetobacter*. The antibiotic susceptibility of *Acinetobacter* strains obtained from the clinical samples was evaluated using the Kirby–Bauer disk diffusion method, adhering to the norms set by the Clinical and Laboratory Standards Institute.[8] *Pseudomonas aeruginosa* ATCC 27853 was used as the reference strain. The Buyyon microdilution method was employed to assess the susceptibility of colistin and tigecycline, with minimum inhibitory concentration (MIC) ≤4 and >8 μg/mL for cholismetate sodium indicating susceptibility and resistance to colistin, respectively.[9] The MIC thresholds for tigecycline in the *Acinetobacter* strains were assessed in accordance with the Food and Drug Administration guidelines (≤2 μg/mL for susceptibility).[10] Commercially acquired antibiotic powders included colistin (cholismetate sodium) and tigecycline. The classification of multidrug-resistant strains was based on the categories provided by Falagas et al.[11]

Repetitive extragenic palindromic polymerase chain reaction (REP–PCR) using the DiversiLab system (bioMerieux, France) was employed to investigate the clonal relationship among *A. baumannii* strains. Pearson's correlation coefficient was used for the band analysis, whereas the unweighted pairwise grouping mathematical averaging was adopted for the clustering analysis.

**Statistical Analysis:** The Statistical Package for Social Sciences version 16.0 was used for data analysis. The Shapiro–Wilk test was employed to evaluate the normality of the groups' distributions. The unpaired t-test, chi-squared test, or Fisher's exact test was used for intragroup comparisons. Univariate logistic regression analysis revealed the risk factors for hospital-acquired *Acinetobacter* infections, including variations with P <0.25 in multivariate logistic regression models. Through retrospective elimination, the best predictive risk factor for *Acinetobacter* infection was identified by computing the odds ratios, 95% confidence intervals, and significance levels. A P-value of 0.05 was deemed statistically significant.

## RESULTS

The predominant *Acinetobacter* infection identified was ventilator-associated pneumonia (VAP), which occurred in 68 (63%) patients. Invasive procedures, such as urinary catheterization, tracheotomy, mechanical breathing, central venous catheterization, and percutaneous endoscopic gastrostomy (PEG), were more prevalent in the case than in the control group ($P = 0.0001$ for each). The case group demonstrated significantly elevated risks for *Acinetobacter* infections, including cerebrovascular and pulmonary illnesses ($P = 0.024$ and $P = 0.033$, respectively). In the case group, it was determined that beta-lactam/beta-lactamase inhibitor-aminoglycoside combina-

tions and carbapenem group antibiotics were used more. Table 1 presents the comparison of the cases and controls.

The independent risk factors were identified as a younger average age, mechanical ventilator use, tracheotomy, PEG, carbapenem administration, and nonuse of third-generation cephalosporin (Table 2).

In the univariate statistical study, potential risk factors influencing mortality were incorporated into a multivariate logistic regression model. The study showed that enteral nutrition and the APACHE II score were independent risk factors for mortality (Table 3). The incidence of *Acinetobacter* infection did not substantially affect the mortality rates.

**Table 1.** Comparison of the case and control groups.

| Variate | | Case group (n=108) | Control group (n=105) | p |
|---|---|---|---|---|
| **Demographic and laboratory data** | Age | 59.1±18.3 | 66.8±16.8 | 0.002 |
| | Gender | 68 male+40 female | 55 male+50 female | 0.129 |
| | White blood cell count ($x10^3/mm^3$) | 13.3±10.2 | 12.4±10.2 | 0.52 |
| | Platelet count ($x10^3/mm^3$) | 241.6±132.9 | 210.6±119.3 | 0.076 |
| | C reactive protein | 13.7±10.8 | 10.0±9.7 | 0.009 |
| | APACHE II score | 23.7±7.3 | 19.6±7.1 | 0.0001 |
| | Mortality | 44 (%40.7) | 32 (%30.5) | 0.118 |
| **Risk factors** | Immunosuppression | 29 (%26.9) | 30 (%28.6) | 0.779 |
| | Malignancy | 15 (%13.9) | 23 (%21.9) | 0.127 |
| | Diabetes mellitus | 17 (%15.7) | 21 (%20) | 0.417 |
| | Cerebrovascular disease | 67 (%62) | 49 (%46.7) | 0.024 |
| | Pulmonary disease | 61 (%56.5) | 44 (%41.9) | 0.033 |
| | Cardiovascular disease | 41 (%38) | 50 (%47.6) | 0.154 |
| | Kidney failure | 13 (%12) | 17 (%16.2) | 0.384 |
| | Nasogastric tube | 6 (%5.6) | 8 (%7.6) | 0.543 |
| | Urinary catheter | 104 (%96.3) | 79 (%75.2) | 0.0001 |
| | Tracheotomy | 41 (%38) | 5 (%4.8) | 0.0001 |
| | Mechanical ventilator use | 67 (%62) | 19 (%18.1) | 0.0001 |
| | Hemodialysis catheter | 10 (%9.3) | 10 (%9.5) | 0.947 |
| | Central venous catheter | 70 (%64.8) | 35 (%33.3) | 0.0001 |
| | PEG | 29 (%26.9) | 4 (%3.8) | 0.0001 |
| **Antibiotic use** | Carbapenem | 49 (%45.4) | 11 (%10.5) | 0.0001 |
| | Beta lactam/beta lactamase inhibitor | 23 (%21.3) | 27 (%25.7) | 0.447 |
| | Third-generation cephalosporin | 3 (%2.8) | 35 (%33.3) | 0.0001 |
| | Carbapenem and quinolone | 5 (%4.6) | 1 (%1) | 0.212 |
| | Beta-lactam/beta-lactamase inhibitor and aminoglycoside | 6 (%5.6) | 0 (%0) | 0.029 |
| | Beta-lactam/beta-lactamase inhibitor and quinolone | 13 (%12) | 15 (%14.3) | 0.627 |
| **Nutrition type** | Enteral | 54 (%50) | 36 (%34.3) | 0.02 |
| | Parenteral | 54 (%50) | 69 (%65.7) | 0.02 |

APACHE II score: Acute Physiology and Chronic Health Evaluation II score; PEG: Percutaneous Endoscopic Gastrostomy.

**Table 2.** Results of the multivariate logistic regression analysis of the risk factors for hospital-acquired *Acinetobacter* infections.

| Variate | Odd's rate | 95% confidence interval | p |
|---|---|---|---|
| Age | 1.03 | 1.00–1.05 | 0.008 |
| Mechanical ventilator use | 5.68 | 2.53–12.72 | 0.0001 |
| Tracheotomy | 5.29 | 1.64–17.08 | 0.005 |
| PEG | 9.49 | 2.41–37.27 | 0.001 |
| Carbapenem administration | 6.02 | 2.42–14.94 | 0.0001 |
| Nonuse of third-generation cephalosporin | 0.11 | 0.02–0.49 | 0.004 |

PEG: Percutaneous Endoscopic Gastrostomy.

**Table 3.** Results of the multivariate logistic regression analysis of the risk factors for mortality.

| Variate | Odd's rate | 95% confidence interval | p |
|---|---|---|---|
| Enteral nutrition | 2.53 | 1.33–4.78 | 0.004 |
| APACHE II score | 1.08 | 1.03–1.13 | 0.0001 |

APACHE II score: Acute Physiology and Chronic Health Evaluation II score.

The sensitivity of the recovered *Acinetobacter* strains to different antibiotics was evaluated. According to the evaluation made based on the categories created by Falagas et al., the rate of multidrug resistance (MDR) in Acinetobacter isolates in this study was found to be 94%. The strains exhibited the highest susceptibility to colistin and the highest resistance to ciprofloxacin, ertapenem, piperacillin, and piperacillin-tazobactam. Table 4 presents the antibiotic susceptibility profiles for all the isolates included in the study.

In our study, sensitivity was found to be 100% for colistin and 99.1% for tigecycline in the evaluation made according to the reference MIC breakpoints. Among the aminoglycoside antibiotics (amikacin, netilmicin, tobramycin, gentamicin), the highest sensitivity was found in netilmicin, and the highest resistance was found in amikacin. Genotypic analysis was conducted on 96 isolates, of which 83 were categorized into 24 distinct clusters (Figure 1). The data showed a clustering rate of 86% among the isolates (Figure 1), indicating a high level of clonal similarity among the *A. baumannii* strains obtained in this study. By examining the isolation dates of 24 strains in the P5 cluster with the highest number of isolates in our study, it was determined that this clone had persisted in our hospital for approximately 14 months.

**Table 4**. Antibiotic susceptibility of the identified *Acinetobacter* strains.

| Antibiotic | Susceptible n (%) | Moderately susceptible n (%) | Resistant n (%) |
|---|---|---|---|
| Amikacin | 22 (20.4) | 7 (6.5) | 79 (73.1) |
| Netilmicin | 62 (93.9) | 1 (1.5) | 3 (4.5) |
| Tobramycin | 44 (86.3) | 1 (2) | 6 (11.8) |
| Gentamicin | 40 (40.8) | 5 (5.1) | 53 (54.1) |
| Ampicillin–sulbactam | 36 (33.6) | 6 (5.6) | 65 (60.7) |
| Cefepime | 6 (5.8) | 4 (3.9) | 93 (90.3) |
| Cefoperazone-sulbactam | 40 (37.7) | 12 (11.3) | 54 (50.9) |
| Cefotaxime | 5 (4.8) | - | 99 (95.2) |
| Ceftazidime | 7 (6.5) | 5 (4.6) | 96 (88.9) |
| Ceftriaxone | 3 (3.3) | - | 87 (96.7 |
| Ciprofloxacin | 8 (7.4) | - | 100 (92.6) |
| Imipenem | 12 (11.1) | 7 (6.5) | 89 (82.4) |
| Meropenem | 10 (9.3) | 3 (2.8) | 95 (88) |
| Piperacillin | 2 (1,9) | 1 (1) | 102 (97,1) |
| Piperacillin–tazobactam | 4 (3.7) | 3 (2.8) | 101 (93.5) |
| Trimethoprim-sulphamethoxazole | 6 (6) | - | 94 (94) |
| Mezlocilline | 4 (4.3) | - | 96 (95.7) |
| Tetracycline | 8 (8.2) | - | 89 (91.8) |

## DISCUSSION AND CONCLUSION

Genotypic analysis is imperative for understanding the dissemination and evolution of *A. baumannii* in healthcare environments. A study that employed enterobacterial repetitive intergenic consensus-polymerase chain reaction for fingerprint genotypic analysis reported that among 59 *A. baumannii* strains, 51 were categorized into 7 clusters. In contrast, the remaining 8 were identified as distinct strains. The significant genetic similarity among these strains was taken as evidence of cross-contamination among hospitalized patients.[12] One study showed that the analyzed strains showed more than 90% similarity and were grouped into 11 distinct genotypes.[13] In our study, we employed REP–PCR using the DiversiLab system (bioMerieux, France) to examine the clonal relationships among *A. baumannii* isolated from the ICU of our hospital. Using this approach, 24 unique clusters were found among the 96 *A. baumannii* isolates. An 86% clustering rate indicated a high level of clonal proximity among isolates, implying a considerable incidence of cross-contamination among patients. This finding is corroborated by a study conducted in our country in which 66 *A. baumannii* isolates collected over a 14-month period were typed via pulsed-field gel electrophoresis, yielding a clustering rate of 80.3%, aligning with our findings.[14] A particularly significant finding in our investigation was the enduring presence of a particular clone (designated as P5) for almost 14 months in our hospital. In this respect, the findings obtained in our study are similar to domestic and international studies.[13,14]

*Acinetobacter* species, although capable of inducing hospital infections in any area, mainly cause respiratory tract, urinary tract, and wound infections. A notable increase in the number of hospital-acquired pneumonia cases attributed to *A. baumannii* has been documented at numerous sites.[15,16] In accordance with existing research, our study identified VAP as the predominant type of hospital-acquired infection, with tracheal aspirate cultures representing

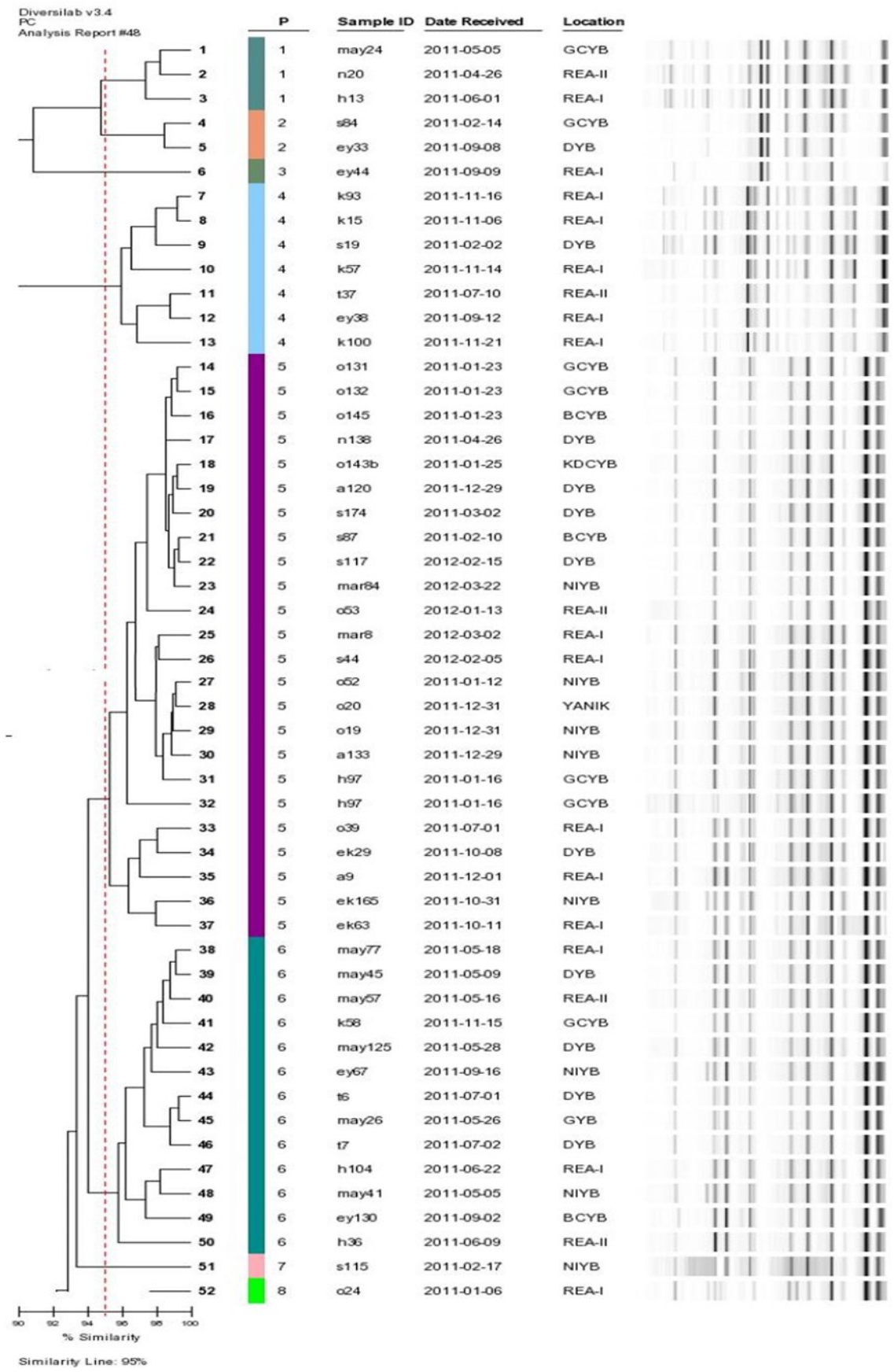


**Figure 1.** Clustering analysis using a 95% similarity coefficient.

the most prevalent site of *Acinetobacter* proliferation.

Previous research on the risk factors for hospital-acquired *Acinetobacter* infections has identified independent risk factors through multivariate analysis. These factors included male sex, advanced age,[1,16,17] high APACHE II score,[1,18] extended hospital and ICU stay,[18] previous ICU and hospital admissions, enteral nutrition,[1] administration of broad-spectrum antibiotics (particularly third-generation cephalosporins),[18,19] invasive procedures (central venous catheterization, mechanical ventilation, urinary catheterization, surgical interventions),[1] and immunosuppression in patients with critical illness.[20]

Through multivariate regression analysis, this study found age, mechanical ventilator use, tracheotomy, PEG, carbapenem administration, and nonuse of cephalosporins as independent risk factors for hospital-acquired *Acinetobacter* infections. Notably, enteral feeding via PEG was found to increase the incidence of hospital-acquired *Acinetobacter* infections. This is consistent with the finding of a previous study indicating that enteral nutrition is a risk factor for *Acinetobacter* colonization or infection.[1]

Similar to other research,[1,16,17] our study found that age is an independent risk factor for hospital-acquired *Acinetobacter* infections.

Consistent with previous literature,[1] the present study also indicated that interventional procedures are critical risk factors for the aforementioned infections. This study specifically demonstrated that patients who underwent tracheotomy exhibited a greater risk of acquiring *Acinetobacter* infection in the hospital.

Retrospective stepwise elimination logistic regression analysis revealed that enteral nutrition and high APACHE II scores were independent risk factors for mortality. This corresponds to previous studies demonstrating a relationship between high APACHE II scores and an increased risk of acquiring ICU-associated infections.[19]

The use of broad-spectrum antibiotics is an important risk factor for the development of antibiotic resistance and colonization/infection by *Acinetobacter* species.[1,21] Our study demonstrated a markedly increased utilization of beta-lactam/beta-lactamase inhibitor–aminoglycoside combinations and carbapenems in the case group compared with the control group. Multivariate analysis revealed that carbapenem administration and nonuse of cephalosporin are independent risk factors, with the former increasing the probability of *Acinetobacter* infection.

The capacity of *Acinetobacter* to develop antimicrobial resistance and persist on many surfaces enhances its importance as a causal agent of hospital infections. A study found the multidrug resistance to be 63% for the *A. baumannii* isolates and has indicated that the prevalence of carbapenem-resistant *A. baumannii* exceeds 40%.[16] A study reported that a carbapenem-resistant *A. baumannii* strain showed resistance to the majority of the evaluated antimicrobial drugs.[17] In a study involving 2,636 *A. baumannii* isolates, MDR was detected in almost 65% of *A. baumannii* isolates.[22] A study reported resistance rates of 52.2% and 47.8% to meropenem and imipenem, respectively, among *Acinetobacter* strains.[13] Some countries in the South and Southeast Asian regions have resistance rates above 40%, representing the highest frequency among important hospital-acquired Gram-negative infections.[23]

Our analysis revealed that the isolates demonstrated a very high rate of MDR. This finding is consistent with the elevated rates of carbapenem resistance (82.4% for imipenem and 88% for meropenem) identified in our study. Within the aminoglycoside antibiotic category, netilmicin showed the greatest susceptibility, whereas amikacin exhibited significant resistance. In a recent study, the resistance rates for tobramycin, gentamicin, and amikacin were found to be 65.2%, 73.9%, and 52.2%, respectively.[13]

The importance of colistin and tigecycline in the treatment of *Acinetobacter* infections has substantially increased. Numerous studies have reported the development of *in vivo* resistance to colistin or tigecycline during the treatment of *A. baumannii* infections, frequently resulting in chronic or recurring infections.[24] In contrast, our study demonstrated a tigecycline susceptibility rate of 99.1%.

A study examining tigecycline heteroresistance in *A. baumannii* revealed the presence of a significant proportion of heteroresistant isolates.[25] Resistance to colistin, which is essential in combination therapy for managing MDR *A. baumannii* infections, has become increasingly prevalent. Asia has reported the highest resistance rates to colistin, followed by Europe.[26] Conversely, our study revealed complete susceptibility to colistin. A separate investigation showed that the polypeptides polymyxin B and colistin had the highest efficacy against *A. baumannii*, with susceptibility rates of 82.6% and 73.9%, respectively.[13]

Our study on Acinetobacter infections, which is an important health problem today, will make a significant contribution to the literature as it simultaneously includes research on risk factors, antibiotic resistance profile and genotypic analysis.

The limitation of our study is that it is a single-center study. This may limit the generalizability of our findings. Multicenter studies may yield even more valuable results.

In conclusion, multiple critical risk factors were discovered for *A. baumannii* infections in our study, including advanced age, particular interventional

procedures, and the administration of specific antibiotics, such as carbapenems. Genotypic analysis revealed significant clonal relatedness among the *A. baumannii* isolates, indicating considerable cross-contamination hazards within the hospital setting. Identification of molecular and epidemiological diagnostic markers that will help identify resistant clones and monitor their spread will guide the management of nosocomial multidrug-resistant Acinetobacter infections.

***Ethics Committee Approval:*** Our study was approved by the XX University Ethics Committee (Date: 01.03.2011, decision no: 2011/14). The study was carried out following the principles of the Declaration of Helsinki.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

***Author Contributions:*** Concept–SED, FM; Supervision–SED; Materials–SED, CK, YE; Data Collection and/or Processing–SED; Analysis and/or Interpretation–SED, BO; Writing–SED.

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# Epidemiologic Evaluation of *Candida* Species in Vaginal Swab Specimens: An 11-Year Retrospective Study

# Vajinal Sürüntü Örneklerindeki *Candida* Türlerinin Epidemiyolojik Değerlendirmesi: 11 Yıllık Retrospektif Bir Çalışma

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**ABSTRACT**

**Objective:** *Candida* species may be part of the normal vulvovaginal flora, and hence their isolation in vaginal cultures does not necessarily indicate infection. However, vulvovaginal candidiasis (VVC) is a clinical condition particularly prevalent among women of reproductive age. The aim of this study was to investigate the epidemiology of *Candida* species isolated from vaginal swab samples (VSS) in the microbiology laboratory.

**Materials and Methods:** This study was designed retrospectively at a university hospital in Istanbul, with a bed capacity of 950, between August 2012 and August 2023. A total of 7050 vaginal swab culture results were analyzed in the microbiology laboratory. VSSs were cultured on *CHROMagar™ Candida (CHROMagar, Paris, France)* to isolate fungal pathogens. Automated systems such as the VITEK 2 (bioMérieux, France) system or MALDI-TOF mass spectrometry (Bruker, United States) were employed for undetermined colonies on this medium. The study evaluated the results of 2594 vaginal swab cultures and identified *Candida* species.

**Results:** The rate of *Candida* species in VSS cultures was 36.79%. The mean age of the patients was 36.1 years (range: 0–85 years), with 97.8% falling within the category of young adults. The highest prevalence of VVC was in patients 29–38 years of age (48%). *Candida albicans* accounted for 70.7%, non-*albicans Candida* for 26.4%, and growth of more than one *Candida* species for 2.8%. The most frequently observed non-*albicans* species was *Candida glabrata*, accounting for 23.1% of the isolates.

**Conclusions:** *C. albicans* was the predominant species in VSSs. However, the emergence of *C. glabrata* as a significant non-*albicans* species is a serious concern due to its potential for azole resistance.

**Keywords:** *Candida albicans*, non-*albicans Candida*, vaginal candidiasis, vaginal swab culture

**ÖZ**

**Amaç:** *Candida* türleri normal vulvovajinal floranın bir parçası olabilir ve bu nedenle vajinal kültürlerde izole edilmeleri mutlaka enfeksiyona işaret etmez. Bununla birlikte, vulvovajinal kandidiyazis özellikle üreme çağındaki kadınlarda yaygın olan klinik bir durumdur. Bu çalışmanın amacı, mikrobiyoloji laboratuvarına gönderilen vajinal sürüntü kültürlerinden izole edilen *Candida* türlerinin epidemiyolojisini incelemektir.

**Materyal ve Metot:** Bu çalışma Ağustos 2012-Ağustos 2023 tarihleri arasında İstanbul'da 950 yatak kapasiteli bir üniversite hastanesinde retrospektif olarak gerçekleştirilmiştir. Toplam 7050 vajinal sürüntü örneği kültürü mikrobiyoloji laboratuvarında analiz edilmiştir. Mantar patojenlerinin izolasyonu için kültür besiyeri olarak *CHROMagar™ Candida (CHROMagar, Paris, France*) kullanılmıştır. Bu besiyerinde belirlenemeyen kolonilerin tanımlanması için VITEK 2 (bioMérieux, Fransa) sistemi veya MALDI-TOF mass spectrometry (Bruker, United States) gibi otomatize sistemler kullanılmıştır. Çalışmada, *Candida* türlerinin tanımlandığı 2594 vajinal sürüntü kültürünün sonuçları değerlendirilmiştir.

**Bulgular:** Vaginal sürüntü kültürlerinden *Candida* türlerinin izolasyon oranı %36.79'dır. Hastaların ortalama yaşı 36.1 (aralık: 0-85 yıl) olup, %97.8'i genç yetişkin kategorisinde yer almaktadır. En yüksek vulvovaginal kandidiyazis prevalansı 29-38 yaş arasındaki hastalarda görülmüştür (% 48). *Candida albicans* %70,7, non-*albicans Candida* % 26.4 ve birden fazla türde *Candida* üremesi %2.8 oranında görülmüştür. En sık gözlenen non-*albicans Candida* türü, izolatların %23.1'ini oluşturan *Candida glabrata* olmuştur. *C. albicans* ve non-*albicans Candida* izolasyon oranlarında çalışma periyodu süresince anlamlı bir değişiklik gözlenmemiştir.

**Sonuç:** On bir yıllık süreçte *C. albicans* vajinal sürüntü örneklerinde baskın tür olarak kalmıştır. Bununla birlikte non-*albicans Candida* türlerinden *C. glabrata*'nın baskın tür olarak ortaya çıkması, azol direnci potansiyeli nedeniyle tedavi güçlüğü açısından endişe kaynağıdır.

**Anahtar Kelimeler:** *Candida albicans*, non-*albicans Candida*, vajinal kandidiyazis, vajinal sürüntü kültürü

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## INTRODUCTION

*Candida* species are present in the gastrointestinal, respiratory, and urogenital systems as part of the human microbiota. They can colonize the mucosa of the genital tract in most women without showing any symptoms of infection. This colonization may turn into invasive mucosal candidiasis in cases such as disruption of the defense mechanism of the vaginal mucosa, a decrease in lactobacilli abundance, and a change in pH.[1,2] Pregnancy, diabetes mellitus, contraceptive practices, hormone replacement therapy, antibiotics and steroids, immunosuppressive diseases, hygienic habits, intrauterine devices, and sexual behaviors are among the facilitating factors for vulvovaginal candidiasis (VVC).[3,4] In symptomatic women, the prevalence of VVC ranges from 17% to 57%.[3]

VVC is one of the main reasons for outpatient visits to gynecology clinics. It is usually treated with topical or oral azole antifungals based on symptoms.[5] The treatment with azoles is successful in VVC caused by *C. albicans* (CA); however, difficulties are experienced in infections caused by non-*albicans Candida* (NAC) species such as *C. glabrata* or *C. krusei*, which have acquired or natural resistance. [6] The most common causative agent in VVC is CA. [5]However, some studies report NAC species at the forefront.[7,8]

This study was conducted to investigate the distribution of *Candida* species isolated from the cultures of VSSs and their epidemiological course over 11 years.

## MATERIALS AND METHODS

***Ethics Committee Approval:*** The study was conducted in accordance with the International Declaration guidelines, and approval for this study was obtained from the Non-Invasive Clinical Research Ethics Committee of Istanbul Medipol University Faculty of Medicine (Date: 27/09/2024, decision no: E-10840098-202.3.02-5918).

***Study Design and Participants:*** A retrospective study was conducted in Istanbul, Türkiye, between August 2012 and August 2023. Our facility was a tertiary-care university hospital with a bed capacity of 950. A total of 7050 VSSs were evaluated in the microbiology laboratory during the study period. The culture results were obtained from the hospital information management system. The results of 2594 cultures in which *Candida* was identified were evaluated. No age restrictions were imposed on patients whose culture results were included in the study.

***Direct microscopic evaluation*:** Microscopic analysis of VSS was conducted using both wet preparations with 10% potassium hydroxide and Gram staining.. These techniques were used to assess the presence of yeast cells and hyphae formation, which are the key indicators of fungal structure.

***Fungal culture and identification*:** The clinical samples were cultured on *CHROMagar™ Candida (CHROMagar, Paris, France)* medium for fungal isolation and incubated at 37 °C for 48–72 h. The colonies grown on the medium were evaluated according to their color and shape. The yeast strains that could not be identified using this medium were subjected to further analysis using automated systems, such as the VITEK 2(bioMérieux, Fransa) system or matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS, Bruker, United States) . The culture results were broadly categorized and reported as CA and NAC during the initial 8 years of the 11-year study period. However, all isolated *Candida* strains were identified and reported at the species level in the subsequent years.

***Statistical analysis:*** Descriptive analysis was performed from the Excel spreadsheet. The continuous variable age was reported as the median. Graphs were created from the data sheet and the frequency of variables was determined as number (n) and percentage (%).

## RESULTS

A total of 7050 VSSs were examined. *Candida* species were detected in 36.79% of the samples (*n* = 2594/7050) in 2329 patients. Among 2594 *Candida* species, CA and NAC species accounted for 70.70% and 26.48%, respectively. The most common *Candida* strain isolated in the cultures was CA (n = 1834, 70.7%), followed by NAC (n = 687, 26.48%) and growth of more than one Candida species (n = 73, 2.82%). The most significant number of VSSs were evaluated in 2019, with the growth of *Candida* detected in 37.92% of the samples from that year. CA was the dominant species for each year, with a small difference between the rates of CA and NAC by year. The distribution of VSSs by year is shown in Table 1.

The median age of the patients was 31 years (min-max: 0–85 years). 96% of patients were of childbearing age, followed by the early menopausal age group with 2%, the pediatric age group with 1% and the elderly age group with 1% (Figure 1).

The highest rate of *Candida* growth was observed among patients in their 30s, accounting for 48% of cases. Patients in the 2nd decade had a prevalence of 35%, while those in the 4th decade had a prevalence of 12%. The distribution of *Candida* growth in vaginal cultures by decade is presented in Figure 2.

**Table 1.** Distribution of *Candida* growth by year in vaginal swab samples.

| Year | Number of VSSs | Yeast growth, *n* (%) | Number of CA, *n* (%) | Number of NAC, *n* (%) | CA + NCA, *n* (%) |
|---|---|---|---|---|---|
| **2012** | 213 | 95 (44.6) | 71 (74.74) | 24 (25.26) | – |
| **2013** | 600 | 240 (40) | 171 (71.25) | 62 (25.83) | 7 (2.92) |
| **2014** | 552 | 209 (37.86) | 144 (68.9) | 60 (28.71) | 5 (2.39) |
| **2015** | 603 | 236 (39.14) | 166 (70.34) | 61 (25.85) | 9 (3.81) |
| **2016** | 527 | 205 (38.9) | 139 (67.80) | 59 (28.78) | 7 (3.42) |
| **2017** | 683 | 260 (38.07) | 177 (68.07) | 76 (29.23) | 7 (2.7) |
| **2018** | 787 | 269 (34.18) | 188 (69.89) | 67 (24.9) | 14 (5.21) |
| **2019** | 836 | 317 (37.92) | 234 (73.82) | 76 (23.97) | 7 (2.21) |
| **2020** | 527 | 191 (36.24) | 134 (70.16) | 54 (28.27) | 3 (1.57) |
| **2021** | 700 | 229 (32.71) | 159 (69.43) | 67 (29.25) | 3 (1.32) |
| **2022** | 683 | 220 (32.21) | 169 (76.82) | 43 (19.54) | 8 (3.64) |
| **2023** | 339 | 123 (36.28) | 82 (66.66) | 38 (30.89) | 3 (2.45) |
| **Total** | 7050 | 2594 (36.79) | 1834 (70.70) | 687 (26.48) | 73 (2.82) |

CA: *Candida albicans*; NAC: Non-*albicans Candida*; VSS: Vaginal swab sample.

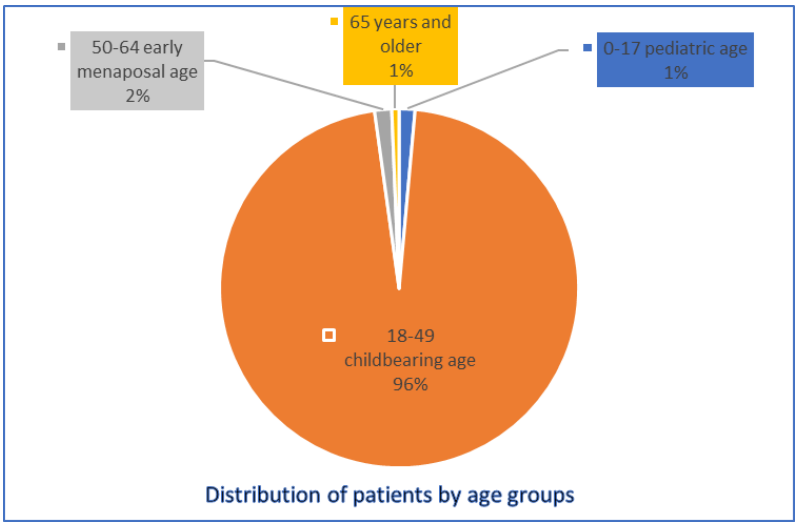


**Figure 1**. Distribution of patients by age groups.

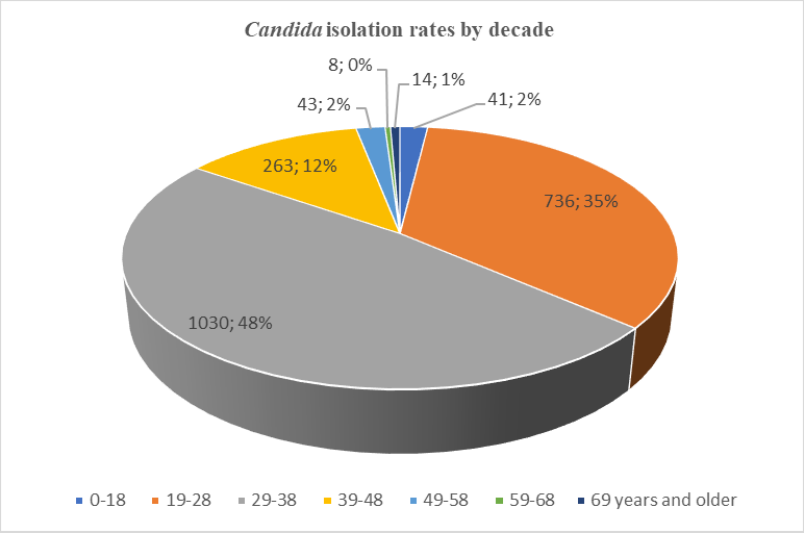


**Figure 2.** Distribution of *Candida* growth in vaginal cultures by decade.

Figure 3 illustrates the rate of CA and NAC growth based on the menopausal age limit of 50 years, which is widely regarded as a theoretical threshold. The results showed that the rate of NAC isolation increased from 26.17 to 42.11 in patients over 50 years of age.

In older patients, NAC species were observed to be the dominant species. Figure 4 presents the age distribution of patients aged 65 years and older.

A total of 459 culture samples were analyzed due to the persistence or recurrence of symptoms in 11.4% of patients. The most frequently identified pathogen in recurrent vaginal samples was CA, which was responsible for 73.2% of cases. All of the repeated samples were from patients in the childbearing age group. Of the NAC isolates, 67.83% remained unidentified at the species level. The following most prevalent species was *C. glabrata*, representing 23.14% of the isolates, followed by *C. kefyr* (4.22%) and *C. krusei* (3.35%). Further, the remaining isolates were identified as *C. krusei* (4), *C. lusitaniae* (3), *C. parapsilosis* (1), *C. dubliniensis* (1), *C. lambica* (1), *C. guilliermondii* (1), and *C. tropicalis* (1).

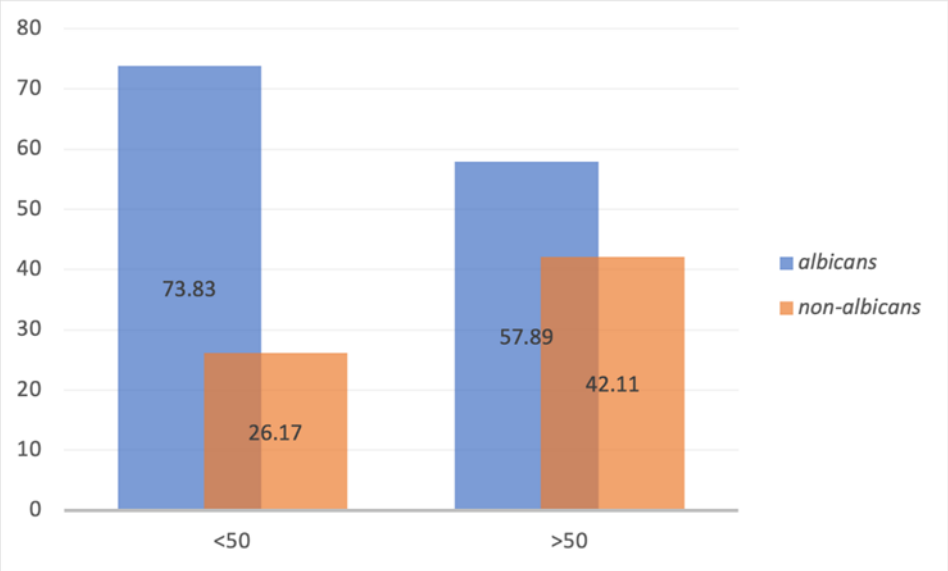


**Figure 3.** Distribution of *Candida* species according to pre- and postmenopausal periods. The age limit for menopause is considered to be 50 years in this analysis.

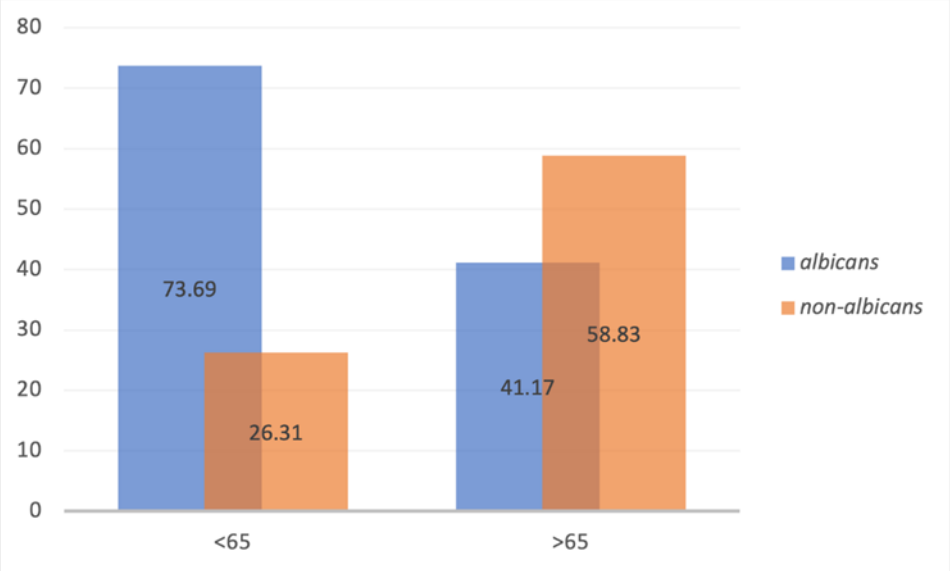


**Figure 4.** Distribution of *Candida* species according to geriatric age limit.

## DISCUSSION AND CONCLUSION

This study investigated the prevalence of *Candida* isolation, the distribution of CA and NAC species, and the epidemiological trends in vaginal swab specimens over 11 years. *Candida* growth was detected in more than one-third of the VSSs. Moreover, 89% of the patients were either pregnant or of childbearing age. CA was the most frequently isolated species in VVC. However, the findings highlight the importance of considering NAC species, particularly *C. glabrata*, which was the most commonly isolated NAC species.

Among two separate studies conducted in the USA,[9,10] 78% of women in one study and 53% in the other reported a history of VVC. The prevalence ranged from 15% to 37.7% in studies based on vaginal swab cultures in Brazil.[11,12] The prevalence of VVC ranged from 5.3% to 28% in Europe, 33% in Africa, and 19.4% to 47% in Asia and the Far East.[13-18] In national studies, these rates ranged from 18.4% to 43%.[19-22] The isolation rate of *Candida* in the present study was 36.8%, which was higher than the reported rates in Europe but lower than those in the USA. This prevalence was compatible with the national data as well as the findings from Asian, Far Eastern, and African countries.

The prevalence of VVC varies significantly worldwide. This variation is likely driven by several factors, including patient demographics, lifestyle habits, and socioeconomic conditions. Additionally, the differences in study design contribute to these variations because some studies rely on patient history and surveys, others on clinical evaluations, and some solely on laboratory findings.

This study confirmed a high prevalence of VVC, particularly among women in their reproductive years. The third-decade patients with the highest *Candida* isolation rate represented 48% of the cases. The prevalence peaked in the third decade of life, indicating that hormonal changes and factors such as pregnancy might significantly contribute to the development of VVC. The increased prevalence in younger women suggested increased exposure to risk factors during this stage of life. Previous studies reported that the prevalence of VVC was higher in the second to third decade compared with other decades among reproductive-age women.[8,10,12,23]

The present study demonstrated that all repeat specimens were obtained from patients of childbearing age, with CA being the most predominant species. This suggests that factors such as pregnancy, hormonal contraceptive use, personal hygiene practices, spermicides, condoms, and intrauterine devices in this age group may contribute to the development of the infection. In this study, CA was the most dominant species, more predominant in the reproductive period and early menopausal age. However, NAC isolates were more predominant in elderly patients. Prior to this study period, between March 2003 and March 2007, Vermitsky et al.[24] reported the presence of CA and *C. glabrata* in 89% and 9% of cases, respectively, among 93,775 cervicovaginal swab specimens. Also, it indicated that CA was more prevalent in women of reproductive age prior to menopause, whereas *C. glabrata* was more prevalent in postmenopausal women. However, subsequent studies[25-27] demonstrated a decline in the isolation rate of CA, with reports indicating a range of 50%–70%. Furthermore, some studies reported that the prevalence of NAC species exceeded the prevalence of CA.[8,19,28,29] *C. glabrata* is a frequently observed NAC species.[15,30] The widespread use of azole antifungals might contribute to this increase. We believe that species-level identification and even antifungal susceptibility surveillance should be emphasized in vaginal samples to evaluate epidemiological shifts. NAC species may resist antifungal treatments, emphasizing the need for tailored therapeutic strategies.

In conclusion, vulvovaginal candidiasis continues to be an important clinical problem, particularly in women of childbearing age. *C. albicans* remains the most dominant species in vaginal swab cultures, with no significant shift observed between CA and NACs. However, *C. glabrata* is the dominant species among NAC species due to its potential for azole resistance, highlighting the importance of species identification in surveillance. The main limitations of this study were its retrospective design and reliance solely on culture results.

***Ethics Committee Approval:*** The study was conducted in accordance with the International Declaration guidelines, and approval for this study was obtained from the Non-Invasive Clinical Research Ethics Committee of Istanbul Medipol University Faculty of Medicine (Date: 27/09/2024, decision no: E-10840098-202.3.02-5918).

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# Examination of Cases Who Had Molecular Testing with the Presumptive Diagnosis of Cystic Fibrosis: Experience of a Single Center

# Kistik Fibrozis Öntanısıyla Moleküler Test Yapılan Olguların İncelenmesi: Tek Merkez Deneyimi

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**ABSTRACT**

**Objective:** Cystic fibrosis (CF) is an autosomal recessive disorder caused by mutations in the Cystic Fibrosis Transmembrane Regulator (CFTR) gene, leading to multisystem involvement. Early diagnosis is crucial for managing complications and improving patient prognosis. This study aimed to evaluate the clinical and demographic characteristics and molecular analysis results of patients who underwent CFTR gene mutation analysis with a preliminary diagnosis of CF.

**Materials and Methods:** A total of 34 patients were included in the study. Clinical and demographic data, along with genetic analysis results, were retrospectively examined. The frequency of symptoms associated with CF was determined, and the relationship between genetic findings and clinical manifestations was analyzed.

**Results:** The most common reason for admission was respiratory symptoms, accounting for 64.7% of cases, followed by gastrointestinal complaints and malnutrition. Malnutrition was found to be significantly associated with a positive CFTR gene mutation (p=0.027). The risk of detecting a CFTR gene mutation was 5.667 times higher in patients with malnutrition.

**Conclusions:** This study highlights the necessity of considering CF in the differential diagnosis of children presenting with recurrent respiratory tract infections and malnutrition, even in the absence of a positive family history. While respiratory symptoms were the most common reason for admission, malnutrition was found to be significantly more prevalent among mutation-positive cases. These findings underscore the importance of supporting careful clinical evaluation with genetic analysis in the diagnostic process of CF. Further large-scale, multicenter studies are needed to confirm and expand upon these results.

**Keywords:** CFTR gene, cystic fibrosis, heterozygous mutation, malnutrition, recurrent lower respiratory tract infection

**ÖZ**

**Giriş:** Kistik fibrozis (KF), Cistic fibrosis Cystic Fibrosis Transmembrane Regulator (CFTR) genindeki mutasyonlar sonucu ortaya çıkan otozomal resesif geçişli bir hastalıktır ve multisistemik tutulum gösterir. Erken tanı, komplikasyonların yönetimi ve hasta prognozu açısından kritik öneme sahiptir. Bu çalışmada, KF ön tanısı ile CFTR gen mutasyon analizi yapılan hastaların klinik ve demografik özellikleri ile moleküler analiz sonuçlarının değerlendirilmesi amaçlandı.

**Materyal ve Metot:** Çalışmaya toplam 34 hasta dahil edilmiştir. Klinik, demografik veriler ve genetik analiz sonuçları retrospektif olarak incelenmiştir. KF ile ilişkili semptomların sıklığı belirlenmiş ve genetik bulgular ile klinik belirtiler arasındaki ilişki analiz edilmiştir.

**Bulgular:** Başvuru nedenleri arasında en yaygın olanı % 64,7 oranıyla solunum yolu semptomlarıydı; bunu gastrointestinal şikayetler ve malnütrisyon izledi. Malnütrisyon, CFTR gen mutasyonu pozitifliği ile anlamlı şekilde ilişkili bulundu (p=0,027). Malnütrisyonu olan hastalarda CFTR gen mutasyonu saptanma riski 5,667 kat daha yüksekti.

**Sonuç:** Bu çalışma, tekrarlayan solunum yolu enfeksiyonları ve malnütrisyon ile başvuran çocuklarda, aile öyküsü olmasa dahi, ayırıcı tanıda kistik fibrozisin mutlaka göz önünde bulundurulması gerektiğini vurgulamaktadır. Solunum semptomları en sık başvuru nedeni olmakla birlikte, malnütrisyonun mutasyon pozitif olgularda anlamlı derecede daha sık görüldüğü saptanmıştır. Bu bulgular, kistik fibrozis tanı sürecinde dikkatli klinik değerlendirmenin genetik analizle desteklenmesinin önemini ortaya koymaktadır. Bulguların doğrulanması ve genişletilmesi için daha geniş çaplı, çok merkezli çalışmalara ihtiyaç vardır.

**Anahtar Kelimeler:** CFTR gen, heterozigot mutasyon, kistik fibrozis, malnutrisyon, tekrarlayan alt solunum yolu enfeksiyonu

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## INTRODUCTION

Cystic fibrosis (CF) is an autosomal recessive disorder caused by mutations in the Cystic Fibrosis Transmembrane Regulator (CFTR) gene, which encodes a chloride channel protein in epithelial cells. It affects approximately 1 in 4.000 live births, with an estimated 89.00 cases worldwide. Over 2.000 CFTR mutations have been identified, with the ΔF508del mutation detected in 85.5% of CF patients.[1,2]

The CFTR protein belongs to the ATP-binding cassette transporter family and consists of 1.480 amino acids. It functions as a chloride channel in the cell membrane, regulated by cAMP-dependent protein kinases. ATP-dependent phosphorylation of CFTR triggers the channel to open, allowing chloride ion transport. Certain CFTR mutations produce defective proteins that fail to reach the cell membrane or remain nonfunctional. This disrupts chloride and water transport, leading to dehydrated mucus and secretions.[3]

CF patients frequently present with recurrent lower respiratory tract infections and malnutrition. *Staphylococcus aureus* and *Pseudomonas aeruginosa* contribute to chronic lung disease, bronchiectasis, progressive lung function decline, and respiratory failure, the primary cause of mortality. Treatment includes mucolytics, anti-inflammatory agents, and antibiotics.[4] Increased viscosity of pancreatic secretions leads to pancreatic duct obstruction, tissue damage, cyst formation, and fibrosis. Exocrine pancreatic insufficiency is present in 60–80% of patients at birth.[5] Other symptoms include excessive salt loss, male infertility, and pseudobartter syndrome.[4]

Diagnosis is based on CF-related symptoms, genetic testing, nasal potential difference measurement, or elevated chloride levels in sweat testing.[6] Newborn screening programs in many countries, including Türkiye, facilitate early detection. Advances in multidisciplinary care, including dietitians, respiratory physiotherapists, and social workers, have significantly improved the CF prognosis. The median survival age increased from 36.3 years in 2006 to 53.1 years in 2021.[2]

This study aimed to evaluate the demographic and clinical characteristics, as well as the molecular analysis findings, of patients who underwent CFTR gene mutation testing with a preliminary diagnosis of CF.

## MATERIALS AND METHODS

***Ethics Committee Approval:*** This research involving human subjects complied with all relevant national regulations and institutional policies and was conducted in accordance with the tenets of the Helsinki Declaration. The study was approved by the Duzce University Faculty of Medicine Ethics Committee (Date: 10.06.2024, decision no: 2024/126). Before inclusion, parents of all study participants were informed about the study's purpose, methodology, and implementation, and written consent was obtained.

***Patient Selection:*** Clinical features such as recurrent lung infections, inadequate weight gain, malnutrition, chronic diarrhea, a history of nasal polyps, ileal obstruction, and a family history of cystic fibrosis are suggestive of cystic fibrosis.[7] This study included 34 cases who presented to the Duzce University Application and Research Hospital, Pediatrics clinics between 01.01.2015 and 01.01.2021.

***Sample Collection and Genetic Analysis:*** Genomic DNA was isolated from peripheral blood samples of the patients, and whole-exome sequencing (WES) was performed using the Illumina SureSelect V6 Exome kit on an Illumina HiSeq4000 platform. The pathogenicity of detected variants was classified according to the guidelines established by the American College of Medical Genetics and Genomics and the Association for Molecular Pathology (ACMG/AMP) for the interpretation of sequence variants (PMID: 25741868) and multiple databases and tools, including Illumina BaseSpace Variant Interpreter, InterVar, SIFT, Mutation Tester, PolyPhen-2, Franklin, VarSome, ClinVar, OMIM, and PubMed. Variants with a population frequency higher than 0.5% were excluded.

With the advancements in next-generation sequencing (NGS) technologies, more comprehensive information has been obtained regarding the diagnosis, prognosis, and etiopathogenesis of various diseases.[8-10] In our study, we evaluated the clinical symptoms and findings of patients who underwent genetic analysis via NGS with a preliminary diagnosis of cystic fibrosis.

***Definition of Malnutrition:*** In our study, malnutrition was defined as a weight-for-age Z score below -2 SD, consistent with established pediatric growth assessment criteria.[11]

***Clinical Data Collection:*** Demographic characteristics (age, sex, etc.) were recorded along with the presence of recurrent lung infections, inadequate weight gain, malnutrition, chronic diarrhea, history of nasal polyps, ileal obstruction, and family history of CF. Height and weight percentiles, respiratory system examination findings, and laboratory parameters [including plasma sodium, potassium, and chloride levels, as well as blood gas analysis (pH, $HCO_3$, and $pCO_2$ levels)] were evaluated alongside CFTR gene mutation analysis results.

***Exclusion Criteria:*** Cases with bronchopulmonary dysplasia, asthma, and immunodeficiency syndromes that could lead to recurrent pulmonary infections, as well as those with celiac disease, other mal-

absorption syndromes, or existing malnutrition, were excluded from the study.

***Statistical Analysis:*** Descriptive statistics were presented as frequency and percentage. Demographic data were presented as mean, standard deviation (SD), median, and Interquartile Range (IQR). For normality analysis, the bell curve was used when $n > 50$, whereas the Shapiro-Wilk test was applied when $n < 50$. The relationship between two independent categorical variables was analyzed using the Pearson Chi-square test or Fisher's Exact test. The Mann-Whitney U test was employed for non-normally distributed continuous variables between two independent groups, while the Student's *t*-test was used for normally distributed continuous variables. Statistical analyses were performed using SPSS software for Windows, version 25 (IBM, Chicago, IL, USA). A $p$ -value < 0.05 was considered statistically significant.

## RESULTS

A total of 34 cases were included in the study. The median age (IQR 25-75) was 6.50 (5-14.25) years, and 19 cases (55.9%) were male. The mean gestational age was 38.71 ± 1.21 weeks, and the mean birth weight was 3127.06 ± 430.84 g. A family history of CF was present in 11 cases (32.4%). The most common symptoms were respiratory-related, with 22 cases (64.7%) having a history of recurrent lower respiratory tract infections, bronchiectasis, or atelectasis. Malnutrition was observed in 10 cases (29.4%), while gastrointestinal symptoms such as vomiting, diarrhea, and feeding intolerance were seen in 11 cases (32.4%). Nasal polyps were detected in 5 cases (14.7%), and ileal atresia in 1 case. The median symptom duration (IQR 25-75) was 1 (1-3) years, and the median number of hospitalizations was 1.50 (1-4.25) (Table 1).

Some demographic data of the patients are presented in Table 1.

The laboratory findings of a cystic fibrosis patient who applied to the Pseudobartter syndrome clinic included plasma sodium of 142 mEq/L, potassium 2.9 mEq/L, chloride 66.4 mEq/L, blood gas pH 7.62, $HCO_3^-$ 39.2 mEq/L, and $pCO_2$ 37.2 mEq/L. Due to a history of recurrent respiratory infections, genetic analysis revealed a compound heterozygous mutation in exon 4 (c.328G>C p.Asp110His rs113993958) and exon 11 (c.1521_1523delCTT p.Phe508delPhe rs113993960). Median (IQR 25-75) plasma electrolyte values were: sodium 138 (135.75-140.25) mEq/L, potassium 4.55 (4.17-4.85) mEq/L, chloride 101.50 (99-104) mEq/L, blood gas pH 7.39 (7.36-7.42), $pCO_2$ 38.40 (36.3-41) mmHg, and $HCO_3^-$ 24 (22.95-24.65) mEq/L (Table 2).

**Table 1.** Descriptive data of patients diagnosed with CF.

| Parameters | | Data |
|---|---|---|
| Age, year [Median (IQR 25-75)] | | 6.50 (5-14.25) |
| Gender, n (%) | Boy | 19 (55.9) |
| | Girl | 15 (44.1) |
| Gestation age, week Mean ± SD | | 38.71 ± 1.21 |
| Birth weight, grams Mean ± SD | | 3127.06 ± 430.84 |
| Family history, n (%) | | 11 (32.4) |
| Hospitalization, Median (IQR 25-75) | | 1.50 (1-4.25) |
| Symptom time, Median (IQR 25-75) | | 1 (1-3) |
| Symptoms and findings, n (%) | Malnutrition | 10 (29.4) |
| | GIS symptoms | 11 (32.4) |
| | Respiratory system symptoms | 22 (64.7) |
| | Nasal polyp | 5 (14.7) |
| | Ileal atresia | 1 (2.9) |
| | Gene Analysis, Positive | 14 (41.1) |

GIS: Gastrointestinal System; CF: Cystic fibrosis.

**Table 2.** Laboratory parameters of patients diagnosed with CF.

| Laboratory Parameters | Median (IQR 25-75) |
|---|---|
| pH | 7.39 (7.36-7.42) |
| $pCO_2$ (mmHg) | 38.40 (36.3-41) |
| $HCO_3^-$ (mEq/L) | 24 (22.95-24.65) |
| Sodium (mEq/L) | 138 (135.75-140.25) |
| Potassium (mEq/L) | 4.55 (4.17-4.85) |
| Chloride (mEq/L) | 101.50 (99-104) |

CF: Cystic fibrosis.

CF results from autosomal recessive CFTR gene mutations. The mutations identified in our cases are presented in Table 3.

When comparing cases with and without detected mutations in genetic analysis, there were no significant differences in age, sex, gestational age, or birth weight (p=0.710, p=0.901, p=0.146, p=0.570). Although a family history of CF was more common in the mutation-positive group, it was not statistically significant (p=0.135). Hospitalization numbers and symptom durations were similar between the groups (p=0.580, p=0.500). Malnutrition was significantly more frequent in the mutation-positive group (p=0.027). No significant differences were found regarding gastrointestinal or respiratory symptoms (p=0.458, p=0.275). None of the five cases with nasal polyps had a detected mutation, and a significant difference was found between the groups (p=0.043) (Table 4).

**Table 3.** Genetic mutations detected variant in the patients.

| Case No | Zygosity | Region (Exon/ Intron) | DNA Change | Protein Change | rs ID |
|---|---|---|---|---|---|
| **1** | Homozygous | Intron 9 | c.1210-11T>G | - | rs73715573 |
| **2** | Compound heterozygous | Exon 10 / Exon 14 | c.1244A>G / c.2002C>T | p.N415S / p.R668C | rs1800100 |
| **3** | Compound heterozygous | Exon 13 / Exon 14 | c.1727G>C / c.2002C>T | p.Gly576Ala / p.Arg668Cys | rs1800098 / rs1800100 |
| **4** | Compound heterozygous | Exon 4 / Exon 11 | c.328G>C / c.1521_1523delCTT | p.Asp110His / p.Phe508delPhe | rs113993958 / rs113993960 |
| **5** | Heterozygous | Exon 2 | c.4332C>T | p.Ser1444Ser | - |
| **6** | Heterozygous | Exon 26 | c.4231C>T | p.Q1411* | rs397508701 |
| **7** | Heterozygous | Exon 6 | c.650A>G | p.Glu217Gly | rs121909046 |
| **8** | Heterozygous | Intron 9 | c.1210-11T>G | - | rs73715573 |
| **9** | Heterozygous | Exon 14 | c.2052dupA | p.Gln685ThrfsTer4 | rs746460279 |
| **10** | Heterozygous | Exon 14 | c.1897C>A | p.Leu633Ile | rs397508317 |
| **11** | Heterozygous | Exon 6 | c.650A>G | p.Glu217Gly | rs121909046 |
| **12** | Heterozygous | Exon 20 | c.3154T>G | p.Phe1052Val | - |
| **13** | Heterozygous | Exon 2 | c.4332C>T | p.Ser1444Ser | - |
| **14** | Heterozygous | Intron 4 | c.489+3A>G | - | rs377729736 |

**Table 4.** Comparison of parameters between patients with positive and negative genetic analysis results.

| Parameters | | Genetic Analysis | | p-value |
|---|---|---|---|---|
| | | Positive, n=14 | Negative, n=20 | |
| Age, year [Median (IQR 25-75)] | | 6 (5.75-15.50) | 8 (5-14) | 0.710* |
| Gender, n (%) | Boy | 8 (57.1) | 11 (55) | 0.901** |
| | Girl | 6 (42.9) | 9 (45) | |
| Gestation age, week Mean ± SD | | 39.07 ± 1.07 | 38.45 ± 1.27 | 0.146*** |
| Birth weight, grams Mean ± SD | | 3178.21 ± 486.80 | 3091.25 ± 396.19 | 0.570*** |
| Family history, n (%) | | 7 (50) | 4 (20) | 0.135**** |
| Hospitalization, Median (IQR 25-75) | | 2.50 (1-3.50) | 1 (0.25-4.75) | 0.580* |
| Symptom time, Median (IQR 25-75) | | 1 (1-3.50) | 1 (1-2.75) | 0.500* |
| Symptoms and findings, n (%) | Malnutrition | 7 (50) | 3 (15) | 0.027**** |
| | GIS Symptoms | 6 (42.9) | 5 (45.5) | 0.458**** |
| | Respiratory System Symptoms | 11 (78.6) | 11 (55) | 0.275**** |
| | Nasal Polyp | 0 (0) | 5 (25) | 0.043**** |
| | Ileal Atresia | 0 (0) | 1 (5) | 0.588**** |
| Laboratory Parameters, Median (IQR 25-75) | pH | 7.42 (7.37-7.43) | 7.38 (7.35-7.41) | 0.094* |
| | $pCO_2$, mmHg | 37. 2 (36.05-39.25) | 39 (36.22-41.75) | 0.361* |
| | $HCO_3^-$, mEq/L | 24 (23.32-24.52) | 24.05 (22.25-24.87) | 0.861* |
| | Sodium, mEq/L | 138.50 (135.50-141) | 138 (135.25-140) | 0.597* |
| | Potassium, mEq/L | 4.65 (4-5.02) | 4.5 (4.2-4.7) | 0.752* |
| | Chloride, mEq/L | 102.50 (101-104.50) | 101 (98.25-102.75) | 0.121* |

*: p-value was obtained by Mann Whitney-U test; **: p-value was obtained by Pearson Chi-Square test; ***: p-value was obtained by Student's t-test; ****: p-value was obtained with Fisher-Exact test; GIS: Gastrointestinal system.

## DISCUSSION AND CONCLUSION

This study retrospectively analyzed the demographic characteristics, clinical findings, and laboratory results of patients with suspected CF at Duzce University Application and Research Hospital. The most frequently recurring respiratory system symptoms, followed by gastrointestinal symptoms and malnutrition, were detected in the patients included in the study. Malnutrition was more frequently observed in cases with detected mutations in genetic analysis.

Priel et al.[12] found that CFTR heterozygous mutations were linked to higher rates of asthma and recurrent neutrophilic bronchitis due to CFTR hypofunction. They also reported that patients with recurrent bronchitis and severe asthma were four times more likely to have a CFTR heterozygous mutation. Studies have shown that individuals carrying heterozygous CFTR gene mutations exhibit a significantly higher prevalence of 57 out of 59 clinical conditions associated with cystic fibrosis, including respiratory diseases such as asthma, chronic rhinosinusitis, and respiratory tract infections, as well as gastrointestinal disorders like gastroesophageal reflux and chronic pancreatitis, compared to control groups.[13] In our study, malnutrition was found to be significantly more frequent in mutation-positive cases. Additionally, patients with malnutrition were 5.667 times more likely to have CF compared to those without malnutrition [OR: 5.667; (CI: 1.129; 28.454)]. This challenges the belief that individuals with CFTR heterozygous mutations are asymptomatic.

Lung disease and malnutrition are significant challenges in CF. Studies show a positive link between good nutritional status and better lung function.[14] Hyperviscous mucus accumulation in the pancreas impairs enzyme secretion, leading to acinar tissue damage and exocrine pancreatic insufficiency, which results in malabsorption and malnutrition.[15] Malnutrition in CF is caused by various factors, including dietary deficiencies, malabsorption, CF-related liver disease, CF-related diabetes, and stress. Malnourished CF patients tend to have a worse prognosis and lower life expectancy.[14] Collectively, these findings reinforce the perspective put forward by Priel et al.[12] that heterozygous CFTR mutations can be clinically relevant and should not be considered entirely benign.

CF pulmonary symptoms involve abnormal chloride and sodium ion movement across airway epithelial cells, leading to poor airway secretion clearance and chronic bronchial infections. The immune response causes intense neutrophilic inflammation, and neutrophil death thickens sputum, further obstructing clearance. This cycle leads to recurrent infections, bronchiectasis, and respiratory failure.[3] In our study, CFTR gene analysis was requested for cases with frequent recurrent respiratory pathologies, and 64.7% had respiratory symptoms. Recurrent lower respiratory tract infections are a leading cause of death in CF patients in early adulthood, making CF a consideration in such cases.[4]

The number of hospitalizations is typically higher in patients with positive CFTR gene mutations.[12] In our study, while the number of hospitalizations was higher in mutation-positive patients, no significant difference was found between the two groups. This may be due to the majority of mutation-positive cases being heterozygous. Schlüter et al.[16] reported that children with CF are more likely to be born prematurely and with low birth weight. In our study, however, no significant difference was found in birth weight or gestational age between the mutation-positive and mutation-negative groups.

Ninety percent of CF cases are diagnosed before the age of 10. The most common symptoms include progressive lung disease or exocrine pancreatic insufficiency, or laboratory findings related to abnormalities in the CFTR gene or protein. In cases where the diagnosis is made later in life, symptoms tend to begin later and are milder, due to partial CFTR gene mutation or protein function. Since the sweat chloride test sensitivity and specificity are low in these cases, genetic testing becomes more prominent for diagnosis.[17] In our study, the median (IQR 25-75) age of diagnosis for mutation-positive cases was 6 (5.75-15.50) years, and all 5 cases with a genetic mutation detected after the age of 10 had heterozygous mutations. This is likely due to the later onset and milder course of symptoms in heterozygous mutation cases.

Studies have reported that boys are more commonly diagnosed with CF than girls, but that the mortality and morbidity in female patients are higher.[18] In our study, 57.1% of the cases were male. When we compared mutation-positive male and female cases, no significant differences were found in terms of symptoms and laboratory findings ($p>0.05$). Although clinical presentations in female patients are reported to be more severe in some studies, since CFTR gene mutations are autosomal recessive, it is not expected that clinical outcomes to vary by sex. Our study also did not find a significant difference.

Studies have reported that 5-15% of children with CF develop nasal polyps, and the likelihood of developing nasal polyps increases with age. The etiology of nasal polyps involves many factors, and although rare, CF should be considered as a possible cause.[19] In our study, genetic analysis was performed on the cases with nasal polyps, but no mutations were detected.

The pulmonary and pancreatic morbidities of CF are well known, but rare complications, such as pseudobartter syndrome, may go unnoticed. Bartter syndrome is a hereditary tubulopathy that affects the

thick ascending limb of the loop of Henle, and is characterized by hypokalemia, hyponatremia, hypochloremia, and metabolic alkalosis. In CF, a similar metabolic disturbance is observed, and this condition is referred to as pseudobartter syndrome.[20] In one of the cases included in our study, pseudobartter syndrome was detected, and genetic analysis revealed compound heterozygous mutations at exon 4 (c.328G>C, p.Asp110His, rs113993958) and exon 11 (c.1521_1523delCTT, p.Phe508delPhe, rs113993960).

In a study by Steinraths et al.[21] on CF cases, the mean age of diagnosis was reported to be 3.6 years, and the average duration between symptom onset and diagnosis was 2.1 years. In our study, the median (IQR 25-75) age of diagnosis in the mutation-positive group was 6 (5.75-15.50) years, and the duration between symptom onset and diagnosis was 1 (1-3.50) year. No significant differences were found between the mutation-positive and mutation-negative groups in terms of age at onset and symptom duration. This is likely due to the fact that the majority of our cases had heterozygous mutations, which are associated with later symptom onset. It is also possible that as the age of the cases increases, earlier genetic testing is requested to address concerns about diagnostic delays, which is why the symptom duration in our study was relatively shorter.

Since CFTR gene mutations are inherited in an autosomal recessive manner, mutation-positive cases are expected to have a higher frequency of CF diagnosis in their family history. However, in our study, although mutation-positive cases were more likely to have a family history of CF, no significant difference was found between the two groups. This may be attributed to the small sample size in our study.

The number of hospitalizations is expected to be higher in cases with positive CFTR gene mutations compared to those with negative mutations. In our study, no significant difference was found between the two groups in terms of hospitalization frequency. It is believed that the majority of mutation-positive cases having heterozygous mutations likely contributed to this result.

In this study, the clinical and demographic characteristics of patients who presented to Duzce University Application and Research Hospital with a prediagnosis of CF and underwent CFTR gene mutation analysis were retrospectively analyzed.

In conclusion, among the cases included in the study, the majority of those with a positive genetic analysis were identified as carriers of CFTR gene mutations. CFTR gene analysis was most frequently requested for patients presenting with recurrent lower respiratory tract symptoms, followed by gastrointestinal symptoms and malnutrition. It was observed that CFTR gene mutations were significantly more prevalent in cases with malnutrition. These findings underscore the critical importance of thorough clinical evaluation of symptoms and the indispensable role of genetic analyses in the diagnosis of cystic fibrosis. It should also be considered that patients carrying heterozygous CFTR mutations may exhibit certain clinical symptoms, necessitating a careful evaluation during the diagnostic process. This study has some limitations. Firstly, since the study was designed retrospectively, patient data were reviewed from the past, and some clinical information may be incomplete or inadequate. Secondly, since the study was conducted at a single center, the findings may not fully reflect the broader population. Additionally, the lack of statistically significant findings in some parts may be due to the small sample size. Finally, only specific mutations were analyzed in the CFTR gene mutation analysis, and rare or new mutations may have been excluded from the evaluation. Therefore, further studies with larger patient groups and multicenter designs are needed.

***Ethics Committee Approval:*** This research involving human subjects complied with all relevant national regulations and institutional policies and was conducted in accordance with the tenets of the Helsinki Declaration. The study was approved by the Duzce University Faculty of Medicine Ethics Committee (Date: 10.06.2024, decision no: 2024/126). Before inclusion, parents of all study participants were informed about the study's purpose, methodology, and implementation, and written consent was obtained.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

***Author Contributions:*** Concept – FK, RE; Supervision – FK, RE; Materials – FK, RE; Data Collection and/or Processing – FK, RE; Analysis and/or Interpretation – RE; Writing –FK.

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# The Relationship Between Health and Media Literacy Among Pregnant Women and Its Predictors

# Gebelerde Sağlık Okuryazarlığı ile Medya Okuryazarlığı Arasındaki İlişki ve Yordayıcıları

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**ABSTRACT**

**Objective:** The study analyzed the correlation and predictive factors between health literacy and media literacy in pregnant women.

**Materials and Methods**: The cross-sectional and correlational study was conducted with 369 pregnant women. Data were collected by a personal information form, the Health Literacy Scale, and the Media Literacy Level Determination Scale. The data were evaluated by number, percentage, mean, Pearson correlation analysis, and multiple linear regression analysis.

**Results:** The mean score of the health literacy scale of the pregnants is 112.28±16.79, the average score of the media literacy scale is 72.21±12.93. It was determined that there was a positive relationship between the mean health literacy and media literacy scale scores of pregnant women ($p<0.001$). Factors predicting the health literacy of pregnant women were determined as age, education level, employment status, gestational week, planned pregnancy, receiving regular prenatal care, following health channels, and frequency of internet use ($p<0.001$). These variables accounted for 75.7% of health literacy. The factors predicting the media literacy of the participants were determined as education level, income level, planned pregnancy, following health channels, and frequency of internet use ($p<0.05$). These variables accounted for 77.1% of media literacy.

**Conclusions:** Pregnant women are sufficiently health literate and good level of media literate. It has been found that health literacy and media literacy are correlated in pregnant women. The main factors predicting health and media literacy were found to be education level, planned pregnancy, following health channels, and frequency of internet use.

**Keywords:** Health literacy, media literacy, nursing, pregnant

**ÖZ**

**Amaç:** Araştırma gebelerde sağlık okuryazarlığı ve medya okuryazarlığı arasındaki ilişkiyi ve yordayan faktörleri incelemek için yapılmıştır.

**Materyal ve Metot:** Kesitsel ve ilişki arayıcı tipteki çalışma 369 gebe ile gerçekleştirilmiştir. Verilerin toplanmasında tanıtıcı bilgi formu, Sağlık Okuryazarlığı Ölçeği, Medya Okuryazarlık Düzey Belirleme Ölçeği kullanılmıştır. Veriler sayı, yüzde, ortalama, Pearson korelasyon analizi ve çoklu doğrusal regresyon analizi ile değerlendirilmiştir.

**Bulgular:** Gebelerin sağlık okuryazarlığı ölçeği puan ortalaması 112,28±16,79, medya okuryazarlığı ölçeği puan ortalaması 72,21±12,93'tür. Gebelerin sağlık okuryazarlığı ve medya okuryazarlığı ölçek puan ortalamaları arasında pozitif yönde bir ilişki olduğu tespit edilmiştir ($p<0,001$). Gebelerin sağlık okuryazarlığını yordayan faktörler yaş, eğitim düzeyi, çalışma durumu, gebelik haftası, gebeliğin planlı olması, düzenli olarak doğum öncesi bakım alma, sağlık kanalı takip etme ve internet kullanma sıklığı olarak belirlenmiştir ($p<0,001$). Bu değişkenler sağlık okuryazarlığının %75,7'sini açıklamıştır. Katılımcıların medya okuryazarlığını yordayan faktörlerin eğitim düzeyi, gelir düzeyi, gebeliğin planlı olması, sağlık kanalı takip etme ve internet kullanma sıklığı olduğu saptanmıştır ($p<0,05$). Bu değişkenler medya okuryazarlığının %77,1'ini açıklamıştır.

**Sonuç:** Gebeler yeterli düzeyde sağlık okuryazarı ve iyi seviyede medya okuryazarıdır. Gebelerde sağlık okuryazarlığı ile medya okuryazarlığının ilişkili olduğu bulunmuştur. Sağlık ve medya okuryazarlığını yordayan temel faktörlerin; eğitim düzeyi, planlı gebeliğe sahip olma, sağlık kanalı takip etme ve internet kullanma sıklığı olduğu saptanmıştır.

**Anahtar Kelimeler:** Sağlık okuryazarlığı, medya okuryazarlığı, hemşirelik, gebe

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## INTRODUCTION

Health literacy is the mental and social competencies necessary for individuals to access, understand and evaluate health information.[1] A woman's competence in healthcare directly affects the health of all individuals in her family.[2] Health literacy assists women in being aware of the problems they may encounter, increasing their self-care, reducing the fear of childbirth, and having a safe and healthy pregnancy, one of the most important processes in their lives.[3]

Pregnancy is a period when women's need for information increases, and different sources such as social environment and the internet are used to access information besides health professionals.[4] In this process, the ability of pregnant women to critically approach the information they receive from media tools affects their health as well as their future babies. At this point, media literacy gains importance. Fundamentally, media literacy is the ability to analyse the information the media conveys.[5] During pregnancy, when the need for information increases, pregnant women are expected to be media literate in the sources to be used to access the accurate information and health literate in the accuracy of the obtained source.[6]

Media and health literacy are related, and being media literate can increase awareness about health. Being health literate enables the correct evaluation of the content presented through the media.[7,8] Although the factors affecting health and media literacy vary, knowledge of these factors provides guidance for health professionals in terms of the organisation of health education given to pregnant women.[8,9]

A review of the existing literature shows that studies on correlation between health and media literacy of pregnant women and their predictors are limited.[2,6,10] This study sought to answer two questions: to determine the relationship between health literacy and media literacy in pregnant women and to determine the variables that predict health literacy and media literacy.

## MATERIALS AND METHODS

***Ethics Committee Approval:*** Approval was received from the University Clinical Research Ethics Committee (Date: 12.04.2022, decision no: 2022/95), and written permission was obtained from the Provincial Health Directorate (Date: 27.05.2022, no: E-38224951). The study was conducted per the principles of the Declaration of Helsinki**.** Written informed consent of the participants, permission of the authors for the scales used were obtained.

***Study Design:*** The cross-sectional and correlational study was carried out between June and December 2022.

***Population and Sample:*** The population consisted of pregnant women who applied to the obstetrics and gynaecology outpatient clinics of two hospitals in a province of the Western Black Sea region of Türkiye. The tables published by the World Health Organisation were used to determine the sample size.[11] Adequate health literacy in pregnant women varies between 15% and 85%.[1] In this study, the level of adequate health literacy in pregnant women was accepted as 40%,[6] and the sample size required to estimate the actual value of this ratio with a sensitivity of 0.05 and 95% confidence was found to be 369. Women aged 18-45 years who were primiparous/ multiparous, literate, without any mental disability, communication problem, or hearing or visual impairment, and who accepted the study were included in the study.

***Data Collection Tools:*** Personal information form, the Health Literacy Scale (HLS), and the Media Literacy Level Determination Scale (MLLDS) were used to collect the data.

***Personal information form:*** The form consists of 14 questions evaluating the socio-demographic (age, education, etc.), obstetric (gestational week, number of pregnancies) and media use (internet use, television viewing, reading newspapers, etc.) characteristics of the participants.

***Health Literacy Scale* (*HLS):*** Toçi et al. in 2013 developed the scale to assess individuals' health literacy.[12] Turkish validity and reliability of the scale was performed by Aras and Bayık Temel.[13] The minimum score that can be obtained from the scale is 25, and the maximum score is 125. A high score indicates very good and adequate health literacy; a low score indicates problematic, inadequate, or poor health literacy. Cronbach's Alpha value was 0.95 in the original study[13] and 0.98 in this study.

***Media Literacy Level Determination Scale (MLLDS)***: The 17-item scale was developed by Karaman and Karataş in 2009.[14] Scale scores range from 17 to 85. The increase in the scores obtained from the scale indicates that individuals' media literacy is enhanced. Cronbach's Alpha value on the scale is 0.84,[14] and 0.98 was found in the study.

***Statistical Analysis:*** The SPSS Statistics 23 programme was used to evaluate the data. Frequency distribution (number, percentage) was used to evaluate categorical variables, and descriptive statistics were used to calculate numerical variables. Pearson correlation analysis was used to examine the relationship between the scales. Multiple linear regression analysis was used to investigate the factors affecting the health and media literacy. Since the skewness and kurtosis indices calculated by dividing the skewness and kurtosis coefficients by their standard errors were close to 0 within the limits of

±1.96, the data were considered normally distributed, and parametric tests were used. For statistical significance, $p<0.05$ was accepted.

## RESULTS

Descriptive characteristics of the pregnant women are shown in Table 1. The mean age of the participants was 27.97 ± 4.08 years; 35.1% had undergraduate or higher education; 55.9% were employed; and 72.4% had an income equivalent to expenses. The mean gestational week of the pregnant women was 27.58 ± 6.28 weeks, and more than half of them (57.6%) had their first pregnancy. Of the pregnant women, 78.0% had a computer that could be used, and 93.2% had internet access. While 77.2% of pregnant women did not read newspapers regularly, 41.4% reported not following health channels. Of the participants, 46.3% said they watched television between 11 and 20 hours per week, and 35.8% said they used the internet between 11 and 20 hours per week. The mean score of the health literacy scale of the pregnant women is 112.28±16.79, and the average score of the media literacy scale is 72.21±12.93 (Table 1).

**Table 1.** Descriptive characteristics of pregnant women (n=369).

| Characteristic | | Data |
|---|---|---|
| **Age**, Mean±Sd, n (%) | Range:19-41 | 27.97±4.08 |
| | 19-25 | 104 (28.2) |
| | 26-33 | 226 (61.2) |
| | 34-41 | 39 (10.6) |
| **Educational status**, n (%) | Elementary school | 54 (14.7) |
| | High school | 104 (28.2) |
| | Associate degree | 81 (22.0) |
| | Bachelor's and above | 130 (35.1) |
| **Working status**, n (%) | Working | 206 (55.9) |
| | Not working | 163 (44.1) |
| **Income level**, n (%) | Income < expenditure | 16 (4.3) |
| | Income = expenditure | 267 (72.4) |
| | Income > expenditure | 86 (23.3) |
| **Gestational week**, Mean±Sd, n (%) | Range:15-40 | 27.58±6.28 |
| | 2nd trimester (14-26 wk) | 159 (43.1) |
| | 3rd trimester (27-40 wk) | 210 (56.9) |
| **Number of pregnancies**, n (%) | 1 | 213 (57.6) |
| | 2 | 99 (26.8) |
| | 3 and ↑ | 57 (15.6) |
| **Planned pregnancy**, n (%) | Yes | 240 (65.0) |
| | No | 129 (35.0) |
| **Getting regular prenatal care**, n (%) | Yes | 338 (91.6) |
| | No | 31 (8.4) |
| **Having computer**, n (%) | Yes | 288 (78.0) |
| | No | 81 (22.0) |
| **Access to internet**, n (%) | Yes | 344 (93.2) |
| | No | 25 (6.8) |
| **Reading newspaper daily**, n (%) | Yes | 84 (22.8) |
| | No | 285 (77.2) |
| **Following health channels**, n (%) | Never | 153 (41.4) |
| | Rarely | 76 (20.6) |
| | Sometimes | 84 (22.8) |
| | Often/always | 56 (15.2) |
| **TV watching frequency (hours per week)**, n (%) | 1-10 | 163 (44.2) |
| | 11-20 | 171 (46.3) |
| | 21 and ↑ | 35 (9.5) |
| **Internet usage frequency (hours per week)**, n (%) | None | 21 (5.6) |
| | 1-10 | 94 (22.5) |
| | 11-20 | 132 (35.8) |
| | 21 and ↑ | 122 (33.1) |
| **Health Literacy Scale**, Mean±Sd | | 112.28±16.79 |
| **Media Literacy Level Determination Scale**, Mean±Sd | | 72.21±12.93 |

The relationship between health and media literacy scale scores of women is shown in Table 2. Accordingly, a strong positive correlation was found between the scale mean scores (Table 2).

Table 3 shows the predictors of health literacy in pregnant women. The effect of pregnant women's age, educational status, employment status, gestational week, planned pregnancy, regular health check-ups, following health channels, and frequency of internet use on health literacy was significant ($p<0.001$). These variables accounted for 75.7% of health literacy. Among the participants, the HLS score of those aged 26-33 years was 2.5 units higher than those aged 19-25 years, and the HLS score of those with a bachelor's degree and above was 19.4 units higher than those with a primary education. The HLS score of employed pregnant women was 3.1 units higher than that of housewives. Regarding obstetric characteristics, the HLS score was 2.7 units higher in the second trimester than in the third trimester, 9.2 units higher in those who received prenatal care than those who did not, and 2.9 units higher in those whose pregnancy was planned than those whose pregnancy was unplanned. The characteristics of media use affected the HLS score; the HLS score of those who frequently followed health channels was 5.7 units higher than those who never followed health channels, and the HLS score of pregnant women who used the internet for 21 hours or more per week was 16.5 units higher than those who never used the internet (Table 3).

**Table 2.** Health literacy and media literacy relationship between scale scores (n=369).

| Scale | | HLS |
|---|---|---|
| **MLLDS** | **r** | 0.865* |
| | **p** | 0.0001 |

r:Pearson correlation; *:p<0.01; HLS: Health Literacy Scale; MLLDS: Media Literacy Level Determination Scale.

**Table 3.** Predictors of health literacy in pregnant women (n=369).

| | Unstandardized coefficient | | Standardized coefficient | t | p | 95.0% CI | |
|---|---|---|---|---|---|---|---|
| | **B** | **SE** | **Beta** | | | **Lower limit** | **Upper limit** |
| **(Constant)** | 9.672 | 5.728 | | 16.004 | 0.0001 | 80.407 | 102.938 |
| **Age (1)** | 2.455 | 1.065 | 0.071 | 2.306 | 0.022 | 0.361 | 4.549 |
| **Age (2)** | -0.605 | 1.666 | -0.011 | -0.363 | 0.717 | -3.883 | 2.672 |
| **Educational status (1)** | 14.144 | 1.888 | 0.380 | 7.490 | 0.0001 | 10.430 | 17.858 |
| **Educational status (2)** | 19.015 | 2.134 | 0.469 | 8.912 | 0.0001 | 14.819 | 23.211 |
| **Educational status (3)** | 19.392 | 2.313 | 0.552 | 8.384 | 0.0001 | 14.843 | 23.941 |
| **Working** | 3.082 | 1.152 | 0.091 | 2.676 | 0.008 | 0.817 | 5.347 |
| **Gestational week** | -2.720 | 0.940 | -0.080 | -2.893 | 0.004 | -4.570 | -0.871 |
| **Planned pregnancy** | -2.941 | 1.207 | -0.084 | -2.437 | 0.015 | -5.315 | -0.567 |
| **Prenatal care** | -9.192 | 2.312 | -0.152 | -3.976 | 0.0001 | -13.740 | -4.645 |
| **Watching the health channel (1)** | 3.046 | 1.236 | 0.090 | 2.464 | 0.014 | 0.615 | 5.477 |
| **Watching the health channel (2)** | 5.658 | 1.769 | 0.121 | 3.199 | 0.002 | 2.180 | 9.137 |
| **Internet usage (1)** | 15.103 | 2.713 | 0.394 | 5.566 | 0.0001 | 9.767 | 20.439 |
| **Internet usage(2)** | 16.922 | 2.878 | 0.484 | 5.881 | 0.0001 | 11.263 | 22.582 |
| **Internet usage (3)** | 16.508 | 2.841 | 0.463 | 5.811 | 0.0001 | 10.921 | 22.095 |
| $F=78.808$, $p<0.001$, $R^2=0.757$ | | | | | | | |

CI: Confidence interval; SE: Standard error; B: Unstandardized coefficient; Beta= Standardized coefficient; F: ANOVA F-test; Age (Reference value =19-25, 1=26-33, 2=34-41); Educational status (Reference value = Elemantary scool 1=High scool 2= Associate degree, 3= Bachelor's and above); Working (Reference value =Not working, 1=Working); Gestational week (Reference value =2nd trimester, 1=3rd trimester); Planned pregnancy (Reference value =Yes, 1=No); Prenatal care (Reference value =Yes, 1=No); Fallowing health channels (Reference value = Never, 1= Rarely, 2= Often); Internet usage frequency (Reference value =None, 1=1-10 hours per week, 2= 11-20 hours per week, 3= More than 20 hours week).

The findings related to the predictors of media literacy in pregnant women are presented in Table 4. The effect of education level, income level, planned pregnancy, following health channels, and frequency of internet use on the media literacy scale score of pregnant women was significant ($p<0.001$). These variables were found to account for 77.1% of media literacy. Analysis of the regression coefficients showed that the MLLDS score of those with a bachelor's degree and above was 20.6 units higher than those with a primary education. The MLLDS score was found to be 6.1 units higher in those whose income was more than their expenses than in those whose income was less, and 4.0 units higher in those whose pregnancy was planned than in those who did not have a planned pregnancy. When the MLLDS score was evaluated according to the characteristics of media use of pregnant women, the MLLDS score of those who frequently followed health channels was 2.9 units higher in than those who never followed health channels, and the MLLDS score of those who used the internet for 21 hours or more per week was 11.6 units higher than those who never used the internet (Table 4).

**Table 4.** Predictors of media literacy in pregnant women ( n=369).

| | Unstandardized coefficient | | Standardized coefficient | t | p | 95.0% CI | |
|---|---|---|---|---|---|---|---|
| | B | SE | Beta | | | Lower limit | Upper limit |
| **(Constant)** | 46.709 | 2.476 | | 18.864 | 0.0001 | 41.840 | 51.579 |
| **Educational status (1)** | 10.074 | 1.341 | 0.351 | 7.511 | 0.0001 | 7.436 | 12.711 |
| **Educational status (2)** | 16.917 | 1.492 | 0.542 | 11.341 | 0.0001 | 13.983 | 19.850 |
| **Educational status (3)** | 20.570 | 1.654 | 0,761 | 12.433 | 0.0001 | 17.316 | 23.824 |
| **Income level (1)** | 4.582 | 1.828 | 0.159 | 2.507 | 0.013 | 0.988 | 8.176 |
| **Income level (2)** | 6.128 | 2.083 | 0.201 | 2.941 | 0.003 | 2.031 | 10.225 |
| **Planned pregnancy** | -3.972 | 0.886 | -0.147 | -4.485 | 0.0001 | -5.713 | -2.230 |
| **Watching the health channel (1)** | 1.865 | 0.909 | 0.072 | 2.051 | 0.041 | 0.077 | 3.653 |
| **Watching the health channel (2)** | 2.905 | 1.374 | 0.081 | 2.114 | 0.035 | 0.202 | 5.607 |
| **Internet usage (1)** | 10.995 | 1.808 | 0.372 | 6.082 | 0.0001 | 7.440 | 14.550 |
| **Internet usage (2)** | 12.286 | 1.938 | 0.456 | 6.339 | 0.0001 | 8.475 | 16.098 |
| **Internet usage (3)** | 11.626 | 1.907 | 0.424 | 6.095 | 0.0001 | 7.875 | 15.377 |
| $F=109.149$, $p<0.001$, $R^2=0.771$ | | | | | | | |

CI: confidence interval; SE: Standard error; B: Unstandardized coefficient; Beta: Standardized coefficient; F: ANOVA F-test; Edicational status(Reference value = Elemantary scool 1=High scool 2= Associate degree, 3= Bachelor's and above); Income level (Reference value = Income<Expenditure, 1=Income = Expenditure 2= Income > Expenditure); Planned pregnancy (Reference value =Yes, 1=No); Watching the health channel (Reference value = Never, 1= Rarely, 2= Often); Internet usage frequancy (Reference value =None, 1=1-10 hours per week, 2= 11-20 hours per week, 3= More than 20 hours week).

## DISCUSSION AND CONCLUSION

Today, there is an increasing amount of news about health in the media. The media conveys health-related information to society, and a broad audience follows this information. The way to raise awareness that the information in the media on health-related issues does not always reflect the truth is to become conscious of health and media literacy.[8] At this point, it can be said that it is necessary to have social and cognitive skills in both health and media. The current study found a strong positive relationship between the health and media literacy of pregnant women. Similar results were found in studies conducted with pregnant women[6] and different sample groups.[8,15]

Individual factors are known to affect health and media literacy.[6,8] In this study, the HLS score was found to be 2.5 units higher in pregnant women aged 26-33 years compared to those aged 19-25 years. While the findings of the study were similar to Korkmaz's study,[16] Tavananezhad et al. found that health literacy level decreased as the average age of pregnant women increased,[17] and Khorasani et al. established that there was no correlation between health literacy level and age.[18] Although the findings regarding the effect of age on health literacy level are different, it can be concluded that health responsibility and health awareness increase in individuals with advancing age and positively impact health literacy.

Education level is an important factor that enables individuals to access health information and understand, interpret, and critically evaluate the information they encounter in the media.[19,20] This study established that the health and media literacy levels of those with bachelor's and higher education degrees were higher than those with primary education.

In previous studies, it was also observed that health literacy,[2,18,21] and media literacy increased as the level of education increased.[22,23] The findings of this study are consistent with the literature.

In this study, health literacy and media literacy were found to be higher in working pregnant women than in non-working women. Studies show that as the income level increases, access to health resources

and mass media improves, enhancing health and media literacy.[7,24-26]

In addition to individual characteristics, obstetric characteristics may also affect health and media literacy. In this study, the HLS score of pregnant women in the second trimester was 2.7 units higher than that in the third trimester. During pregnancy, women are exposed to many physical and psychosocial changes. Women with increased awareness of pregnancy may seek more health information during this period, which may have positively affected health literacy. In this study, the HLS score was found to be higher in pregnant women who received regular antenatal care compared to those who did not receive regular care. This was an expected result. In the study conducted by Rostamzadeh et al., it was found that the health literacy level of pregnant women who went to antenatal monitoring five or more times during pregnancy was higher than those who went less.[27] The health and media literacy scale score was found to be higher in women with planned pregnancies than in women with unplanned pregnancies. This study finding is similar to the study of Öztürk et al.[28] planned pregnancies may have encouraged pregnant women to obtain more information about maternal and foetal health and to use mass media.

Media use affects health and media literacy levels. The health and media literacy levels of those who follow the media on health-related issues were found to be higher than those who do not follow the media, and those who use the internet were found to have higher health and media literacy levels than those who do not use the internet in this study. The study findings are similar to studies showing that following health channels and social media predicts health literacy and affects media literacy in adults.[8,29] It is observed that pregnant women prefer the internet and television to obtain information about health-related issues.[30] Health channels are media sources that provide information on health, medical practices, healthy lifestyles, and disease prevention. It may be concluded that following these channels provides more conscious behaviour on issues such as access to information, evaluation of information, critical thinking, health-related decision-making, healthy lifestyles, and disease prevention.

In conclusion, it was observed that health literacy and media literacy were positively correlated in pregnant women. The main factors predicting health literacy and media literacy were found to be age, education level, employment status, income level, gestational week, planned pregnancy, receiving regular prenatal care, following health channels, and frequency of internet use. Nurses and other health professionals should be aware of the factors affecting media and health literacy. They should provide training on how to access accurate information, how to use this information and how to evaluate it according to the needs of pregnant women in prenatal follow-up. This study was limited to second- and third-trimester pregnant women admitted to two hospitals in a city centre.

***Ethics Committee Approval:*** Our study was approved by the Bolu Izzet Baysal University Clinical Research Ethics Committee (date:12.04.2022, no: 2022/95). The research was conducted in accordance with the principles of the Declaration of Helsinki.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

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# Determination of Pressure Injury Risk Factors in COVID-19 Patients Hospitalized in the Intensive Care Unit

# Yoğun Bakım Ünitesinde Yatan COVID-19 Hastalarının Basınç Yaralanması Risk Faktörlerinin Belirlenmesi

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**ABSTRACT**

**Objective:** This study aimed to determine the risk factors for pressure injury in COVID-19 in intensive care unit.

**Materials and Methods:** A retrospective study was conducted using COVID-19 Intensive Care Unit archive data from April 2020 to July 2022. The study included patients aged 18 and over, with no pre-existing pressure injury, at high risk (Braden Score not between 6-12), and hospitalized in the ICU for at least 24 hours.

**Results:** A pressure injury developed in 25.2% of the patients. Among those who developed a pressure injury, 79.4% were classified as Stage I, characterized by redness, and 36.8% of the injuries occurred in the sacral region. A significant difference was observed in relation to age, length of stay, Braden score, albumin levels, hemoglobin levels, oxygen levels, and medications used between patients with pressure injuries and those without ($p < 0.05$). The Braden scale was used for risk assessment. Factors independently associated with pressure injury were hemoglobin (1.398 [1.122-1.742]), hemoglobin (0.067 [0.007-0.643]), high-dose steroids (0.026 [0.002-0.317]) and oxygen (0.108 [0.012-0.964]).

**Conclusions:** It was found that stage I developed in patients, and the most pressure injuries were in the sacrum. The risk of pressure injury was associated with the Braden score, hemoglobin, high-dose steroids, and oxygen. Nurses should evaluate the risk of developing pressure injury in the intensive care unit. They should minimize the conditions that will threaten the safety of patients at risk.

**Keywords:** COVID-19, intensive care unit, pressure injury, risk factors

**ÖZ**

**Amaç:** Bu çalışmanın amacı yoğun bakım ünitesinde COVID-19'a bağlı bası yarası risk faktörlerini belirlemektir.

**Materyal ve Metot:** Nisan 2020 ile Temmuz 2022 tarihleri arasında COVID-19 yoğun bakım arşiv verileri kullanılarak retrospektif bir çalışma gerçekleştirildi. Çalışmaya 18 yaş ve üzeri, önceden mevcut basınç yarası olmayan, yüksek risk altında olan (Braden Skoru 6-12 puan arasında olmayan) ve en az 24 saat yoğun bakımda yatan hastalar dâhil edildi.

**Bulgular:** Bir basınç yarası, hastaların %25.2'sinde gelişti. Basınç yarası gelişenlerin %79.4'ü, kızarıklıkla karakterize edilen Evre I olarak sınıflandırıldı ve yaraların %36.8'i sakral bölgede meydana geldi. Basınç yarası olan ve olmayan hastalar arasında yaş, yatış süresi, Braden skoru, albümin seviyesi, hemoglobin düzeyi, oksijen seviyesi ve kullanılan ilaçlarla ilgili anlamlı bir fark gözlendi ($p<0.05$). Risk değerlendirmesi için Braden ölçeği kullanıldı. Basınç yaralanmasıyla bağımsız olarak ilişkili faktörler (1,398 [1,122-1,742]), hemoglobin (0,067 [0,007-0,643]), yüksek doz steroid (0,026 [0,002-0,317]) ve oksijen (0,108 [0,012 -0,964]) bulundu.

**Sonuç:** Hastalarda evre I geliştiği ve en fazla basınç yaralanmasının sakrumda olduğu bulundu. Basınç yaralanması riski Braden skoru, hemoglobin, yüksek doz steroid ve oksijen ile ilişkiliydi. Hemşireler yoğun bakım ünitesinde basınç yaralanması gelişme riskini değerlendirmelidir. Risk altındaki hastaların güvenliğini tehdit edecek koşulları en aza indirmelidirler.

**Anahtar Kelimeler:** Basınç yaralanması, COVID-19, risk faktörleri, yoğun bakım ünitesi

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## INTRODUCTION

Coronavirus 2019 (COVID-19) was characterized by severe respiratory infection (severe pneumonia), acute respiratory distress syndrome (ARDS), sepsis, septic shock, myocarditis, arrhythmia and cardiogenic shock, and multiple organ failure.[1] Disease management was also very challenging due to decreased oxygenation and the risk of infection in COVID-19.[2] The inability to frequently change patients' position due to the severity of the disease, their medical characteristics, practices related to treatment interventions, and health personnel-related reasons impaired oxygenation and tissue perfusion.[2,3] Therefore, prolonged disease management also caused pressure injuries (PIs) in the patient.[2] Healthcare professionals may have overlooked PI as they often focused on the hemodynamic responses of COVID-19 patients who had severe respiratory problems in the ICU (Intensive Care Unit).[4,5]

In a study conducted in New York, it was found that the prevalence of PIs in COVID-19 patients who needed ICU was three times higher than in patients without a COVID-19 diagnosis who needed ICU.[6] The pathophysiology of COVID-19 and the risk of developing PI were evaluated at the European Pressure Ulcer Advisory Panel Virtual Meeting held in September 2020. In this evaluation, inflammation and medical device-related tissue damage were stated as the causes of PIs.[5,6] Patient-related medical conditions (low oxygenation due to lung involvement, anemia, malnutrition, hypovolemia, etc.) needed to be assessed in patients who had COVID-19 and were admitted to the ICU. In addition, the use of devices related to diagnosis, treatment, and care and diagnostic conditions (non-invasive mechanical ventilation (NIMV), immobilization, oxygen treatment methods, prone position, etc.) needed to be assessed, too.[6,7]

Prone positioning improves mortality in ARDS by optimizing oxygen recruitment, reducing lung strain, and improving oxygenation. While the benefits of prone positioning far outweighed the risks, placing patients with COVID-19 in a prone position was likely to put them at risk of other complications, including PIs of the soft tissues and skin.[5,8] However, prone positioning was widely used to reduce ventilator-induced lung injury and improve oxygenation in patients with severe COVID-19.[5,9-11]

Practices performed depending on the patient's medical condition and diagnosis, therapeutic interventions[1,5] needed to be considered as risk factors that accelerated the development of PI and delayed wound healing in some cases,[6,9-11] and risks needed to be minimized using preventable holistic nursing interventions (e.g., supporting the PIs region, frequent positioning, skin monitoring, etc.).[4,11,12] In this context, this study was carried out to determine the risk factors for PIs in ICU patients diagnosed with COVID-19.

## MATERIALS AND METHODS

**Ethics Committee Approval:** Written approval to conduct the study was obtained from the Non-Interventional Clinical Research Ethics Committee of Cukurova University Faculty of Medicine (Date: 13.05.2022, decision no: 52). The requirement for individual patient consent was waived by the Clinical Research Ethics Committee due to the retrospective and anonymous nature of the study. The study was conducted in accordance with the tenets of the Declaration of Helsinki.

**Study Design and Sample:** This was a retrospective observational study. This study was conducted with 270 COVID-19 patients in the ICU between April 2020 and July 2022. The study was carried out retrospectively by using patients' records. The records of 2,110 patients diagnosed with COVID-19 from April 2020 to July 2022 were analyzed. Only 348 of the patients were admitted to the ICU, and therefore, the remaining 1762 records were excluded. The study setting was the 9-bed COVID-19 ICU of a university hospital. Patient files that met the inclusion criteria were recorded. Patients aged 18 and over, patients who did not have an existing PIs, who were patients at high risk for PIs (Braden Score 6-12 points) on admitted to the ICU, and who were hospitalized in the intensive care unit for at least 24 hours were included in the study.

**Data Collection Tools:** Patient characteristics were required to compile data from electronic records, so we created a Patient Descriptive Information Form. We also used the Braden Pressure Injury Risk Assessment Scale.[13,14]

Patient Descriptive Information Form (PDIF): This form consisted of 17 questions about patients' descriptive and medical characteristics, including age, length of stay in the ICU, gender, chronic disease, body mass index (BMI), skin status, nutrition status, serum albumin level, oxygen level, hemoglobin level, smoking status, vasopressor medicines treatment and high-dose steroids (at least 40 mg of equivalent prednisone per day), the duration of sedation, the duration of the prone position, and systemic infection.

Braden Pressure Injury Risk Assessment Scale (BPIRAS): The scale was developed in 1989,[13] and its validity and reliability study in our country was performed in 1997.[14] The scale consists of 6 subscales: sensory perception, activity, mobility, skin moisture, nutrition, and friction and shear. The six subscales reflect critical determinants of pressure and factors that influence the pressure tolerance of

the skin and supporting structures. Each item is scored between 1 and 3 or 4, and the total scale score ranges from 6 to 23. The lower the score is, the higher the patient's risk of PIs is. A lower Braden score indicates higher levels of risk for PI development. Scores from 6 to 12 indicate a very high risk.

**Data Collection:** We obtained the data from patients' records between April 2020 and July 2022. The data were reviewed by the researcher, and it took approximately 20-25 minutes to review each patient file.

**Data Analysis:** The SPSS (IBM-Statistical Package for Social Sciences for Windows, Version 24.0) was applied to analyze the data of the study. Descriptive analysis included frequency, percentage, mean, standard deviation, minimum, and maximum values. The Kolmogorov-Smirnov test was used to determine whether the data were normally distributed. Parametric tests were applied as the data were normally distributed. Categorical variables were expressed as percentages and compared using the chi-square or Fisher exact test. After applying multivariate logistic regression (LR), the variables associated with the risk of developing PI were analyzed. According to our findings from univariate analysis, we included variables that were significant at the $p<0.2$ threshold into the forward model and performed a stepwise-decreasing analysis that removed variables with a $p>0.05$ threshold from the model. The link between estimators was assessed by examining the Variance Inflation Factor. $p<0.05$ was considered significant in all tests.

## RESULTS

Table 1 compares PI development based on patients' descriptive and clinical characteristics. The average age of patients was 64.12±14.55 years, with 60.9% being male, and the average ICU stay was 12.28±7.07 days. No significant differences were found in gender, BMI, chronic diseases, or smoking status between patients with and without PI. However, significant differences were observed in albumin levels, hemoglobin levels, oxygen treatment, age, ICU stay length, and Braden total scores ($p<0.05$).

**Table 1.** Comparison of PI development according to the descriptive and clinical characteristics of the patients

| **Descriptive and clinical characteristics** | **PI Mean±SD (n=68)** | **Non-PI Mean±SD (n=202)** | **Test/p** |
|---|---|---|---|
| **Age (years)** | 64.12±14.55 | 59.11±16.15 | t=2.472/ **p=0.019** |
| **Length of ICU stay (days)** | 12.28±7,07 | 8.02±4.94 | t=4.484/ **p=0.000** |
| **Scale for the evaluation of the risk of PI (BRADEN)** | 8.19±2.53 | 11.47±4.04 | t=-7.831/ **p=0.000** |
| **Albumin** | 2,21±1,12 | 3,20±2,63 | t=-4.398/ **p=0.000** |
| **Length of MV (days)** | 9.84±5,17 | 6.05±3.24 | t=-4.926/ **p=0.000** |
| **Hemoglobin** | 9.34±3.42 | 11.94±6.14 | t=-6.430/ **p=0.000** |
| **Length of steroids (days)** | 9.48±2.56 | 10.86±3.31 | t=-5.102/ **p=0.000** |
| **Length of vasopressors (days)** | 4,88±2,71 | 3,00±0,00 | t=-.451/ p=0.596 |
| **Sedation duration (hours)** | 3,79±2,10 | 3,96±2,98 | t=-.369/ p=0.713 |
| **Prone position duration (n=40)/hours** | 9,08±3,31 | 8,79±3,33 | t=.564/ p=0.517 |
| | **n(%)** | **n(%)** | |
| **Gender** | | | |
| Male | 38 (55.9) | 123 (60.9) | $x^2$=0.530/ |
| Female | 30 (44.1) | 79 (39.1) | p=0.467 |
| **BMI** | | | |
| Less than 18.5 kg/m2: Underweight | 13 (19.1) | 7 (20.8) | |
| 18.5-24.9 kg/m2: Normal | 0 (0.0) | 6 (3.0) | $x^2$=2.232/ |
| 25-30 kg/m2: Overweight | 26 (38.2) | 73 (36.1) | p=0.526 |
| ≥30 kg/m2: Obese | 29 (42.6) | 81 (40.1) | |
| **Chronic Disease*** | | | |
| Yes | 62 (91.2) | 159 (78.7) | $x^2$=0.241 |
| No | 6 (8.8) | 43 (21.3) | p=0.621 |
| **Smoking** | | | |
| Yes | 28 (41.2) | 91 (45.0) | $x^2$=0.310/ |
| No | 40 (58.8) | 111 (55.0) | p=0.578 |
| **Oxygen Treatment** | | | |
| MV [a] | 57 (83.3) | 92 (45.5) | |
| NIMV | 8 (11.8) | 23 (11.4) | $x^2$=36.578/ |
| Mask | 2 (2.9) | 35 (17.3) | **p=0.000** |
| Nasal | 1 (1.5) | 24 (11.9) | |
| HFT[a**] | 0 (0.0) | 28 (13.9) | |

*: DM, Heart Diseases; HT: Hypertension; Respiratory diseases- COPD, ARDS, PNEUMONIA; **: HFT, high flow therapy; SD: Standard Deviation; t: Independent groups t-test, test; a: Groups causing significance according to Bonferonni test; High-dose steroids: >40 mg of equivalent prednisolone per day.

Multivariate LR analysis is shown in Table 2. According to the findings obtained from the univariate analysis, we included age, length of ICU stay (days), albumin, oxygen therapy, hemoglobin, Braden Scale score, and high-dose steroid use in the advanced model, and performed a stepwise backward elimination analysis that excluded variables with a p-value > .05. The factors independently associated with oxygen levels (OR:0.108 [95% Cl:0.012,p=0.964]), PI in the scale for the evaluation of the risk of PI (Braden) (OR:1.398 [95% Cl:1.122- p=1.742]), hemoglobin levels (OR:0.067 [95% Cl:0.007, p=0.643]) and high-dose steroids (OR:0.026 [95% Cl:0.002, p=0.317]). Collinearity between these four variables was low, with the variable inflation factor ranging between 1.0 and 1.2. BMI, chronic disease, smoking, low albumin level, nutrition and skin condition were not associated with PIs.

PIs were identified in 25.2% of the patients. Among those affected, the majority (79.4%) had stage I injuries, followed by 17.6% with stage II and 2.9% with stage III injuries. The anatomical distribution of PIs, detailed in Table 3, shows that the most frequently affected sites were the sacral region (36.8%) and the gluteal region (35.3%).

**Table 2.** Multivariate analysis of the factors associated with pi among COVID-19 patients hospitalized in the ICU.

| Variable | Odds ratio | 95% Confidence interval | | p-value |
|---|---|---|---|---|
| | | Lower | Upper | |
| **Oxygen levels*** | 0.108 | 0.012 | 0.964 | **0.046** |
| **Hemoglobin levels** | 0.067 | 0.007 | 0.643 | **0.019** |
| **Scale for the evaluation of the risk of PI (BRADEN)** | 1.398 | 1.122 | 1.742 | **0.003** |
| **High-dose steroids** | 0.026 | 0.002 | 0.317 | **0.004** |

*oxygen-treatment: MV, NIMV, Mask, Nasal, HFT.

**Table 3.** PIs characteristics (n=270).

| PI characteristic | n (%) |
|---|---|
| Total Number of Patients | **270 (100)** |
| Total PI | **68 (25.2)** |
| **Stage of PIs*** | **68 (100)** |
| Stage I: redness | 54 (79.4) |
| Stage II: partial-thickness skin loss | 12 (17.6) |
| Stage III: full-thickness skin loss | 2 (2.9) |
| **Location of PIs*** | **68 (100)** |
| Sacrum | 25 (36.8) |
| Gluteal | 24(35.3) |
| Face | 10 (14.7) |
| Heel | 5 (7.4) |
| Scapula | 4 (5.9) |

*Regardless of the total number of patients, the location of PI and Stage of PI were considered as n=68, %=100.

## DISCUSSION AND CONCLUSION

PIs were likely to be overlooked since health professionals usually focused on the hemodynamic responses of patients with COVID-19 in the ICU who had severe respiratory problems.[4,5] There were various risk factors for PIs due to decreased physical activity in the ICU,[15] and necessary precautions had to be taken to prevent PIs development in case of risks.[16]

The mean age of patients who had developed PIs was determined as 64.12±14.55 in this study and 67.5±17 in the study by Kıraner et al.[12] With aging, patients are prone to PIs development due to changes, such as delayed infiltration of macrophages and lymphocytes, decreased secretion of growth factors,[16] and decreased partial O2 pressure.[17] In elderly patients with severe respiratory failure, weakening of the immune system and slowing of respiratory functions may increase PIs by impairing tissue perfusion.

Albumin levels are as important as oxygenation in ensuring tissue perfusion.[18,19] In this study, 91% of patients with PIs were found to have low levels of albumin. Some studies conducted with patients in the ICU have shown that low albumin levels may cause PIs development.[18-21] In the transition from the early to late phase of COVID-19, the breakdown of the extracellular matrix caused fluid to accumulate in the lungs, impairing the oxygenation capacity over time,[21] and preventing the passage of nutrients

and oxygen to damaged tissues.[20,21] The decrease in the albumin level caused edema, which led to PIs development by impairing tissue perfusion due to decreased oxygen transmission.

According to our results, we found that LR yielded the best model to predict that oxygen, hemoglobin, the Braden Risk Assessment Scale, and high-dose steroid treatment played a role in PIs. Our study yielded results similar to those of studies in the literature,[21-25] and we determined that a statistical approach (LR- oxygen, hemoglobin and high-dose steroid treatment) similar to that of the Braden risk assessment scale existed.

Patients with COVID-19 were often applied mechanical ventilation (MV) or non-invasive mechanical ventilation (NIMV) due to the treatment of acute respiratory failure and acute pulmonary edema, and maintenance of oxygenation.[24-26] In our study, MV was applied to 83% of the patients to maintain oxygenation. Since patients with COVID-19 experienced an atypical form of ARDS,[27] according to its prognosis, it was likely to lead to hypoxia and ischemia unless the oxygen need for peripheral tissues in the human body was met.[26] It is known that prolonged MV of about >96 hours is a known risk factor for PIs in the general ICU population; however, the decrease in oxygenation required for the prevention of tissue damage would inevitably pave the way for PIs development.

In our study, PIs had developed in 97.1% of the patients with low hemoglobin levels, and we determined that hemoglobin levels were a risk factor. While Akan and Sayın[22] determined that hemoglobin levels did not affect the prevention of PIs, Kıraner et al.[12] found that low hemoglobin and albumin levels increased the risk of PIs. In addition, there are different studies in the literature showing that low hemoglobin levels increase PIs development.[12,20] Low hemoglobin and decreased oxygen transport may be risk factors for the development of injury by causing hypoxia and impaired tissue perfusion.

One of the most important risk factors for the development of PIs are the use of high-dose steroids and vasopressors.[20,24,28] We found that high-dose steroids were associated with PIs (OR:0.026 [%95 Cl:0.002,p=0.317]). Labeau et al. defined the use of corticosteroids and vasopressors as risk factors for ICU-related PIs.[29] High-dose steroids and vasopressors are thought to cause PIs development because they impair tissue perfusion in patients at risk for tissue ischemia.

In this study, it was found that approximately 25.2% of the patients with COVID-19 hospitalized in the ICU had PIs and that this was associated with various risk factors (Table 1 and Table 2). This rate was found as 56.8% by Kıraner et al[12] and 57.5% by Şengül et al.[4] ın our study, approximately 25% of the patients had developed stage I (redness) and stage II (partial-thickness skin loss) injuries and the most common injury site was the sacrum (Table 3). Similarly, some studies conducted with COVID-19 patients in the literature indicated that approximately half of the patients had developed deep tissue injury and stage II injuries and that the most common injury site was the sacrum.[4,12,28] As a result, the peak interface pressure at the sacrum increased, and it resulted in an increased risk of sacral PIs. Also, since the majority of PIs were on the sacrum, it seems that the most critical time interval for PIs risk was when the patient was not placed in a prone position. Some studies conducted with COVID-19 patients indicated that PIs were usually tool-induced or were due to the prone position, and also occurred in the facial area.[4,5,7,11,12,15,29] However, in this study, we found that[20-22,24,30] they were more prevalent in the sacrum and gluteal regions. Healthcare professionals were likely to neglect PIs as they often focused on the hemodynamic responses of COVID-19 patients.[4,7] In addition, we think that healthcare workers were reluctant to provide care for patients due to the delay in positioning because of staff shortage, the necessity of wearing PPE, and the high rate of patient contamination. These findings suggest that the sacral and gluteal regions are particularly vulnerable to pressure injuries, likely due to prolonged immobility and sustained pressure in these areas during critical care. This highlights the need for targeted preventive measures focused on these high-risk anatomical sites.

In our study, patients who developed PIs were placed in the prone position for a mean of 9.08±3.31 hours, and no significant difference was found for PIs development (Table 1). As stated in studies conducted with patients with severe ARDS and COVID -19 in the literature, prolonged prone position caused PIs.[4,6,7,29,30] Patients with COVID-19 were placed in a prone position for long periods between 12 and 24 hours, depending on their medical condition, to improve oxygenation.[4,29,30] The reason for the development of PIs in this position may have been due to the medical characteristics of the patient or the prevention of frequent position changes due to having to stay in this position for a long time.

In our study, 14.7% of the patients developed PIs in the facial region, and this rate was approximately 30% in studies in the literature.[4,12,16] In the literature, medical device-related PIs development in COVID-19 patients was reported to be mostly due to respiratory devices such as NIMV masks and tracheal tubes.[1,4,12,16] In studies conducted in the ICU, medical device-related PIs development was reported to range between 30% and 79.4%.[4,12,30] The pressure created by the medical device and the inadequate oxygenation increased the risk of PIs in patients with

COVID-19.

In conclusion, the results of this study have limitations of record studies (such as the reliability of records) as they are based on data from records on risk assessment in patients with PIs cared for during the COVID-19 pandemic in a single center. The study found that 25.2% of patients developed PIs, of which 79.4% were stage I (redness). The most common sites were the sacrum (36.8%) and gluteal region (35.3%). Risk factors for PIs included oxygen level, Braden score, hemoglobin levels and high-dose steroids. Stage I injuries were more common in the sacrum and gluteal regions. PIs were often overlooked as healthcare professionals focused on severe respiratory problems in ICU patients with COVID-19. Risk factors such as prolonged ICU stay, low hemoglobin, low albumin and corticosteroid use were consistent with findings from other studies. Nurses should regularly assess the risk of PIs and apply evidence-based interventions to prevent complications and enhance patients' quality of life.

***Ethics Committee Approval:*** Written approval to conduct the study was obtained from the Non-Interventional Clinical Research Ethics Committee of Cukurova University Faculty of Medicine (Date: 13.05.2022, decision no: 52). The requirement for individual patient consent was waived by the Clinical Research Ethics Committee due to the retrospective and anonymous nature of the study. The study was conducted in accordance with the tenets of the Declaration of Helsinki.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

***Author Contributions:*** Concept – IT, FÜ; Supervision – IT, FÜ, SE; Materials – IT, FÜ, SE; Data Collection and/or Processing – IT, FÜ; Analysis and/or Interpretation – IT, FÜ, SE; Writing – IT, FÜ, SE.

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# Evaluation of Cases Diagnosed with Cervical Myelopathy or Syringomyelia Referred with a Preliminary Diagnosis of Amyotrophic Lateral Sclerosis

# Amiyotrofik Lateral Skleroz Ön Tanısıyla Sevk Edilen Servikal Miyelopati veya Siringomiyeli Tanısı Almış Olguların Değerlendirilmesi

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**ABSTRACT**

**Objective:** Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease involving both upper and lower motor neurons. Upper motor neuron signs include spasticity and hyperreflexia, while lower motor neuron signs include weakness, muscle atrophy, and fasciculations. Because of these signs, ALS can be confused with cervical spondylotic myelopathy (CSM), syringomyelia, and similar diseases. This study aimed to evaluate the clinical and demographic characteristics of patients diagnosed with CSM or syringomyelia after initially being referred with suspected ALS.

**Materials and Methods:** Ten patients referred to our neurology clinic between January 2018 and June 2020, with a preliminary diagnosis of ALS, were evaluated. Those patients later diagnosed with CSM or syringomyelia after neurological examination, including electromyography (EMG) and magnetic resonance imaging (MRI), were included in the study.

**Results:** Ten patients (mean age 65.6 years) were analysed. Thenar and hypothenar atrophy was observed in 8 patients (80%). EMG revealed fasciculations and subacute denervation in cervical myotomes in all patients; 1patietnt had lumbar involvement. EMG of rectus abdominis and genioglossus muscles was normal. Thenar and hypothenar atrophy, fasciculation, and denervation in cervical and lumbar myotomes on EMG are similar to ALS signs. A normal rectus abdominis and genioglossus muscle EMG excludes the diagnosis of ALS.

**Conclusions:** CSM and syringomyelia should be considered in the differential diagnosis of ALS. A detailed history, neurological examination, EMG, and MRI are essential for diagnostic accuracy.

**Keywords:** Amyotrophic lateral sclerosis, cervical spondylotic myelopathy, syringomyelia

**ÖZ**

**Amaç:** Amiyotrofik lateral skleroz (ALS), hem üst hem de alt motor nöronların dejenerasyonu ile karakterize, ilerleyici bir nörodejeneratif hastalıktır. Üst motor nöron bulguları arasında spastisite ve hiperrefleksi; alt motor nöron bulguları arasında ise kas güçsüzlüğü, atrofi ve fasikülasyonlar yer alır. Bu bulgular nedeniyle ALS, servikal spondilotik miyelopati (SSM), siringomiyeli ve benzeri hastalıklarla karıştırılabilir Bu çalışmada, ALS şüphesiyle sevk edilen ve CSM veya siringomiyeli tanısı alan hastaların klinik ve demografik özelliklerinin değerlendirilmesi amaçlanmıştır.

**Materyal ve Metot:** Ocak 2018 – Haziran 2020 tarihleri arasında nöroloji kliniğimize ALS ön tanısıyla sevk edilen 10 hasta değerlendirildi. Nörolojik muayene, elektromiyografi (EMG) ve manyetik rezonans görüntüleme (MRG) sonrasında CSM veya siringomiyeli tanısı konulan hastalar çalışmaya alındı.

**Bulgular:** On hasta (ortalama yaş 65,6 yıl) analiz edildi. 8 hastada (%80) tenar ve hipotenar atrofi gözlendi. EMG'de tüm hastalarda servikal miyotomlarda fasikülasyonlar ve denervasyon görüldü; 1 hastada lomber bölgede tutulum vardı. Rektus abdominis ve genioglossus kaslarının EMG'si normaldi. Tenar ve hipotenar atrofi gözlenmesi, EMG'de servikal ve lomber miyotomlarda fasikülasyon ve denervasyon görülmesi ALS ile benzerlik göstermektedir. Rektus abdominis ve genioglossus kaslarının EMG'sinin normal olması ALS tanısından uzaklaştırmaktadır.

**Sonuç:** ALS ayırıcı tanısında CSM ve siringomiyeli düşünülmelidir. Ayrıntılı öykü, nörolojik muayene, EMG ve MRG tanı doğruluğu için gereklidir.

**Anahtar Kelimeler:** Amiyotrofik lateral skleroz, servikal spondilotik miyelopati, siringomiyeli

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## INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a gradually worsening neurodegenerative disease involving the motor neurons situated in the spinal cord, cerebral cortex, and brainstem. Its incidence is reportedly 1.68 per 100,000, and recent data show a rising prevalence worldwide. Male sex is a known risk factor, and disease onset typically occurs between the ages of 51 and 66 years. An ALS diagnosis is based on clinical history, findings, neurophysiological testing, and exclusion of other diseases. It presents with simultaneous upper and lower motor neuron degeneration.[1] Upper motor neuron (UMN) signs are detected clinically, while lower motor neuron (LMN) signs are confirmed by diagnostic procedures such as nerve conduction analysis and needle electromyography (EMG).[2]

Cervical spondylotic myelopathy (CSM), the most severe outcome of cervical spondylosis, is the leading cause of acquired spinal cord dysfunction. Its incidence in North America is at least 4 per 100,000.[3] CSM usually develops between the ages of 50 and 60 years and presents with neck, shoulder, or arm pain as well as hand weakness, leg weakness, and gait disorder. Upon examination, findings include muscle atrophy, hyperreflexia, sensory loss, and spastic paresis of the lower limbs.[4] LMN signs appear at the lesion level, while UMN signs appear below. Upper limb signs may be unilateral; lower limb signs are always bilateral.[5] Diagnosis is supported by magnetic resonance imaging (MRI) showing spinal cord changes such as oedema, gliosis, or myelomalacia on T2 sequences.[6] Electromyography (EMG) helps in ruling out ALS.

Syringomyelia is a fluid-filled cavity (syrinx) in the spinal cord (typically in the mid-lower cervical region), which causes chronic sensory and motor loss.[7,8] Symptoms vary by syrinx location. Involvement of the anterior horns causes segmental atrophy and weakness. Damage to the central grey matter causes temperature sensation and loss of pain. Involvement of lateral columns leads to spasticity, paraparesis, and hyperreflexia. Syringomyelia can mimic ALS but progresses slowly and includes sensory symptoms. MRI confirms diagnosis.[9] CSM may also mimic ALS and cause diagnostic delays.

This study aimed to evaluate and compare the clinical, radiological and electrophysiological features of patients who were initially referred with a preliminary diagnosis of ALS. Still, it was later diagnosed with CSM or syringomyelia after detailed examinations.

## MATERIALS AND METHODS

***Ethics Committee Approval***: Approval was granted by the Ethics Committee of Sakarya University Faculty of Medicine (Date: 10.07.2020, decision no: E.6172), and all procedures were performed in accordance with the Helsinki Declaration

***Study:*** This study retrospectively reviewed the medical records of 10 patients who presented to our neurology clinic in Turkey with a preliminary diagnosis of ALS between 1 January 2018 and 1 June 2020. Based on medical history, detailed neurological examination, spinal MRI, sensory and motor nerve conduction studies and concentric needle electromyography (EMG), ALS was excluded in all patients. These patients were diagnosed with CSM or syringomyelia. The radiological findings were evaluated by MRI. We selected only patients for whom cervical cord MRI showed radiological signs of CSM and syringomyelia.

***Analysis***: All participants underwent sensory and motor nerve conduction studies and EMG of the thenar and hypothenar muscles as a conventional diagnosis method. During motor nerve examination, thenar and hypothenar compound muscle action potential (CMAP) values were recorded at the abductor pollicis brevis (APB) and abductor digiti minimi (ADM) in response to stimulation of the median and ulnar nerves, respectively. In sensory nerve examination, the median and ulnar nerves were stimulated at the wrist.

Deep tendon reflexes are an important part of the neurological examination used to assess the integrity of the peripheral and central nervous systems. Reflex responses are graded on a scale from 0 to 4+:

Grade 0: No response.

Grade 1+: Diminished or sluggish response.

Grade 2+: Average, normal response.

Grade 3+: Brisker than average (the reflex is more active than normal, but not necessarily abnormal).

Grade 4+: Very brisk, hyperactive with clonus (this is an exaggerated reflex response, often accompanied by clonus, which is typically abnormal and suggests an upper motor neurone lesion or central nervous system pathology).

***Exclusion Criteria:*** 1) history of spinal cord tumor or abnormalities of the cervical vertebrae; 2) focal or multifocal neuropathy; 3) brachial plexus lesion; 4) muscular dystrophy; or 5) injury or infection at presentation.

***Statistical Analyses:*** The statistical component of the study was handled via SPSS version 21.0, with numerical results presented as mean ± standard deviation, number, and percentage.

## RESULTS

The mean age of the patients in this research was 64.90 ± 9.26 years, with an age range of 51 to 78 years. The 10 patients comparised 6 (60%) males and 4 (40%) females. Four patients (40%) took med-

ications for hypertension, and 2 (20%) for diabetes mellitus. One patient (10%) was diagnosed with chronic kidney disease (CKD). The mean time from onset to diagnosis was 3.25 ± 3.01 years. Table 1 shows a summary of the demographic characteristics of the study participants. These patients, along with their demographic characteristics, are detailed in Table 1.

Regarding the presenting symptoms, five patients exhibited isolated unilateral upper extremity weakness, two had bilateral upper extremity weakness, three demonstrated lower extremity weakness accompanied by gait disorder, and one patient displayed weakness in both the upper and lower extremities, coupled with gait disorder. In addition to these complaints, all patients had neck and back pain, and two patients had spasticity in the lower extremities.

Neurological examination findings included thenar and hypothenar muscle atrophy in eight patients, gait disorder and mild spasticity in the lower extremities in four patients, increased deep tendon reflexes in the lower extremities in eight patients, and cape-like sensory deficits in three patients. Seven patients had significant muscle atrophy. No patients were diagnosed with dysphagia or dyspnoea. In six patients, spinal MRI showed narrowing of the canal diameter, low signal intensity on the T1-weighted sequence, high signal intensity on the T2-weighted sequence, and atrophy of the medulla spinalis on cervical spinal MRI, so they were evaluated in favour of CSM. In four patients, cervical spinal MRI showed hypointensity on T1, hyperintensity on T2, and no contrast enhancement on contrast-enhanced examinations, which are findings compatible with syringomyelia. A 78-year-old male patient (Case 6) presented complaining of weakness in the left hand. During the general physical examination, muscle atrophy and contracture were observed in the left hand. Upon neurological examination, atrophy was observed in the left-hand intrinsic muscles and hypoesthesia in the left upper extremity. Cervical MRI showed a syrinx extending from C3 to C7. The dilated spinal canal appears as a centrally located intramedullary elongated/ tubular structure with high T2W and low T1W signal intensity. There is no evidence of contrast-enhancing intraspinal masses or abnormal enhancement. Figure 1 shows the cervical spinal MRI findings of Case 6: atrophy in the left-hand intrinsic muscles.

**Table 1.** Demographic characteristics of patients.

| Demographic characteristics | Data |
|---|---|
| Age (years), Mean±SD | 64.90 ± 9.26 |
| Gender (male), n (%) | 6 (60.0) |
| Hypertension, n (%) | 4 (40.0) |
| Diabetes mellitus, n (%) | 2 (20.0) |
| Chronic kidney disease, n (%) | 1 (10.0) |
| Time to final diagnosis (years), Mean±SD | 3.25 ± 3.01 |

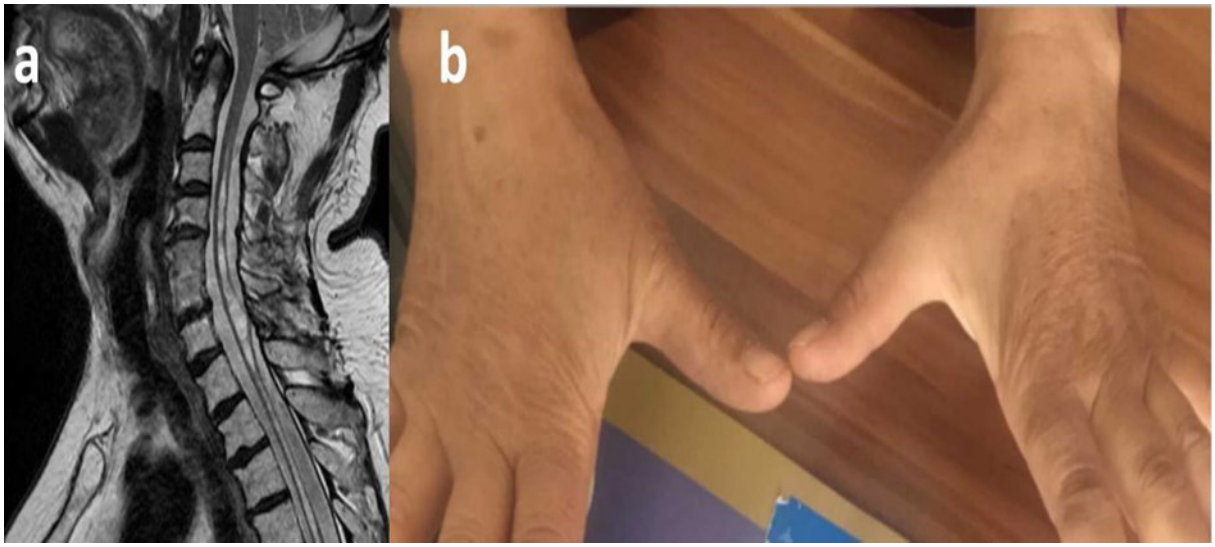


**Figure 1.** MRI of the cervical spine in a patient with cervical syringomyelia (case 6) (a) and atrophy of the intrinsic muscles of the left hand (b).

Another 78-year-old male patient (Case 7) presented complaining of weakness in the right-hand. This patient had no sensory complaints or pain. Upon examination, atrophy was observed in the right-hand intrinsic muscles. Cervical spondylotic myelopathy was detected on cervical spinal MRI. Cervical spinal MRI findings and atrophy in the hand muscles are shown in Figure 2.

Table 2 illustrates a summary of the clinical features of the study participants.

Sensory nerve action potentials and conduction velocities were normal, even in advanced atrophic extremities. The paraspinal muscle, rectus abdominis, and genioglossus concentric needle EMG examinations of the patients were normal. These findings were atypical for ALS, and the predominance of denervation in the upper extremities suggested an underlying spinal cord pathology. Based on spinal MRI results and concentric needle EMG findings, six patients were diagnosed with CSM, and four patients were diagnosed with syringomyelia. The patients were referred for neurosurgical consultation and evaluated for the need for surgery. Table 3 summarises the neurological symptoms/neurological examination findings, and laboratory findings. Performed as part of the general screening protocol, six patients were diagnosed with CSM and four patients with syringomyelia. All these individuals were directed towards the neurosurgery department.

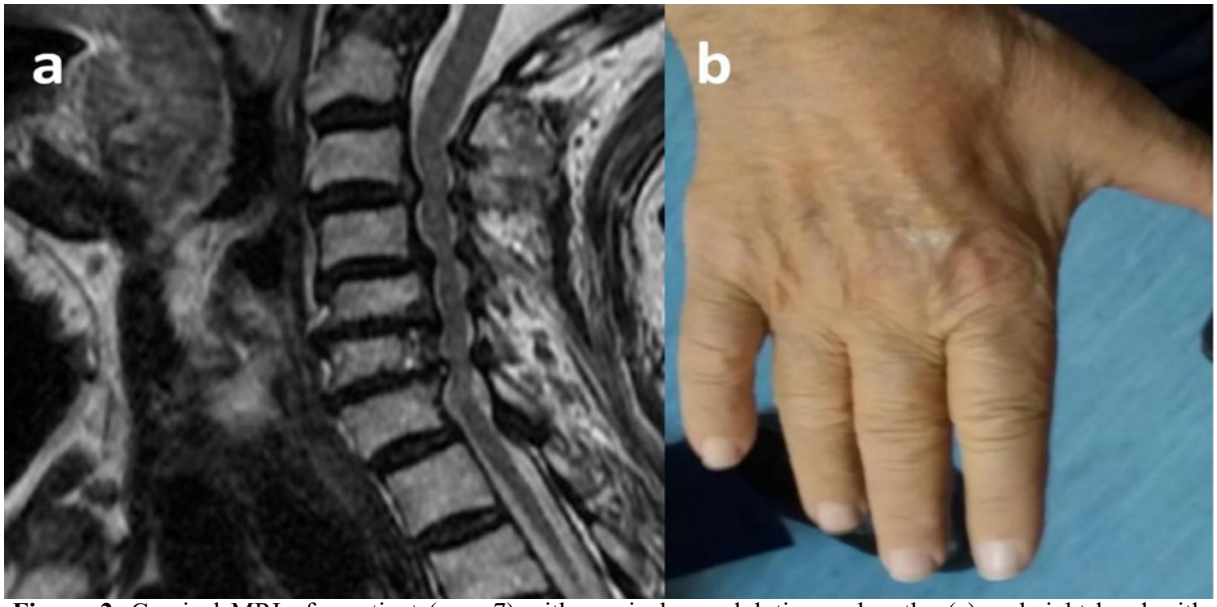


**Figure 2.** Cervical MRI of a patient (case 7) with cervical spondylotic myelopathy (a) and right hand with marked intrinsic muscle atrophy (b).

**Table 2.** Clinical features of the participants.

| Clinical Features | n (%) |
|---|---|
| Unilateral upper extremity weakness | 5 (50.0) |
| Bilateral upper extremity weakness | 2 (20.0) |
| Lower extremity weakness and gait disorder | 3 (30.0) |
| Weakness in both the upper and lower extremities, with a gait disorder | 1 (10.0) |
| Unilateral thenar and hypothenar atrophy | 5 (50.0) |
| Bilateral thenar and hypothenar atrophy | 3 (30.0) |
| Gait disorders and spasticity in the lower extremities | 4 (40.0) |
| Increased deep tendon reflexes in both lower extremities | 8 (80.0) |
| Cape-like sensory deficits (pain and temperature sensation) | 3 (30.0) |
| Cervical spinal MRI findings consistent with CSM | 6 (60.0) |
| Cervical spinal MRI findings consistent with syringomyelia, | 4 (40.0) |

**Table 3.** Clinical characteristics, neurological symptoms/neurological examination findings, and laboratory findings of the patients (N=10).

| | Gender | Age (years) | Comorbidities | Time from symptom onset to diagnosis (years) | Complaints | Neurological examination | MRI | EMG | Diagnosis |
|---|---|---|---|---|---|---|---|---|---|
| **Patient 1** | M | 73 | HT | 0.5 | Paraesthesia and loss of muscle strength in legs, gait disorder | Exaggerated DTR and spasticity in both lower extremities | C3-C4, C4-C5, C5-C6, C6-C7, C7-C8 disc protrusions and spinal cord compression C5-C7 myelomalacia | Chronic neurogenic MUPs and positive spikes and fibrillations in bilateral C5-C6-C7 roots innervated muscles | CSM |
| **Patient 2** | M | 65 | HT | 10 | Paraesthesia and loss of muscle strength in the left hand | Atrophy of the intrinsic muscles of the left hand, hypoesthesia in the left arm | C2-C3, C4-C5, C5-C6 disc protrusions and spinal cord compression, myelomalacia in the spinal cord at C5-C6 level | Chronic neurogenic MUPs and positive spikes and fibrillations in bilateral C5-C6 roots innervated muscles | CSM |
| **Patient 3** | M | 60 | DM | 4 | Paraesthesia and loss of muscle strength in both hands, gait disorder | Intrinsic muscle atrophy of both hands, loss of muscle strength in both hands, exaggerated DTR in both lower extremities | C3-T1 levels syrinx cavity | Chronic neurogenic MUPs and positive spikes and fibrillations in bilateral C4-C5-C6-C7-C8-T1 roots innervated muscles | Syringomyelia |
| **Patient 4** | F | 67 | | 0.5 | Paraesthesia and loss of muscle strength in both legs, gait disorder | Mild spasticity and exaggerated DTR in both lower extremities and gait disorder | C4-C5, C5-C6, C6-C7 protrusions and spinal cord compressions | Chronic neurogenic MUPs and positive spikes and fibrillations in C5-C6-C7 roots innervated muscles | CSM |
| **Patient 5** | F | 54 | | 2 | Paraesthesia and loss of muscle strength in both hands | Mild weakness and hypoesthesia in both upper extremities, atrophy of intrinsic muscles in both hands | C4-C5 and C5-C6 paracentral bulging, spinal cord compression, C5-C6 myelomalacia | Chronic neurogenic MUPs and positive spikes and fibrillation in bilateral C5-C6 root innervated muscles. | CSM |
| **Patient 6** | M | 78 | | 3 | Paraesthesia and loss of muscle strength in the left hand | Intrinsic muscle atrophy of the left hand | C3-C7 syrinx cavity in the spinal cord | Positive spikes and fibrillations in left C3-C7 roots innervated muscles | Syringomyelia |

C: Cervical; CKD: Chronic kidney disease; CSM: Cervical spondylotic myelopathy; DM: Diabetes Mellitus; DTR: Deep tendon reflex; F: Female; HT: Hypertension; M: Male; MRI: Magnetic resonance imaging; MUP: Motor unit potentials.

**Table 3.** Continue.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Patient 7** | M | 78 | DM | 8 | Paraesthesia and loss of muscle strength in the right hand | Intrinsic muscle atrophy of the right hand | C3-C4, C4-C5, C5-C6, C6-C7 bulging, right C6-C7 nerve root compression | Positive spikes and fibrillations in right C6-C7 roots innervated muscles | CSM |
| **Patient 8** | F | 51 | | 5 | Paraesthesia and loss of muscle strength in the left hand | Hypoesthesia in the left arm and intrinsic muscle atrophy of the left hand | C5-C7 syrinx cavity in the spinal cord | Fibrillations in C5-C6-C7 innervated muscles on the left and chronic neurogenic MUPs in the same muscles | Syringo-myelia |
| **Patient 9** | F | 62 | HT, CKD | 0.5 | Paraesthesia and loss of muscle strength in the right hand | Intrinsic muscle atrophy of the right hand | C4-C6 syrinx cavity in the spinal cord | Fibrillations in C5-C6 innervated muscles on the right and neurogen-ic MUPs in the same muscles | Syringo-myelia |
| **Patient 10** | M | 61 | HT | 1 | Paraesthesia and loss of muscle strength in both hands and legs, gait disor-der | Mild weakness in both upper extremities, intrin-sic muscle atrophy of both hands, spasticity and ex-aggerated DTR in both lower extremities | C3-C4, C4-C5, C5-C6, C6-C7 disc compressions, myelomalacia at the C4-C7 level | Fibrillations and posi-tive spike activities in muscles with bilateral C4-C5-C6-C7 innerva-tion and thinning in the same muscles, chronic neurogenic MUPs | CSM |

C: Cervical; CKD: Chronic kidney disease; CSM: Cervical spondylotic myelopathy; DM: Diabetes Mellitus; DTR: Deep tendon reflex; F: Female; HT: Hypertension; M: Male; MRI: Magnetic resonance imaging; MUP: Motor unit potentials.

## DISCUSSION AND CONCLUSION

ALS is characterised by the widespread degeneration of lower and upper motor neurons, which typically leads to death (often from respiratory failure) approximately 3 years after symptoms first appear.[10] The disease is 90–95% sporadic and 3–10% familial. In Europe, the annual incidence is 2.1/100,000.[11] Although genetics, glutamate excitotoxicity, viral infections, autoimmunity, and heavy metal intoxication, such as lead, mercury, and aluminium, are thought to be implicated in the pathogenesis of the disease, the exact cause remains unknown. The diagnosis of the disease relies on an in-depth medical history and neurological examination results. There is no definitive test for an ALS diagnosis.[12] A confirmed diagnosis typically takes 1–2 years from the onset of symptoms. CSM and syringomyelia are two conditions that are often mistaken for ALS. Early diagnosis often leads to more favourable outcomes for patients.

Wu et al. reported that myelopathy was more common in men, especially those working in physically demanding jobs. They also found that CSM was more common in older and male patients.[13] Similarly, the proportion of male patients was also higher in our study. Degenerative changes in the spine in CSM lead to the compression of the nerve roots and spinal cord, causing symptoms both at and below the site of compression. Patients typically present with motor deficits due to damage to both upper and lower motor neurons. In addition to motor dysfunction, patients with CSM often experience a variety of sensory deficits related to the compression of specific sensory pathways.[14]

In our study, all patients reported sensory complaints. Lower motor neuron symptoms, such as upper extremity weakness, muscle atrophy, fasciculations, hyporeflexia, and hypotonia, are common at the affected vertebral level in CSM. In addition, 75% of patients have difficulty with fine motor skills, such as writing or buttoning, due to weakness of the intrinsic hand muscles.[15,16] Of our patients, eight had a loss of strength in the upper extremities, including intrinsic hand muscle weakness. Gait dysfunction is seen in most cases of CSM and is a differentiating characteristic.[16] In our study, four patients had this symptom. Lower extremity symptoms, such as clonus, are less sensitive (11%) but highly specific (96%) to CSM.[17] Clonus was observed in two of our patients. Cervical spine MRI is considered the definitive diagnostic tool for CSM.[18] In our study, all patients underwent both cervical spine MRI and concentric needle EMG for differential diagnosis.

Syringomyelia manifests as a disorder due to the disturbed circulation of cerebrospinal fluid (CSF) within the spinal cord, resulting in a fluid-filled cavity, or syrinx, within the spinal cord parenchyma or central canal.[19] The clinical manifestations of syringomyelia vary widely. Patients often present with pain, weakness, and atrophy, especially in the hands and arms, along with sensory disturbances in the upper extremities and spasticity or stiffness in the lower extremities.[20,21] A significant number of patients are in the 20 to 50-year range. The increased use of MRI for the routine evaluation of back and neck pain has led to more frequent diagnoses of syringomyelia.[22] In a study by Bogdanov et al. of 103 patients (35 females and 68 males) with syringomyelia, all participants had symptoms of syringomyelia. Bilateral segmental sensory deficits in the trunk and upper extremities were found in 35 (34%) patients, whereas unilateral deficits were observed in 58 (56%) patients. Upper limb weakness or atrophy was bilateral in 36 (35%) patients, unilateral in 45 (44%), and absent in 22 (21%). Pain was reported in 24 (23%) patients.[23] In our study, of the four patients with syringomyelia, three had unilateral upper extremity weakness and atrophy, while one patient had bilateral symptoms. In our study, the patients sent to our clinic with an initial diagnosis of ALS were ultimately diagnosed with CSM or syringomyelia after a thorough evaluation of clinical symptoms, neurological examination findings, concentric needle EMG, and spinal MRI findings.

In conclusion, the findings suggest that careful consideration of the combined clinical signs, physical examination findings, EMG, and MRI results is critical when evaluating patients with a preliminary diagnosis of ALS. Given the overlapping age range and symptom presentation, conditions such as CSM and syringomyelia should be carefully considered as potential differential diagnoses. Due to the small cohort and retrospective nature of the study, it underscores the requirement for further research with larger groups. The study's main limitations include being at a single institution with a limited number of patients. Furthermore, the small sample size precluded the opportunity to make reliable comparisons of the clinical and radiological features of CSM and syringomyelia.

***Ethics Committee Approval:*** The study was approved by the Sakarya University Faculty of Medicine Ethical Committee (Date:10.07.2020, decision No: E.6172), and conducted in compliance with the Helsinki Declaration.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

***Author Contributions:*** Concept - NUC; Supervision - NUC; Materials - NUC; Data Collection and/or Processing - NUC; Analysis and/or Interpretation - NUC; Writing - NUC.

***Peer-review:*** Externally peer-reviewed.

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# Nearing Old Age: Technological Aging

# Yaşlanmaya Ramak Kala: Teknolojik Yaşlanma

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**ABSTRACT**

**Objective:** The study aimed to determine the Awareness of age-related change (AARC) and attitudes of adults between the ages of 40-64 years towards artificial intelligence (AI).

**Materials and Methods:** It was conducted in a descriptive and correlational type. The study included 255 individuals aged 40-64 years, who were not bedridden and had no neuropsychiatric problems. The data for this study were collected using a personal information form, the AARC scale, and the General Attitudes Towards Artificial Intelligence Scale (GAAIS). Data were analyzed using the SPSS 25 software package. The Skewness-Kurtosis test was used to check the normality of distribution. Correlation analysis was performed for the connection between the scale total scores and sub-dimension scores.

**Results:** The majority (79.2%) of the participants thought positively about aging, 71.8% were afraid of the stigma of old age, 67.1% had positive attitudes towards AI, and 91.4% used AI tools. When the participants' scale scores were examined, it was determined that the average AARC Gains score was 19.55±3.31 (5-25), the average AARC Losses score was 13.71±3.89 (5-25), and the average GAAIS score was 62.74±15.60 (23-98). It was determined that the connection between the participants' AARC Gains and GAAIS (r=0.152) was positive and significant. It was also determined that there was no connection between AARC Losses and GAAIS (r<0.001).

**Conclusions:** It is recommended that the views of adults aged 40 years and over, who are nearing old age, be increased, their awareness be raised, and training be organized to improve their attitudes towards AI.

**Keywords**: Aging, artificial intelligence, awareness of age -related changes, technology

**ÖZ**

**Amaç**: Çalışmada 40-64 yaş arası yetişkinlerin yaşa bağlı değişim farkındalığını (YBDF) ve yapay zekaya (YZ) yönelik tutumlarını belirlemek amaçlanmıştır.

**Materyal ve Metot:** Tanımlayıcı ve ilişki arayıcı türde yürütülmüştür. Çalışmaya 40-64 yaş aralığında, yatağa bağımlı olmayan ve nöropsikiyatrik problemi olmayan 255 birey dahil edildi. Bu çalışma için veriler kişisel bilgi formu, Yaşa Bağlı Değişim Farkındalığı Ölçeği (YBDFÖ) ve Yapay Zekaya Yönelik Genel Tutum Ölçeği (YZYGTÖ) kullanılarak toplanmıştır. Veriler SPSS 25 yazılım paketi kullanılarak analiz edilmiştir. Dağılımın normalliğini kontrol etmek için Skewness-Kurtosis testi kullanılmıştır. Ölçek toplam puanları ile alt boyut puanları arasındaki ilişkiler için korelasyon analizi yapılmıştır.

**Bulgular:** Katılımcıların %79.2'si yaş almayı olumlu olarak düşünmekte, %71.8'inin yaşlılık damgalamasından korkmakta, %67.1'inin yapay zekaya yönelik olumlu tutum sergilemekte ve %91.4'ünün yapay zeka araçlarını kullanmaktadır. Katılımcıların ölçek skorları incelendiğinde YBDFÖ-Kazanç puan ortalaması 19.55±3.31 (5-25), YBDFÖ-Kayıp puan ortalaması 13.71±3.89 (5-25) ve YZYGTÖ puan ortalamasının ise 62.74±15.60 (23-98) olduğu belirlenmiştir. Katılımcıların YBDFÖ-Kazanç ile YZYGTÖ ilişkisinin (r=0.152) pozitif yönde ve anlamlı olduğu saptanmıştır. YBDFÖ-Kayıp ile YZYGTÖ ilişkisinin de olmadığı (r<0.001) belirlenmiştir.

**Sonuç:** Yaşlanmaya ramak kala olan 40 yaş ve üzeri yetişkin bireylerin yaşlanmayla ilgili pozitif görüşlerinin artırılması, yapay zekaya yönelik tutumlarının iyileştirilmesi için farkındalıklarının oluşturulması ve eğitimlerin düzenlenmesi önerilmektedir.

**Anahtar Kelimeler**: Teknoloji, yapay zekâ, yaşa bağlı değişim farkındalığı, yaşlanma

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## INTRODUCTION

It is predicted that the number of older people in the world, which is currently one billion, will be approximately two billion by 2050[1] and that older people in our country, which is 10.6%, will increase even more in coming years. In such case,[2] it becomes important to be prepared for old age before aging. It is important to know the age-related change awareness attitudes of adults. Awareness of age-related change (AARC) is defined as awareness that person's behavior, performance level, or way of experiencing life changes as a result of aging.[3,4] Adults may have positive or negative attitudes, prejudices, concerns, and hopes towards aging. Their self-perception and views on lifestyle towards these situations may vary from individual to individual.[3,5] The concept of AARC has featured regularly in international literature in recent years,[6-9] but it is still very new in national literature.[4]

Considering the advancements in technology, it is becoming important that older people in society can use artificial intelligence (AI) tools. The use of many technological tools and AI by individuals while continuing their daily lives will make their lives easier.[10] It has become essential for individuals to use these current approaches, which include many AI algorithms, in mobile applications, accessing health services online, using health equipment technologies, and using wearable technology.[11,12] For society that can live healthy, long, and quality life, it is indispensable for adults to adapt to technologies that are products of AI. In this respect, adults' attitudes towards AI have an important place in both national and international literature.[13-18]

Given that it is important for adults to be prepared for old age and to be able to use applications that will make their lives easier, their thoughts and needs regarding these issues need to be determined.[4] To facilitate adults' awareness and adaptation to digital age, it is first necessary to determine individuals' perceptions of AARC and their attitudes towards AI.[19]

In this context, the study aimed to determine the AARC and attitudes of adults between the ages of 40-64 years towards AI.

## MATERIALS AND METHODS

***Ethical Aspects of the Research:*** A university's Ethics Committee granted permission to conduct research (Date: 15.03.2024, decision no: 2024/94). Research conforms to provisions of Declaration of Helsinki. Permission was obtained from scale owners via e-mail to use scales in research. Consents of volunteer adults who participated in study were obtained via an online consent form.

***Type of Research:*** Research was conducted in a descriptive and correlational type to determine AARC (gain and loss situations) and attitudes towards AI of adults aged 40-64 years. STROBE checklist was used in reporting of research.[20]

***Research Questions:*** (1) What is the AARC among adults aged 40-64 years? (2) What are the attitudes of adults aged 40-64 years towards AI? (3) Is there a connection between the AARC among adults aged 40-64 years and their attitudes towards AI?

***Population and Sample:*** Population of this research consisted of adults aged 40-64 years living in Türkiye. G*Power program was used in sample calculation of research. It was determined that a minimum of 138 individuals should be studied in study, assuming that connection between AARC and attitudes towards AI of adults aged 40-64 years was at a moderate level (r=0.30). Of 279 individuals who participated in survey, 10 did not give consent, 13 were not included in study because they were under 40 years, and one was not included because they were over 65 years. Research was completed with a total of 255 individuals. When the data collection process was completed, a post-hoc analysis was performed by entering sample size as 255, correlation coefficient as 0.152 and type 1 error (alpha coefficient) (0.05). As a result of post-hoc analysis, it was determined that researcher's power was 99%.

***Research Inclusion Criteria:*** All individuals between ages of 40-64 years, who were not bedridden and had no neuropsychiatric problems, were included in study.

***Data Collection Method:*** In this study, data were collected from adults aged 40-64 years using the snowball method via a data collection form created online via Google Drive in May 2024. Adult volunteers who participated in study were asked to read consent form prepared online, tick checkbox, and then answer the questions. When the informed consent form was clicked, form that opened was read. After consent was read, they were able to answer research questions after ticking option "I approve of participating in study". Individuals who did not consent were allowed to exit form without answering the questions.

***Data Collection Forms:*** *Personal Information Form:* Information form was created by researchers in line with literature and included 12 questions.[4,16,17,21,22]

*Awareness of Age-Related Change Scale (AARC-10):* AARC refers to awareness that an individual's life has changed due to aging. Scale sub-dimensions, including two positive (AARC-gains) and negative (AARC-losses) aspects of their own aging experiences. Scale is a five-point Likert-type scale with 10 items. Individuals can respond to scale items ranging from not at all (1) to very much (5). An increase in

score indicates that AARC is high. Scale (AARC-10), developed by Kaspar et al.,[23] was adapted to Turkish by Genç et al.[4] Total Cronbach alpha (Cr α) value of AARC-10 scale was found as 0.717, loss factor was 0.806, and gain factor was 0.642.[4] In present study, total Cr α value of AARC-10 was determined as 0.71, AARC Losses factor was 0.77, and AARC Gains factor was 0.70.

*The General Attitudes Towards Artificial Intelligence Scale (GAAIS):* A Scale developed by Schepman and Rodway[19] was adapted to Turkish by Kaya et al.[24] Scale has two sub-dimensions and 20 questions: negative attitudes towards AI and positive attitudes towards AI. There are 12 positive and eight negative items. Scale score is calculated by reverse coding eight items towards AI. Individuals can respond to scale items from strongly disagree (1) to strongly agree (5). Total possible score from scale is 100, and increase in scale score means more positive attitude towards AI. Cr α values were determined as 0.82 for positive attitudes and 0.84 for negative attitudes.[24] In present study, Cr α values were determined as 0.93 for positive attitudes, 0.90 for negative attitudes, and 0.92 for total attitudes.

***Data Analysis***: Data were analyzed using IBM SPSS Statistics 25 software package. Personal data and scale scores are in Tables 1 and 2. Correlation analysis was performed for connections between scale total scores and sub-dimension scores. A normality test was performed to decide on type of correlation analysis (Pearson correlations). Normality of data distribution was determined using Skewness-Kurtosis values of between -1.5 and +1.5, and research data was found to be normally distributed. Significance level was taken as $p < 0.05$.

## RESULTS

Average identity age of participants was 52.60 ± 7.82 (40-68) years, and average age they felt was 42.34 ± 12.17 (16-80) years. Of participants, 59.2% were female, 84.7% were married, 76.5% were university graduates, and 40.8% were working full time. It was determined that 63.9% of participants had no chronic disease and 55.7% did not use regular medication. Majority (79.2%) of participants thought positively about aging, 71.8% were afraid of stigma of old age, 67.1% had positive attitudes towards AI, and 91.4% used AI tools (Table 1).

**Table 1.** Characteristics of people aged 40 and over (n=255).

| Characteristics | | Date |
|---|---|---|
| **Identity age,** Mean ± SD / Median (Min-Max) | | 52.60 ± 7.82 / 53 (40 – 68) |
| **Perceived age,** Mean ± SD / Median (Min-Max) | | 42.34 ± 12.17 / 42 (16 – 80) |
| **Sex,** n (%) | Male | 104 (40.8) |
| | Female | 151 (59.2) |
| **Marital status,** n (%) | Single | 39 (15.3) |
| | Married | 216 (84.7) |
| **Education status,** n (%) | Primary-Secondary Education | 25 (9.8) |
| | High School | 35 (13.7) |
| | University | 195 (76.5) |
| **Employment status,** n (%) | Full time | 104 (40.8) |
| | Part-time | 24 (9.4) |
| | Retired | 69 (27.1) |
| | Unemployed | 13 (5.1) |
| | Other | 45 (17.6) |
| **Chronic illness,** n (%) | Yes | 92 (36.1) |
| | No | 163 (63.9) |
| **Continuous use of medication,** n (%) | Yes | 113 (44.3) |
| | No | 142 (55.7) |
| **Thinking positively about ageing,** n (%) | Yes | 202 (79.2) |
| | No | 53 (20.8) |
| **Fear of stigmatisation of old age,** n (%) | Yes | 72 (28.2) |
| | No | 183 (71.8) |
| **Attitude towards artificial intelligence,** n (%) | Positive | 171 (67.1) |
| | Negative | 84 (32.9) |
| **Using artificial intelligence tools,** n (%) | Yes | 233 (91.4) |
| | No | 22 (8.6) |

When the participants' scale scores were examined, it was determined that average AARC Gains score was 19.55 ± 3.31 (5-25), average AARC Losses score was 13.71 ± 3.89 (5-25), and average GAAIS score was 62.74 ± 15.60 (23-98) (Table 2).

Total AARC and GAAIS scale scores and subdimensions are presented in Table 3. It was determined that connection between participants' AARC Gains and GAAIS (r=0.152, p=0.015, n=255) was positive, weak, and significant. It was also determined that there was no connection between AARC Losses and GAAIS (r<0.001, p=0.995, n=255) (Table 3).

**Table 2.** Date on scale scores.

| | Mean ± SD | Median (Min-Max) |
|---|---|---|
| AARC_Gains | 19.55 ± 3.31 | 20 (5 – 25) |
| AARC_Losses | 13.71 ± 3.89 | 14 (5 – 25) |
| GAAIS | 62.74 ± 15.60 | 64 (23 – 98) |

AARC: Awareness of Age-Related Change Scale; GAAIS: The General Attitudes Towards Artificial Intelligence Scale.

**Table 3.** The relation between the total GAISS, AARC Gains, AARC Losses.

| | | Total_GAISS | AARC_Gains | AARC_Losses |
|---|---|---|---|---|
| Total_GAISS | r | 1 | | |
| | p | | | |
| AARC_Gains | r | 0.152 | 1 | |
| | p | **0.015** | | |
| AARC_Losses | r | **0.001** | 0.127 | 1 |
| | p | 0.995 | **0.043** | |

r: Pearson Correlation; p: Sig. (2-tailed); AARC: Awareness of Age-Related Change Scale; GAAIS: The General Attitudes Towards Artificial Intelligence Scale.

## DISCUSSION AND CONCLUSION

In this study, which was conducted to determine AARC of adults aged 40 years and over, their attitudes towards AI, and connection between them, it was found that individuals' AARC Gains scores were generally good and their attitudes towards AI were moderate. In addition, it was seen that there was a positive and significant connection between adults' AARC Gains scores and their attitudes towards AI.

Chronologic (identity) age refers to age measured from a person's birth to a certain date, and subjective age is related to how old a person feels.[9] Genç et al.[4] found that average age of individuals was 53.4±10.4 (40-92) years and average perceived subjective age was 44.8±13.9 (12-100) years. The present study was similar, finding that average chronologic age of individuals was 52.60±7.82 (40-68) years and average subjective age perception was 42.34±12.17 (16-80) years. Genç et al.[4] found that 68.9% of individuals had more positive aspects of aging, but this rate was determined to be higher (79.2%) in our study. Individuals' feeling of youth is related to their perspectives and expresses that they live in a healthy environment.

When the literature was examined, it was determined that average AARC Gains score was higher than average AARC Losses score in many studies.[4,8,9,21,22] Present study was similar to literature, and participants' views on aging were positive, thinking that gains of old age were higher. In addition, present study revealed that 71.8% of individuals were not afraid of stigma of old age. In this country, where healthy and active aging is at forefront, it is seen that it has positive effects on thoughts of individuals who will age. It is thought that older people are ready for natural process of aging due to reasons such as having a social health policy and knowing how to cope with problems of aging. It is thought that they are ready for natural process of old age due to reasons such as having a social health policy and knowing how to deal with possible situations.

Considering the mega trends echoing in gray revolution, technological transition and its obvious social transformations, the conceptual connection between old age and technology emerges.[22,26] Huxhold et al.[26] addressed the concept of gray digital divide in their study with individuals aged 40 years and over. According to Compaine,[27] digital divide is defined as 'perceived difference between those who have access to latest information technologies and those who do not'. Over time, the gray digital divide has determined that social inequalities have decreased. An important way to minimize the digital divide is attitudes of individuals towards AI. Considering these

situations, the attitudes of older individuals towards AI have been addressed with their AARC. Older individuals' views on aging may prevent use of technology. Older people may internalize negative age-related stereotypes about their ability to use technology and social media, which can hinder their efforts to use these technologies effectively. Reducing negative age-related stereotypes and self-perceptions about aging has potential to encourage the use of AI-based technologies and improve positive self-perceptions about aging.[21] Our study found that individuals who were not yet old had positive attitudes toward AI, in line with literature.

AI is an important phenomenon that has emerged with development of technology and affects life in many areas and offers opportunities.[15,18] Target group of this study was 40-64 years age group, which was not considered older people but is on verge of old age. Determining attitudes is a strong indicator of actual use and acceptance of individuals' attitudes towards AI technologies.[15] In this study, it was determined that individuals' attitudes towards AI were positive and almost all participants (91.4%) used AI tools. It is thought that reason for this situation is sex homogeneity of study group (59.2% female) and high level of education (76.5% university). Studies on AI also show that individuals have highly positive attitudes towards AI.[13,16-18] Despite these positive attitudes of individuals towards AI, it has been determined that they are sceptical about cooperating with AI[17] and that level of anxiety about AI increases with age.[14] Hong et al.[13] stated that although AI and its applications were socially accepted, it was a fact that older people abandoned them after short-term use. In addition, Fang and Sim[28] determined that attitudes towards lifelong learning played a role in shaping well-being of older people, especially their quality of life. Many factors, such as conditions offered to older people, their lifestyles, and order in which they exist affect their use of AI and change their attitudes towards it. For this reason, it is important to determine attitudes towards AI before aging, take precautions accordingly, and develop practical applications.

In present study, it was determined that there was a significant positive connection between adults' AARC Gains scores and their attitudes towards AI. Although positive correlation is statistically significant, its practical impact may be limited. No connection was found between AARC Losses scores and attitudes towards AI. In literature, there are two studies investigating connection between AARC and technology[22] and social media use.[21] Schlomann et al.[22] found that there was a positive connection between AARC Gains and technology skills and technology attitudes. Sabatini et al.[21] found that individuals' AARC Gains and social media use were positively correlated, but AARC Losses and social media use were not correlated. It has been emphasized that reducing negative views about aging can help increase interaction of middle-aged and older individuals with social media and encouraging social media use can encourage positive self-perceptions about aging.[21] It is desired/expected that attitudes about losses do not affect the results. Training should be provided in minimizing AARC Losses and it is recommended that it be converted to AARC Gains. It is recommended that initiatives be planned to increase positive attitudes and increase use of AI. Preparing individuals who are about to age technologically for old age will make their lives easier and increase their quality.

In conclusion, this study, which determined AARC in adults aged 40 years and over, their attitudes towards AI, and connection between them, found that individuals' AARC Gains scores were good, their attitudes towards AI were moderate, and there was a positive and significant connection between adults' AARC Gains scores and their attitudes towards AI. It is recommended that views of adults aged 40 years and over, who are nearing old age, be increased, their awareness be raised, and training be organized to improve their attitudes towards AI. In intervention studies, individuals' views on aging and their attitudes towards AI should be evaluated together. Because non-probability (snowball) sampling method was used, study findings can only be generalized to sample studied. In addition, scales used were based on self-reporting and were in line with individual's statement. Conducting research in online environment may have affected the results, considering that research was only conducted with individuals who had potential to use technology. Results should be interpreted with caution in terms of participation bias. Despite these limitations, research is important in terms of revealing adults' views on ageing, their attitudes towards AI and connection between the two. Research is pioneering for studies that will address individuals' views on aging and their attitudes towards AI.

***Ethics Committee Approval:*** A university's Ethics Committee granted permission to conduct research (Date: 15.03.2024, decision no: 2024/94). Research conforms to provisions of Declaration of Helsinki. Permission was obtained from scale owners via e-mail to use scales in research. Consents of volunteer adults who participated in study were obtained via an online consent form.

***Conflict of Interest:*** No conflict of interest was declared by the authors. The authors have no relevant financial or non-financial interests to disclose.

***Author Contributions:*** Concept – FZG, AU; Supervision– FZG, AU; Materials – FZG; Data Collection

and Processing – FZG, AU; Analysis and Interpretation – FZG; Writing – FZG, AU

***Peer-review:*** Externally peer-reviewed.

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# The Effects of Kinesiological Taping and Exercise on Pain, Proprioception, Sleep, and Psychological State in Individuals with Bruxism

# Bruksizmi Olan Bireylerde Kinezyolojik Bantlama ve Egzersizin Ağrı, Propriyosepsiyon, Uyku ve Psikolojik Durum Üzerine Etkisi

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**ABSTRACT**

**Objective:** Bruxism, characterized by involuntary teeth grinding or clenching, can lead to pain, functional impairments, and reduced quality of life. This study aimed to evaluate the effects of combining kinesiology taping with exercise on pain, temporomandibular joint (TMJ) range of motion, sleep quality, depression levels, and cervical proprioception in individuals with bruxism.

**Materials and Methods:** A total of 30 participants were randomly assigned to two groups: a conventional therapy (CT) group and a conventional exercise + kinesiology taping (KT) group. Both groups underwent a two-week treatment program. Pain, cervical joint position sense (CJPS), range of motion (ROM), sleep quality, and depression levels were assessed before and after treatment.

**Results:** Both groups showed significant improvements in pain, depression levels, and sleep quality after treatment ($p<0.05$). The KT group demonstrated enhanced CJPS and maximum mouth opening, while the CT group showed significant improvements in ROM ($p<0.05$). However, no significant differences were found between the groups in any outcomes ($p>0.05$).

**Conclusions:** The findings of this study indicate that exercise exerts beneficial effects on pain, sleep quality, depressive symptoms, and joint functionality in individuals diagnosed with bruxism. Comparable positive outcomes were observed when exercise was applied alone and in combination with kinesiology taping; however, the addition of taping did not confer any additional clinical benefit.

**Keywords:** Bruxism, exercise, kinesiology taping, physiotherapy

**ÖZ**

**Amaç:** Bruksizm, istemsiz diş sıkma veya gıcırdatma ile karakterize olup ağrıya, fonksiyonel bozulmalara ve yaşam kalitesinde azalmaya yol açabilir. Bu çalışmanın amacı, kinezyoloji bantlaması ile egzersizin birlikte uygulanmasının, bruksizmi olan bireylerde ağrı, temporomandibular eklem (TME) hareket açıklığı, uyku kalitesi, depresyon düzeyi ve servikal propriyosepsiyon üzerindeki etkilerini değerlendirmeyi amaçlamaktadır.

**Materyal ve Metot:** Çalışmaya toplam 30 katılımcı rastgele geleneksel tedavi (GT) grubu ve geleneksel egzersiz + kinezyolojik bantlama (KT) grubuna ayrıldı. Her iki grup da iki haftalık bir tedavi programına dahil edildi. Tedavi öncesi ve sonrası ağrı, servikal eklem pozisyon hissi (CJPS), hareket açıklığı (ROM), uyku kalitesi ve depresyon düzeyleri değerlendirildi.

**Bulgular:** Tedavi sonrasında her iki grupta da ağrı, depresyon düzeyleri ve uyku kalitesinde anlamlı iyileşmeler sağlandı ($p<0,05$). KT grubunda servikal eklem pozisyon hissi (CJPS) ve maksimum ağız açıklığında, GT grubunda ise hareket açıklığında (ROM) belirgin gelişmeler gözlendi ($p<0,05$). Ancak, tedavi sonrası elde edilen tüm sonuçlar açısından iki grup arasında istatistiksel olarak anlamlı bir fark bulunmadı ($p>0,05$).

**Sonuç:** Bu çalışma, egzersizin bruksizmi olan bireylerde ağrı, uyku kalitesi, depresyon düzeyleri ve eklem fonksiyonu üzerinde olumlu etkileri olduğunu göstermektedir. Egzersizin tek başına veya kinezyoloji bantlaması ile birlikte uygulanmasında benzer olumlu sonuçlar elde edilmiştir; ancak bantlamanın ek bir klinik fayda sağlamadığı görülmüştür.

**Anahtar Kelimeler:** Bruksizm, egzersiz, fizyoterapi, kinezyolojik bantlama

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## INTRODUCTION

Bruxism, once defined solely as teeth clenching or grinding, is now recognized as a complex motor activity that may occur during sleep (sleep bruxism) or wakefulness (awake bruxism), with potential physiological or protective functions.[1] Sleep bruxism involves rhythmic or sustained muscle activity, while awake bruxism is characterized by repetitive tooth contact and mandibular movements.[1] The global prevalence of sleep and awake bruxism is reported as 15.9% and 23.8%, respectively, while in Turkey, these rates are 14.1% and 28.2%, with a combined prevalence of 38.8%.[2] Bruxism is a multifactorial condition influenced by psychosocial, biological, genetic, and environmental factors. Gender-related hormonal differences, particularly in women, may affect the severity and prevalence of both temporomandibular disorders (TMDs) and bruxism.[3] Although the role of morphological features remains debated, psychosocial factors, especially stress and anxiety, are increasingly acknowledged as key contributors, particularly in awake bruxism.[4,5]

The main objectives of bruxism treatment include pain relief, reduction of muscle tension, restoration of normal temporomandibular joint function, improvement of sleep quality, and enhancement of overall quality of life.[6] Although there is no definitive treatment for bruxism, both invasive and non-invasive methods are used. Recently, reversible and non-invasive approaches such as exercise, electrical stimulation, manual therapy, and kinesiology taping have gained prominence due to their safety and patient comfort, making them increasingly preferred in clinical practice.[7,8]

Physiotherapy for bruxism focuses on pain relief, jaw function, and muscle relaxation.[9] Bruxism is a centrally mediated behavioral activity, while TMDs are musculoskeletal disorders with local pathology. Though related, bruxism is a separate clinical condition and a potential risk factor for TMD.[10]

Kinesiology taping is used to support muscle function, improve proprioception, and reduce pain, and may be as effective as occlusal splints in managing bruxism symptoms.[11,12] Bruxism is closely linked to poor sleep quality and elevated psychological distress.[13] Thus, evaluating both physical and psychosocial outcomes is crucial in assessing treatment effectiveness.

This study aims to investigate the combined effects of kinesiology taping and exercise on pain, proprioception, sleep quality, and psychological status in individuals with bruxism. Existing literature offers limited evidence on the integrated use of these interventions, particularly regarding proprioceptive outcomes. Therefore, this study seeks to provide novel insights into multidisciplinary physiotherapy approaches for improving sensorimotor function and overall symptom management in bruxism.

## MATERIALS AND METHODS

***Ethics Committee Approval:*** Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Istanbul Medipol University (Date: 08.06.2023, decision no: 526). All procedures adhered to the ethical standards set forth in the Declaration of Helsinki for research involving human subjects. Informed consent was obtained from all participants prior to their enrollment in the study.

***Study Design:*** This single-blind, randomized study included 36 participants aged 20–55 years, diagnosed with bruxism at Batident Clinic based on dental history, clinical signs (e.g., tooth wear, jaw discomfort), and masticatory muscle examination. Individuals with prior temporomandibular joint (TMJ) trauma/surgery, facial pain (e.g., sinusitis, neuralgia), inflammatory TMJ conditions, cervical limitations, recent bruxism treatment, or kinesiology tape allergy were excluded. Of the 52 individuals assessed, 16 were excluded or declined participation. Participants were randomly assigned (1:1) to either a Conventional Exercise (CE) group (n=17) or a Kinesiology Taping (KT) group (n=19) using randomizer.org. During the study, 4 participants from the KT group and 2 from the CE group withdrew. All participants were blinded to group allocation and intervention content.

***Interventions:***

***Conventional Exercise Group:*** Each participant in the study received patient education and a brochure detailing the prescribed exercises to be performed as a home program three days per week for a duration of two weeks. The brochure included isometric neck exercises and temporomandibular joint range of motion exercises, such as protrusion and retrusion movements. To ensure correct and controlled execution, participants were instructed to perform all exercises in front of a mirror. Each exercise was accompanied by step-by-step instructions, visual illustrations, and specified repetition counts. The exercise protocol was designed to be simple, reproducible, and feasible for home application.[14] Participants were contacted via phone every four days to monitor their adherence and to provide individualized feedback. Based on these follow-ups, the number of sets for each exercise was adjusted according to individual needs. The two-week intervention period was selected based on previous findings suggesting that short-term interventions can lead to clinically meaningful improvements in proprioception and symptom relief among individuals with bruxism.[11,15] Additionally, shorter programs may enhance patient compli-

ance and facilitate applicability in routine physiotherapy practice. Importantly, isometric neck exercises were intentionally performed in different joint positions (e.g., neutral, shortened, and lengthened), while ensuring appropriate head and neck alignment to optimize activation of the targeted cervical muscle groups and proprioceptive stimulation. This approach is supported by literature indicating that performing isometric contractions at varied joint angles stimulates muscle spindles and joint receptors across a broader range, thereby contributing to improvements in joint position sense.[16] (Figure 1)

***Kinesiology Taping Group:*** In the KT group, kinesiology taping was applied to the temporomandibular region alongside the conventional exercise program. A 24-hour patch test using a 2×2 cm tape on the inner forearm was conducted to screen for allergic reactions. Participants with adverse skin responses were excluded. Taping was performed every three days for two weeks by a certified physiotherapist using 5 cm-wide Kinesio® Tape Tex Gold. The tape edges were rounded to prevent peeling, and skin was prepared to ensure proper adhesion. During application, participants maintained relaxed facial and cervical posture without jaw clenching. The tape was cut into a Y-shape, stretched 10–15%, and applied over the masseter muscle.[11,15] (Figure 2).

***Outcome Measures:*** The participants were evaluated at baseline and after the two-week intervention for pain intensity, jaw joint range of motion, joint position sense, psychological status using the Beck Depression Inventory, and sleep quality using the Pittsburgh Sleep Quality Index.

***Pain:*** The Visual Analog Scale (VAS) is a tool used to measure the intensity of pain experienced by an individual on a scale from 0 to 10. A score of 0 rep-

**Figure 1.** Conventional Exercise Program.

**Figure 2.** Kinesiology Taping Application.

resents no pain, while a score of 10 indicates unbearable pain. Pain assessment was conducted through palpation of the masseter and temporalis muscles, which are commonly involved in bruxism-related discomfort.[17]

***Assessment of Range of Motion:*** The active TMJ range of motion was measured in centimeters using a linear ruler. Maximum mouth opening, lateral movements (right and left), and protrusion were assessed by measuring the distance between the teeth during specific mandibular movements. During these assessments, the participants were seated in an upright position with their heads in a neutral alignment and their eyes directed forward. For the mouth opening measurement, the mandible was allowed to move freely, and the maximum vertical distance between the upper and lower central incisors was measured in centimeters using a ruler.[18]

***Cervical Joint Position Error Test:*** The Cervical Joint Position Error Test assesses an individual's ability to return their head to its original neutral position after performing maximal rotation in the transverse and sagittal planes. In this study, cervical joint position sense was assessed using a laser pointer and target system. Participants performed head movements (flexion, extension, right and left rotation) with eyes open and then closed, and the deviation from the original neutral position was measured to determine joint position error.[19]

***Beck Depression Inventory:*** The Beck Depression Inventory (BDI) is a 21-item questionnaire that evaluates the severity of depression symptoms. Each item is scored from 0 to 3, yielding a total score between 0 and 63. Higher scores indicate greater levels of depression, categorized as minimal, mild, moderate, or severe.[20]

***The Pittsburgh Sleep Quality Index:*** The Pittsburgh Sleep Quality Index (PSQI) assesses sleep quality based on seven components, each scored from 0 to 3. The total score ranges from 0 to 21, with scores above 5 indicating poor sleep quality. The majority of items are completed through participant self-reporting.[21]

***Statistical Analysis:*** Data were analyzed using IBM SPSS Statistics v26. Descriptive statistics included frequency, percentage, mean, SD, median, minimum, and maximum. Scale reliability was assessed with Cronbach's Alpha (≥0.60 acceptable). Normality was evaluated via skewness (±2) and kurtosis (<7). Between-group comparisons used the Independent Samples t-test; within-group comparisons used the Paired Samples t-test. A p-value <0.05 was considered statistically significant.

## RESULTS

A total of 30 participants were included in the study, with 15 in the Conventional Therapy (CT) group and 15 in the Kinesiology Tape (KT) group. The mean age was 32.13 ± 10.58 years in the CT group and 36.73 ± 10.92 years in the KT group. The gender distribution differed notably between the groups: in the CT group, 11 participants (73%) were male and 4 (27%) were female, whereas in the KT group, only 1 participant (7%) was male and 14 (93%) were female. The mean Body Mass Index (BMI) was 26.19 ± 4.80 kg/m² in the CT group and 23.78 ± 3.98 kg/m² in the KT group. There were no statistically significant differences between groups in pre-treatment measurements for pain (VAS), maximum mouth opening, protrusion, cervical joint position error flexion, right rotation and left rotation (CJPE), depression (BDI), or sleep quality (PSQI). However, the KT group showed significantly higher baseline values for right and left lateral TMJ motion (p=0.001 and p=0.003) and lower CJPE in extension compared to the CT group (p=0.035) (Table 1).

**Table 1.** Intergroup distribution of pre-treatment measurements.

| Variables | CT Group (n=15) | KT Group (n=15) | t | p | d |
|---|---|---|---|---|---|
| **VAS** | 3.47±1.36 | 4.20±1.97 | 1.187 | 0.245 | 0.433 |
| **Maximum Mouth Opening (cm)** | 5.26±0.77 | 4.87±0.79 | -1.361 | 0.184 | -0.497 |
| **Right Lateral ROM** ° | 0.93±0.18 | 1.41±0.48 | 3.584 | **0.001** | 1.309 |
| **Left Lateral ROM**° | 0.94±0.28 | 1.45±0.55 | 3.191 | **0.003** | 1.165 |
| **Protrusion** | 0.45±0.20 | 0.72±0.47 | 2.014 | 0.054 | 0.735 |
| **Cervical Joint Position Error** Flexion° | 9.49±7.01 | 7.47±3.49 | -0.996 | 0.328 | -0.364 |
| **Cervical Joint Position Error** Extension° | 9.83±6.63 | 5.43±3.91 | -2.218 | **0.035** | -0.810 |
| **Cervical Joint Position Error** Right Rotation° | 10.75±7.24 | 9.47±6.89 | -0.493 | 0.626 | -0.180 |
| **Cervical Joint Position Error** Left Rotation° | 10.50±4.62 | 9.30±6.63 | -0.575 | 0.570 | -0.210 |
| **Beck Depression Inventory** | 10.67±5.96 | 14.27±7.16 | 1.497 | 0.146 | 0.547 |
| **Pittsburgh Sleep Quality Index** | 5.80±3.19 | 6.13±2.50 | 0.318 | 0.753 | 0.116 |
| **Age (yrs)** | 32.13±10.58 | 36.73±10.92 | - | - | - |
| **Male, n (%)** | 11 (%73) | 1 (7) | - | - | - |
| **Female, n (%)** | 4 (%27) | 14 (93) | - | - | - |
| **BMI** | 26.19±4.80 | 23.78±3.98 | - | - | - |

CT: Conventional Therapy Group; KT: Kinesiology Tape Group; ROM: range of Motion; VAS: Visual Analog Scale. Statistical Method: Independent Samples t-test for between-group comparisons; BMI: Body Mass Index.

VAS significantly decreased in both groups: from 3.47±1.36 to 1.80±1.26 in the CT group (p<0.05, d=1.235), and from 4.20±1.97 to 2.13±1.77 in the KT group (p=0.001, d=1.154). Maximum mouth opening also improved significantly, increasing from 5.26±0.77 cm to 5.54 ± 0.76 cm in the CT group (p=0.004, d= -0.909), and from 4.87±0.79 cm to 5.23±0.77 cm in the KT group (p<0.05, d= -1.253). Right lateral ROM increased from 0.93 ± 0.18° to 1.11 ± 0.18° in the CT group (p=0.009, d= -0.808), and from 1.41 ± 0.48° to 1.58 ± 0.67° in the KT group (p=0.104, d= -0.449). Similarly, left lateral ROM showed improvement in the CT group (0.94±0.28° to 1.07±0.29°, p=0.036, d= -0.620), while the change in the KT group was not significant (1.45±0.55° to 1.51±0.51°, p=0.464, d= -0.194). Protrusion increased significantly in the CT group (0.45±0.20 to 0.58±0.19, p=0.003, d= -0.945), but not in the KT group (0.72±0.47 to 0.82±0.35, p=0.140, d=-0.404). Regarding CJPE, flexion improved significantly in the KT group (7.47±3.49° to 5.09±2.57°, p=0.024, d=0.656), but not in the CT group (9.49±7.01° to 8.52±5.63°, p=0.625, d=0.133). Similarly, improvements were observed in extension (KT: p=0.045, d=0.568; CT: p=0.234, d=0.332), right rotation (KT: p=0.049, d=0.558; CT: p=0.354, d=0.256), and left rotation (KT: p=0.012, d=0.741; CT: p = 0.001, d = 1.185), with the KT group showing statistically significant reductions in all directions except flexion in the CT group. Psychological parameters also improved significantly. BDI scores decreased from 10.67±5.96 to 6.07±3.45 in the CT group (p=0.002, d=1.040), and from 14.27±7.16 to 7.73±5.69 in the KT group (p=0.004, d=0.899). Likewise, PSQI scores improved in both groups (CT: 5.80±3.19 to 4.93±2.49, p=0.010, d=0.797; KT: 6.13±2.50 to 4.20±2.11, p=0.005, d=0.847) (Table 2).

**Table 2.** Comparison of within-group changes in pre- and post-treatment measurements for the groups.

| | CT Group | | | | | KT Group | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Pre-tre** | **Post-tre** | **t** | **p** | **d** | **Pre-tre** | **Post-tre** | **t** | **p** | **d** |
| **VAS** | 3.47±1.36 | 1.80±1.26 | 4.620 | **0.0001** | 1.235 | 4.20±1.97 | 2.13±1.77 | 4.468 | **0.001** | 1.154 |
| **Maximum Mouth Opening (cm)** | 5.26±0.77 | 5.54±0.76 | -3.400 | **0.004** | -0.909 | 4.87±0.79 | 5.23±0.77 | -4.852 | **0.0001** | -1.253 |
| **Right Lateral ROM°** | 0.93±0.18 | 1.11±0.18 | -3.025 | **0.009** | -0.808 | 1.41±0.48 | 1.58±0.67 | -1.738 | 0.104 | -0.449 |
| **Left Lateral ROM°** | 0.94±0.28 | 1.07±0.29 | -2.320 | **0.036** | -0.620 | 1.45±0.55 | 1.51±0.51 | -0.752 | 0.464 | -0.194 |
| **Protrusion** | 0.45±0.20 | 0.58±0.19 | -3.537 | **0.003** | -0.945 | 0.72±0.47 | 0.82±0.35 | -1.563 | 0.140 | -0.404 |
| **Cervical Joint Position Error** Flexion° | 9.49±7.01 | 8.52±5.63 | 0.499 | 0.625 | 0.133 | 7.47±3.49 | 5.09±2.57 | 2.540 | **0.024** | 0.656 |
| **Cervical Joint Position Error** Extension° | 9.83±6.63 | 7.78±4.24 | 1.243 | 0.234 | 0.332 | 5.43±3.91 | 4.09±2.45 | 2.198 | **0.045** | 0.568 |
| **Cervical Joint Position Error** Right Rotation | 10.75±7.24 | 8.71±5.97 | 0.958 | 0.354 | 0.256 | 9.47±6.89 | 7.01±5.28 | 2.160 | **0.049** | 0.558 |
| **Cervical Joint Position Error** Left Rotation° | 10.50±4.62 | 5.37±3.04 | 4.433 | **0.001** | 1.185 | 9.30±6.63 | 4.53±2.46 | 2.868 | **0.012** | 0.741 |
| **Beck Depression Inventory** | 10.67±5.96 | 6.07±3.45 | 3.890 | **0.002** | 1.040 | 14.27±7.16 | 7.73±5.69 | 3.481 | **0.004** | 0.899 |
| **Pittsburgh Sleep Quality Index** | 5.80±3.19 | 4.93±2.49 | 2.982 | **0.010** | 0.797 | 6.13±2.50 | 4.20±2.11 | 3.281 | **0.005** | 0.847 |

CT: Conventional Therapy Group; KT: Kinesiology Tape Group; ROM: range of motion; VAS: Visual Analog Scale. Statistical Method: Paired Samples t-test for within-group comparisons; Pre-tre: Pre-treatment; Post-tre: Post-treatment.

Despite these within-group improvements, no statistically significant differences were found between the CT and KT groups when comparing post-treatment change scores for any outcome variable ($p>0.05$ for all). Between-group effect sizes were small (e.g., VAS: d=–0.249; BDI: d=–0.318; PSQI: d=–0.593), suggesting that kinesiology taping did not yield superior outcomes over conventional exercise alone (Table 3).

**Table 3.** Comparison of the differences in measurements between pre- and post-treatment across groups.

| Variables | CT Group (n=15) | KT Group (n=15) | t | p | d |
|---|---|---|---|---|---|
| **VAS** | -1.67±1.40 | -2.07±1.79 | -0.682 | 0.501 | -0.249 |
| **Maximum Mouth Opening (cm)** | 0.28±0.32 | 0.36±0.29 | 0.722 | 0.476 | 0.264 |
| **Right Lateral ROM°** | 0.17±0.22 | 0.17±0.39 | 0.001 | 0.999 | 0.001 |
| **Left Lateral ROM°** | 0.13±0.22 | 0.06±0.31 | -0.746 | 0.462 | -0.272 |
| **Protrusion (cm)** | 0.13±0.14 | 0.10±0.25 | -0.364 | 0.719 | -0.133 |
| **Cervical Joint Position Error** Flexion° | -0.97±7.50 | -2.39±3.64 | -0.660 | 0.515 | -0.241 |
| **Cervical Joint Position Error** Extension° | -2.05±6.40 | -1.33±2.35 | 0.409 | 0.686 | 0.149 |
| **Cervical Joint Position Error** Right Rotation° | -2.04±8.24 | -2.46±4.41 | -0.174 | 0.863 | -0.064 |
| **Cervical Joint Position Error** Left Rotation° | -5.13±4.49 | -4.77±6.44 | 0.181 | 0.858 | 0.066 |
| **Beck Depression Inventory** | -4.60±4.58 | -6.53±7.27 | -0.872 | 0.391 | -0.318 |
| **Pittsburgh Sleep Quality Index** | -0.87±1.13 | -1.93±2.28 | -1.623 | 0.116 | -0.593 |

CT: Conventional Therapy Group; KT: Kinesiology Tape Group; ROM: range of motion; VAS: Visual Analog Scale. Statistical Method: Independent Samples t-test for comparison of change scores between groups.

## DISCUSSION AND CONCLUSION

This study demonstrated that both exercise and kinesiology taping effectively improved pain, jaw mobility, cervical proprioception, sleep quality, and depressive symptoms in individuals with bruxism. Although intergroup differences were not significant, greater improvements in cervical joint position sense and sleep quality were observed in the taping group, highlighting the value of combined interventions targeting both jaw and cervical regions.

Findings support the growing evidence that supervised jaw exercises, especially with stretching, are effective for TMD, as confirmed by a recent network meta-analysis.[22] Additionally, improved cervical proprioception in the taping group aligns with research linking TMD and bruxism to cranio-cervical sensorimotor deficits.[23-25] Kinesiology taping may enhance joint position sense by stimulating mechanoreceptors, and previous studies have shown it reduces cervical joint position error.[26] These results underscore the importance of incorporating cervical-focused strategies in bruxism rehabilitation.

Our study demonstrated significant reductions in jaw pain and improvements in mandibular range of motion following an exercise and kinesiology taping protocol. These findings align with existing evidence supporting physiotherapy as an effective approach for managing TMD and bruxism. Zhang et al. reported that jaw exercises are as effective as stabilization splints in improving pain and mouth opening.[27] Similarly, Kadıoğlu et al. found that an 8-week physiotherapy program reduced TMD pain and symptom severity in bruxism patients.[14] Conservative interventions were shown to be as effective as occlusal appliances in improving function.[13,28] Although some studies suggest that adding kinesiology taping to exercise enhances outcomes.[28] We found no additional benefit, possibly due to differences in taping techniques or shorter treatment duration. This contrasts with findings by Yazici et al., who reported immediate pain reduction with taping and manual therapy in bruxism.[15] Notably, our protocol did not include manual therapy, which may have influenced results. Overall, these findings support the use of multimodal physiotherapy including exercise, taping, and manual techniques as a non-invasive, evidence based strategy for TMD and bruxism management.[13,14,27,28]

This study observed a reduction in self-reported depression levels following the intervention, highlighting the link between bruxism and psychological well-being. Psychological factors such as stress, anxiety, and depression play a key role in the etiology and severity of bruxism.[13] Bruxism is often considered a psychosomatic condition, with higher anxiety levels frequently reported among affected individuals.[13] Improvements in mood may result from reduced pain and improved sleep, while pre-existing psychological distress may also contribute to bruxism onset.[29] The type of bruxism may influence this relationship: while stress and anxiety are linked to both awake and sleep bruxism, depression appears more closely associated with awake bruxism.[30] These findings underscore the importance of incorporating stress management and psychological support into physiotherapeutic care.

The improvements in sleep quality observed in individuals with bruxism emphasize the importance of addressing sleep-related factors in physiotherapy. Bruxism is frequently associated with disrupted

sleep architecture, psychological distress, and increased daytime fatigue.[22,29] Evidence suggests that physiotherapeutic interventions, such as exercise and manual therapy, can reduce pain and enhance sleep quality.[14] By targeting nocturnal muscle hyperactivity, these approaches may help restore healthier sleep patterns. Therefore, sleep assessment should be considered a routine component of physiotherapy in bruxism management.

In conclusion, both exercise and kinesiology taping were effective in alleviating bruxism symptoms and enhancing physical and psychological well-being. However, limitations such as short intervention duration, lack of long-term follow-up, gender imbalance, and unassessed sleep-related factors should be addressed in future studies with larger and more diverse populations.

***Ethics Committee Approval:*** Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Istanbul Medipol University (Date: 08.06.2023, decision no: 526). All procedures adhered to the ethical standards set forth in the Declaration of Helsinki for research involving human subjects. Informed consent was obtained from all participants prior to their enrollment in the study.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

***Author Contributions:*** Concept – SC, BM; Supervision – SC, BM; Materials – SC, BM; Data Collection and/or Processing – SC, BM; Analysis and/or Interpretation – SC, BM; Writing –SC, BM.

***Peer-review:*** Externally peer-reviewed.

***Other Information:*** This study is based on research conducted as part of a Master's thesis.

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# Curcumin Reduces High-dose Morphine-Induced Apoptosis and Oxidative Neurotoxicity via TRPV4 Cation Channel Suppression

# Kurkumin Yüksek Doz Morfinin Neden Olduğu Apoptozis ve Oksidatif Nörotoksisiteyi TRPV4 Katyon Kanalını Düzenleyerek Azaltır

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**ABSTRACT**

**Objective:** Long-term and high-dose morphine (H-MRP) treatments for neuropathic pain cause the body to become extremely susceptible to morphine tolerance, which increases the amount of toxic reactive oxygen species (ROS), apoptosis, and calcium ($Ca^{2+}$) entering the neuron. It has been known that curcumin (CRC) decreased these increases in ROS-damaged SH-SY5Y cells by blocking the TRPV4 cation channel. It has not been studied whether CRC can also suppress the high levels of ROS and apoptosis caused by H-MRP in SH-SY5Y cells by affecting TRPV4. So, the study was carried out to investigate whether CRC can suppress the high level of mitochondrial ROS and apoptosis.

**Materials and Methods:** In the SH-SY5Y, four primary groups were induced as control, normal morphine (N-MRP) (50 µM for 24h), H-MRP (500 µM for 24h), H-MRP + CRC (5 µM for 24h).

**Results:** While the incubations of TRPV4 antagonist (ruthenium red) and CRC decreased the H-MRP-induced increases of apoptosis, caspase-3, caspase-8, caspase-9, ROS, mitochondrial dysfunction, debris number, and lipid peroxidation levels, the TRPV4 agonist (GSK1016790A) stimulation further increased these levels. The CRC increased glutathione, glutathione peroxidase, live cell number, and cell viability percentage, all of which were decreased by H-MRP.

**Conclusions:** The levels of H-MRP-induced neuronal death and mitochondrial oxidative stress were reduced by CRC treatment through TRPV4 inhibition. For H-MRP-induced mitochondrial oxidative neuronal injury, CRC is a potential treatment option.

**Keywords**: Curcumin, neuronal injury, mitochondrial oxidative stress, morphine, TRPV4 channel

**ÖZ**

**Amaç:** Nöropatik ağrıyı tedavi etmek için yüksek doz (H-MRP) ve uzun süreli morfin uygulanması kullanılır. Bununla birlikte, H-MRP tedavisi, morfin toleransı, aşırı reaktif oksijen türleri (ROS) üretimi, apoptozis ve $Ca^{+2}$ akışının artmasına neden olur. Sinir hasarı nedeniyle zarar gören SH-SY5Y sinir hücrelerinde, kurkumin (CRC) TRPV4 katyon kanalını inhibe ederek ROS'un neden olduğu apoptozis artışını azaltır. H-MRP, SH-SY5Y hücrelerinde TRPV4 katyon kanalını inhibe ederek aşırı ROS ve apoptozis oluşumunu önlemek için CRC etkisi henüz araştırılmamıştır. Bu çalışmada, CRC tedavisinin TRPV4 kanalını düzenleyerek mitokondriyal ROS üretimini ve apoptozis oluşumunu H-MRP inkübasyonunu nasıl etkilediğini SH-SY5Y hücrelerinde araştırıldı.

**Materyal ve Metot:** SH-SY5Y hücrelerinde dört ana grup oluşturuldu. Bunlar; kontrol, normal morfin (N-MRP) (50 µM ve 24 saat), H-MRP (500 µM ve 24 saat) ve H-MRP + CRC (5 µM ve 24 saat).

**Bulgular:** TRPV4 agonisti (GSK1016790A) ile inkübasyon, ROS, mitokondriyal fonksiyon bozukluğu, debris (ölü hücre artığı), apoptosis, kaspaz -3, kaspaz -8, kaspaz -9 ve lipit peroksidasyon düzeylerini artırdı. Bununla birlikte, TRPV4 antagonisti (rutenyum kırmızısı) ve CRC inkübasyonları bu artışları azalttı. Rutenyum kırmızısı ve CRC inkübasyonları, H-MRP inkübasyonunun neden olduğu hücre canlılığı yüzdesi, canlı hücre sayısı, glutatyon ve glutatyon peroksidaz düzeyleri azalışlarını artırdı.

**Sonuç:** CRC tedavisi, TRPV4 kanalını baskılayarak H-MRP'nin mitokondriyal oksidan ve sinir hücre ölümü etkilerini azalttı. H-MRP neden olduğu mitokondriyal oksidatif stres ve sinir hücre harabiyetini önlemek için CRC tedavisi alternatif bir kaynak tedavi olarak gözükmektedir.

**Anahtar Kelimeler**: Kurkumin, sinir hasarı, mitokondriyal oksidatif stres, morfin, TRPV4 kanalı

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## INTRODUCTION

Present chronic pain management methods are typically ineffective and insufficient. Neuropathic pain is commonly treated with opioids, such as morphine.[1] Conversely, prolonged exposure to large doses of morphine causes analgesic tolerance.[1] Morphine analgesic tolerance lowers endogenous antioxidant levels and induces oxidative stress in a dose-dependent manner.[2] So, morphine has antiapoptotic and antioxidant properties at normal dosages, but at high doses (H-MRP), it can increase $Ca^{2+}$ influx and cause cell death and damage in neuronal cell lines and experimental animal models due to mitochondrial reactive oxygen species (ROS).[3,4,5]

As a natural taste and polyphenol with numerous neuroprotective and cognitive-increasing features, curcumin (CRC) is one of the therapeutic plants that has a significant impact on opioid dependence in cells.[6,7] There is evidence that CRC reduces morphine dependency in the hippocampus via having anti-apoptotic and antioxidant properties.[8] Furthermore, CRC has been demonstrated to prevent opioid tolerance and dependence by inhibiting $Ca^{2+}$ influx through the modification of $Ca^{2+}$/calmodulin-dependent protein kinase II.[9] In an animal model of neurodegenerative disorders, CRC has also been shown to inhibit neuronal cells.[10]

Numerous biological processes, including as morphine-induced oxidative stress and death, have been shown to need the TRP, a non-selective cation channel superfamily.[7,11] In the TRP superfamily, TRP vanilloid 4 (TRPV4) is a member. GSK1016790A (GSK) and $H_2O_2$ are two examples of pharmaceutical substances that activate TRPV4.[12] Prior research showed that non-selective TRPV4 inhibitors, such as ruthenium red (RuR), reduced oxidant and apoptotic indicators.[12,13,14] Moreover, TRPV4 has been demonstrated to be highly expressed in SH-SY5Y neuronal cells,[15] and it has been reported that TRPV4 inhibition in SH-SY5Y cells results in oxidative and apoptotic effects via stimulating GSK.[16]

CRC improves mitochondrial activity, scavenges free radicals, including ROS and lipid peroxidation (LPO), and reduces tissue oxidative damage in SH-SY5Y neural cells.[13,14] CRC also inhibits ROS-sensitive TRP channels, including TRPV4 and TRP melastatin 2 (TRPM2).[12,13,14,16, 17] The injection of resveratrol in diabetes mellitus reduced the increases caused by morphine-mediated stimulation, which increased ROS, caspases, and apoptosis due to an excessive $Ca^{2+}$ influx.[5,11,16]

The suppression of oxidative stress-dependent TRP channel inhibition thereby influenced the degree of morphine-induced oxidative damage and apoptosis. CRC has not yet been investigated for its ability to suppress the disruptive effects of H-MRP on neuronal cells via modulating TRPV4. Thus, this investigation was realized to determine the protective effect of CRC on H-MRP-induced mitochondrial oxidative stress and apoptosis in SH-SY5Y neuronal cells.

## MATERIALS AND METHODS

***Ethics Committee Approval:*** The ethics committee accepted the study, which used cells cultivated using commercial cell culture. Ethics committee approval of this project is not required.

***Cells:*** A common cell line used in TRPV4 research, including morphine addiction and numerous neurological disorders, is SH-SY5Y.[12,13,18] For this reason, the cells (ATCC, VA, USA) were employed in the current investigation as a model for neural cell culture. The SH-SY5Y was cultivated in a cell culture setting, as documented in earlier research.[12,14,17] 90% DMEM/Ham's F12 equal mixture, 10% fetal bovine serum, and 1% antibiotic mixture comprised the medium mixture.[12, 17]

***Experimental Groups:*** Four groups—control (CON), N-MRP, H-MRP, and H-MRP + CRC—were each given a 25 $cm^2$ sterile flask with $1x10^7$ SH-SY5Y cells. In the plate reader experiments, the TRPV4 channel in the cells of four groups was activated with 100 nM GSK despite being blocked by 1 μM RuR incubation.[13,17]

In the incubator, the SH-SY5Y cells in the CON group were maintained for twenty-four hours. The cells in the N-MRP and H-MRP groups were cultured for 24h after being treated with 50 μM and 500 μM of MRP, respectively.[23] 500 μM morphine and 5 μM CRC (Sigma–Aldrich Inc., St. Louis, MO, USA) were administered to the cells of the H-MRP and CRC combination group for a duration of 24h.[13,17]

N-MRP doses were reported in different cells between 10 μM and 50 μM, although the H-MRP dose in the cells was reported between 500 μM and 1000 μM.[5,19,20] Hence, the N-MRP dose was used as 50 μM, although the H-MRP dose was used as 500 μM in the SH-SY5Y cells of the current study.

Stock solutions of CRC, GSK, and RuR were prepared in dimethyl sulfoxide. Then their appropriate concentrations were added to the cell culture medium.

***Cell Viability, Number and Debris Counts*:** Debris (organic waste left over after cell death) and cells were counted using a Casy Modell TT automatic cell counter (Roche, Reutlingen, Germany).[13,17] The percentage changes were used to display the cell viability. But for viable cell counts, $x10^7$ per milliliter was employed, and for debris numbers, $x10^6$ per milliliter.

***Analyses for Apoptosis, Cell Viability, Caspase-3, -8, and -9:*** A commercial APOPercentage kit

(Biocolor Ltd., Co Antrim, UK) was utilised to measure the apoptosis of SH-SY5Y. By employing the Infinite PRO 200 microplate reader (Tecan Austria GmbH, Groedig, Austria), changes in apoptosis were identified in absorbance at 550 nm.[16,17]

The CASY cell viability electronic count analysis was performed in conjunction with MTT for the cell viability experiments. Each white well received 100 microliters of MTT (five mg per ml) in 1xPBS, and the cells were then incubated for 3–4 hours at 37 °C. Five hundred microliters of dimethyl sulfoxide were employed to dissolve the formazan crystals. Following a minute of shaking the 96 white well plates, a microplate reader (Infinite 200 PRO) was used to measure the absorbance at 492 nm.[16,17]

The Infinite PRO 200 microplate reader was used to measure the cleavage of the substrates for caspase-3 (Ac-DEVD-AMC), caspase-8 (Ac-VETD-AMC), and caspase-9 (Ac-LEHD-AFC) (Bachem, Heidelberg, Germany). Under the Infinite PRO 200, the excitation (380 nm) and emission (460 nm) wavelengths were kept constant. The alterations of the caspases were captured by the fluorescence units.[16,17]

These ApoPercentage and substrate loadings were followed by 30-minute cell stimulation with 100 nM GSK, either with or without a TRPV4 inhibitor (1 μM RuR), in order to quantify the TRPV4-dependent apoptosis induction and caspase releases in the cells of four groups. Once the fluorescence units were determined, the results related to caspases and apoptosis were shown as percentage changes from the control (fold increase).

***Analyses for Measuring ROS Generation and Mitochondrial Membrane Dysfunction:*** The ROS probe (DCFH-DA) (Cat # D399, Thermo Fisher Scientific) and JC-1 dye (2 μg/ml; Cat # T3168, Thermo Fisher Scientific) were used to incubate the cells in order to analyze ROS generation and mitochondrial membrane malfunction. Following that, the cells were incubated for 30 minutes at 37 °C in the dark. After that, the changes of DCFH-DA and JC-1-stained cells in fluorescence intensity were recorded using an Infinite Pro 200 plate reader. Following the measurement of fluorescence intensity, the results were displayed as a percentage of the control (experiment/control).

The cells of four groups were stimulated with 100 nM GSK for 30 minutes, either with or without a TRPV4 inhibitor (1 μM RuR), after these DCFH-DA and JC-1 loadings, in order to quantify the TRPV4-dependent ROS and mitochondrial dysfunction. Following the calculation of fluorescence units, the ROS and mitochondrial dysfunction data were shown as percentage changes from the control (fold increase).

***Glutathione (GSH), Lipid Peroxidation (LPO) and Glutathione Peroxidase (GSH-Px) Analysis:*** In the frozen SH-SY5Y samples, the total protein content and the optic density (absorbance) values of LPO (532 nm), GSH (412 nm), and GSH-Px (412 nm) were measured using a spectrophotometer (Shimadzu-UV1800, Kyoto, Japan). The concentrations of GSH and LPO in SH-SY5Y were expressed in micromoles per gram of protein. IU per g of protein is the measure of GSH-Px activity in the SH-SY5Y cells.

***Analysis of the Data:*** The data is presented as mean standard deviation (SD). The comparison was done using one-way analysis of variance followed by Tukey's post hoc test to compare between groups (SPSS, Inc., Chicago, IL, USA), where p-values less than 0.05 were identified.

## RESULTS

The cell viability percentage (Figure 1A) and viable cell number (Figure 1B) of H-MRP groups were lower than those of the control (CON) and N-MRP groups, but they were higher in the H-MRP + CRC group than in the H-MRP group ($p < 0.05$). The H-MRP group had a higher debris number (Figure 1C) CON and N-MRP groups, whereas the supplementation of CRC in the H-MRP + CRC group had a lower debris number than the H-MRP group ($p < 0.05$).

Compared to the CON, H-MRP, and H-MRP + CRC, the CON + GSK, H-MRP + GSK, and H-MRP + CRC + GSK groups showed higher percentages of apoptosis (Figure 2), caspase-3 (Figure 3A), caspase -8 (Figure 3B), and caspase-9 (Figure 3C) ($p < 0.05$). For the CON + GSK + RuR, H-MRP + GSK + RuR, and H-MRP + CRC + GSK + RuR groups, however, the treatments of RuR and CRC reduced their percentages ($p < 0.05$).

In the CON + GSK, H-MRP + GSK, and H-MRP + CRC + GSK groups, JC-1 (Figure 4A) and DCFH-DA (Figure 4B) were higher than in the CON, H-MRP, and H-MRP + CRC, respectively ($p < 0.05$). For the CON + GSK + RuR, H-MRP + GSK + RuR, and H-MRP + CRC + GSK + RuR groups, however, the treatments of RuR and CRC reduced their percentages ($p < 0.05$).

In comparison to the H-MRP + CRC group, the GSH level (Figure 5A) and GSH-Px activity (Figure 5B) of the H-MRP groups were lower ($p < 0.05$) but higher than those of the CON and N-MRP groups. The LPO level was lower in the H-MRP + CRC group than in the H-MRP group ($p < 0.05$), whereas the LPO level was greater in the H-MRP group (Figure 5C) than in the control (CON) and N-MRP groups.

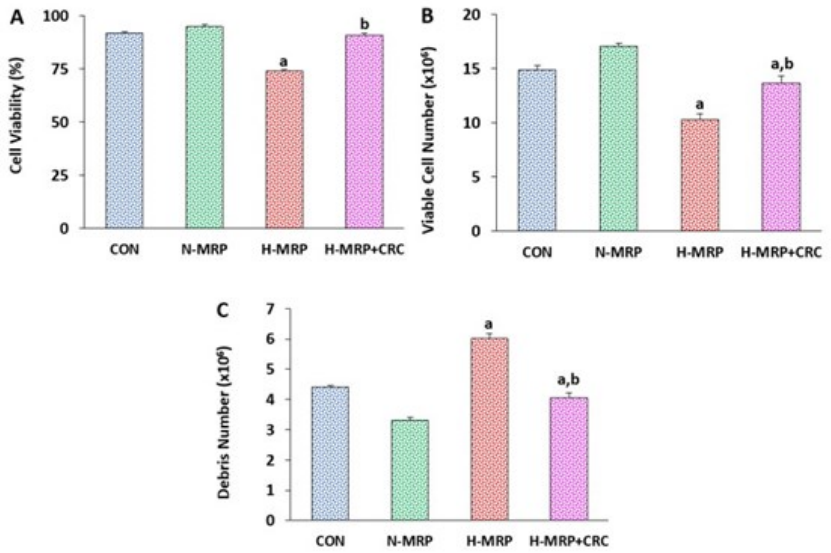


**Figure 1.** The cell viability percentage, viable cell count, and debris number of SH-SY5Y cells changed when CRC (5 µM) was incubated with H-MRP (500 µM). (Mean ± SD). **A**. cell viability percentage. **B.** Viable cell number. **C**. Debris number. ([a]p < 0.05 versus (*vrs.)* CON and N-MRP. [b]p < 0.05 *vrs.* H-MRP).

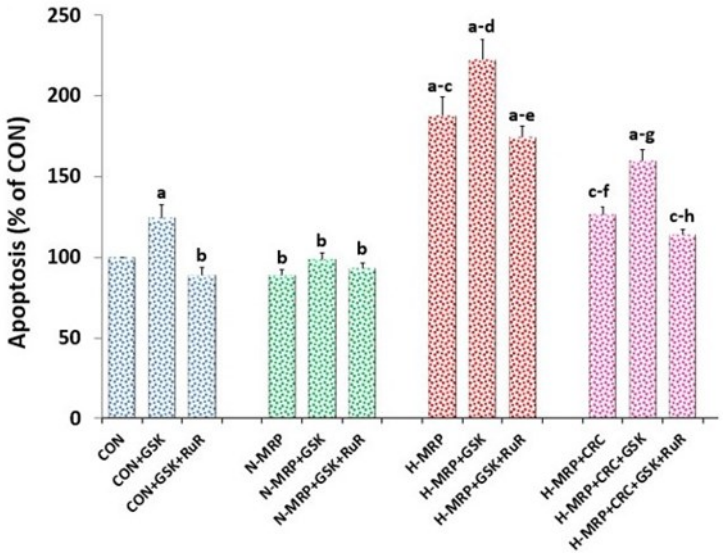


**Figure 2.** The incubation of CRC (5 µM) modulated H-MRP (500 µM), causing an increase in apoptosis in the SH-SY5Y. (Mean ± SD and n=3). Apoptosis percentage. The TRPV4 channel in the cells was stimulated by 100 nM GSK, although it was inhibited by 1 µM RuR. ([a]p < 0.05 versus (*vrs.)* control (CON) and N-MRP. [b]p < 0.05 *vrs.* CON+GSK. [c]p < 0.05 *vrs.* N-MRP, N-MRP + GSK, and N-MRP + GSK + RuR. [d]p < 0.05 *vrs.* H-MRP. [e]p < 0.05 *vrs.* H-MRP + GSK. [f]p < 0.05 *vrs.* H-MRP + GSK + RuR. [g]p < 0.05 *vrs.* H-MRP + CRC. [h]p < 0.05 *vrs.* H-MRP + CRC + GSK).

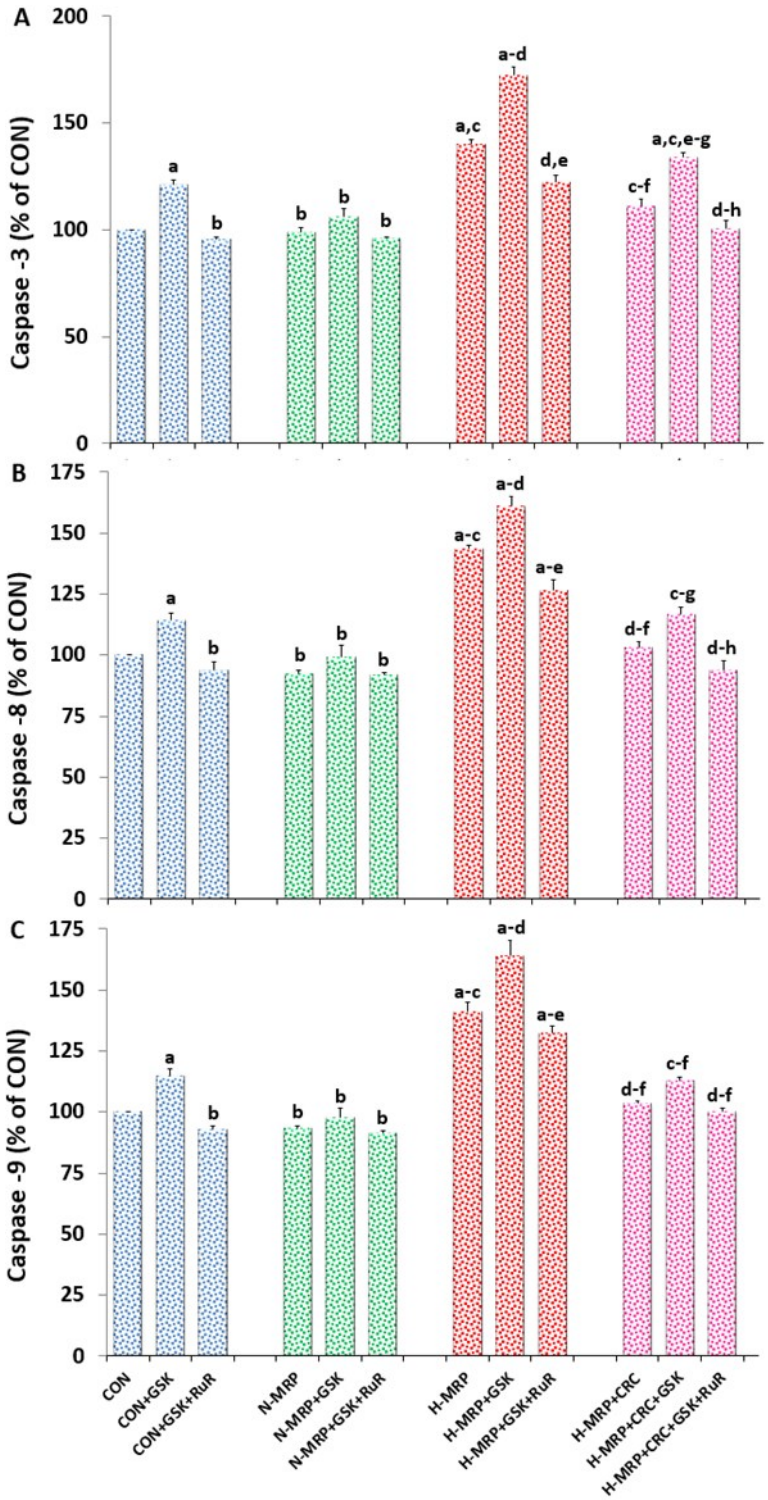


**Figure 3.** The incubation of CRC (5 µM) modulated H-MRP (500 µM), causing an increase in caspase percentages in the SH-SY5Y. (Mean ± SD and n=3). **A.** Caspase-3 percentage. **B**. Caspase -8 percentage. **C**. Caspase -9 percentage. TRPV4 channel in the cells was stimulated by 100 nM GSK, although it was inhibited by 1 µM RuR. ($^{a}p < 0.05$ versus (*vrs.)* control (CON) and N-MRP. $^{b}p < 0.05$ *vrs.* CON+GSK. $^{c}p < 0.05$ *vrs.* N-MRP, N-MRP + GSK, and N-MRP + GSK + RuR. $^{d}p < 0.05$ *vrs.* H-MRP. $^{e}p < 0.05$ *vrs.* H-MRP + GSK. $^{f}p < 0.05$ *vrs.* H-MRP + GSK + RuR. $^{g}p < 0.05$ *vrs.* H-MRP + CRC. $^{h}p < 0.05$ *vrs.* H-MRP + CRC + GSK).

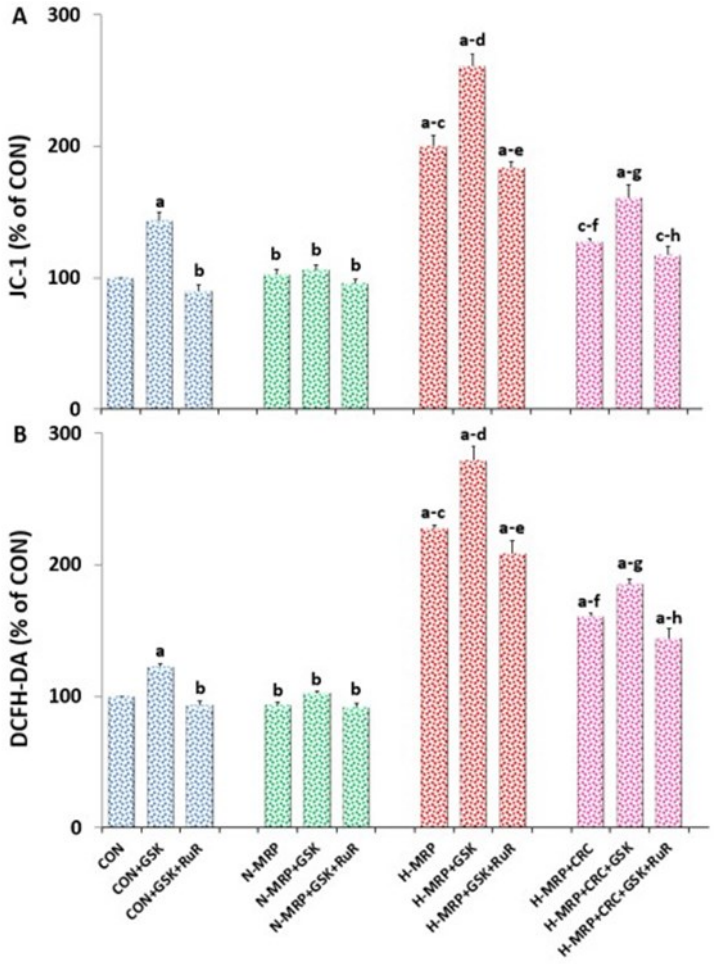


**Figure 4.** The incubation of CRC (5 µM) modulated H-MRP (500 µM), causing an increase in mitochondrial dysfunction (JC-1) and ROS (DCFH-DA) percentages in the SH-SY5Y**.** (Mean ± SD and n=3). A. JC-1 percentage. B. DCFH-DA percentage. TRPV4 channel in the cells was stimulated by 100 nM GSK, although it was inhibited by 1 µM RuR. ($^{a}p < 0.05$ versus (*vrs.)* control (CON) and N-MRP. $^{b}p < 0.05$ *vrs.* CON+GSK. $^{c}p < 0.05$ *vrs.* N-MRP, N-MRP + GSK, and N-MRP + GSK + RuR. $^{d}p < 0.05$ *vrs.* H-MRP. $^{e}p < 0.05$ *vrs.* H-MRP + GSK. $^{f}p < 0.05$ *vrs.* H-MRP + GSK + RuR. $^{g}p < 0.05$ *vrs.* H-MRP + CRC. $^{h}p < 0.05$ *vrs.* H-MRP + CRC + GSK).

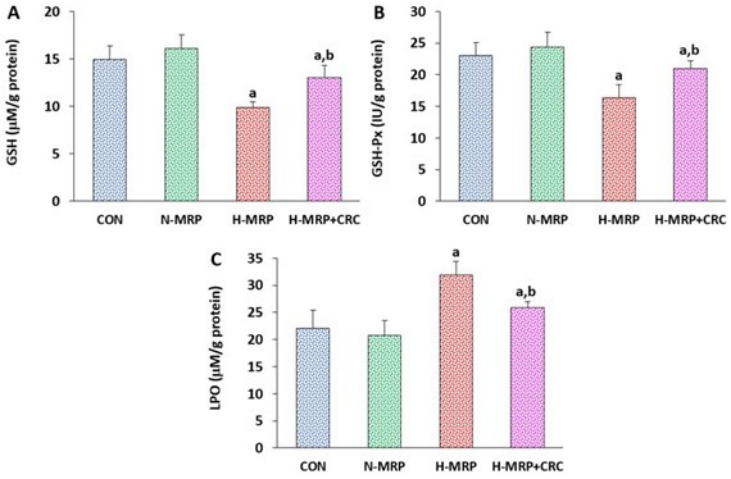


**Figure 5.** The incubation of CRC (5 µM) modulated H-MRP (500 µM), causing changes in glutathione (GSH), glutathione peroxidase (GSH-Px), and lipid peroxidation (LPO) in the SH-SY5Y cells. (Mean ± SD). A. GSH. B. GSH-Px. C. LPO. ($^{a}p < 0.05$ versus (*vrs.)* CON and N-MRP. $^{b}p < 0.05$ *vrs.* H-MRP.

## DISCUSSION AND CONCLUSION

I found that giving CRC to the neuronal cells reduced the H-MRP-mediated increase in oxidative neurotoxicity and apoptosis in the current study by inhibiting the TRPV4 cation channel and increasing GSH and GSH-Px.

Morphine affects intracellular $Ca^{2+}$ levels in two ways. According to certain research, administering H-MRP reduced the level of $Ca^{2+}$ in many brain regions.[4] Increased binding sites to voltage-gated calcium channel blockers (nimodipine) are prevented when morphine and $Ca^{2+}$ channel blockers are administered at the same time.[4] TRPM2 channel blockers may increase ATP generation in SH-SY5Y and experimental animal neurons while reducing mitochondrial oxidative damage.[12–16] TRPM2 cation channel stimulation enhanced the oxidant and apoptotic effects of morphine, while its inhibition reduced these effects in the mouse and rat dorsal root ganglion.[16,22] The results in the dorsal root ganglion showed a comparable protective effect from TRPV1 channel blockage.[23] To the best of my knowledge, no studies have examined how TRPV4 affects the oxidative and apoptotic characteristics of H-MRP in brain cells. While the TRPV4 antagonist (RuR) decreased the apoptotic and oxidant activities of H-MRP in the SH-SY5Y cells, TRPV4 activation in the current study further increased them. It seems that while oxidative damage and neuronal death were decreased when TRPV4 stimulation-mediated $Ca^{2+}$ influx was decreased, both events were increased when TRPV4 stimulation-mediated $Ca^{2+}$ influx was increased.

TRPV4 stimulation results in increased mitochondrial $Ca^{2+}$ uptake in the kidney, dorsal root ganglion, and SH-SY5Y cells. This leads to an increase in ROS production and cell death indicators (apoptosis, caspase-3, caspase-8, and caspase-9) that are caused by dysfunction of the mitochondrial membrane.[12,13,16] The effects of morphine on the rat hippocampal TRPM2 stimulator have been reported.[7] The oxidant (ROS and LPO) and apoptotic (caspase-3, caspase-8, and caspase-9) indicators are thus enhanced as a result of TRPV4 stimulations and increased mitochondrial membrane failure.[4] Conversely, the percentage of oxidant and apoptotic indicators, such as SH-SY5Y, in neural cells is decreased when TRPV4 is suppressed.[12,13,16] The information that is now available indicates that H-MRP-induced TRPV4 activation was the source of the increased mitochondrial membrane dysfunction in SH-SY5Y. In turn, this resulted in a decrease in cell viability but an increase in caspase-3, -8, and -9, ROS, LPO, and apoptosis. TRPV4 blocker (RuR) and CRC treatment influenced the changes. According to the current findings, CRC incubation decreased Parkinsonism-induced increases in mitochondrial dysfunction, ROS, LPO, caspases, and apoptosis in SH-SY5Y cells by inhibiting TRPV4.[13] In mice, morphine therapy altered the anti-hyperalgesic effects of neurotoxin GsMTx4-based 17-residue peptide, which inhibits TRPV4.[24] By raising GSH-Px activity and GSH levels in the rat hippocampal region, the CRC therapy enhanced H-MRP-induced elevations in LPO, caspase-3, and caspase-9 activities.[8] The TRPV4 channel was stimulated in human embryonic kidney 293 and mesenteric artery endothelial cells by CRC, which is contrary to the findings.[25] The CRC treatment reduced the rise in nitric oxide radicals and H-MRP-induced memory impairment in the brain of rats.[7]

The observed reductions in GSH-Px activity and GSH level suggest that components of the thiol redox antioxidant system contribute to regulating the oxidative imbalance induced by H-MRP. After incubation with CRC or TRPV4 suppression with RuR, the oxidative effects of H-MRP decreased, as shown by lower levels of ROS and LPO, while GSH levels and GSH-Px activity increased. These findings imply that RuR and CRC increase GSH levels and GSH-Px activity while decreasing LPO and ROS. It is well-known that GSH-Px transforms $H_2O_2$ into water. GSH is used as a substrate by GSH-Px during the process. The antioxidant property of CRC is responsible for its strong scavenging of a range of oxidants, such as superoxide radicals, hydroxyl radicals, and $H_2O_2$.[26,27,28] Consistent with the findings, CRC therapy has been shown to restore GSH level and GSH-Px activity in SH-SY5Y cells while lowering LPO concentration.[13] The LPO caused by H-MRP was also reduced by the CRC treatment by raising GSH-Px activity and GSH levels in the rat hippocampal region.[8] Present results are in line with these observations.[8,13]

In conclusion, TRPV4 attenuation during CRC incubation protected SH-SY5Y cells from H-MRP-mediated apoptotic and oxidative mediators because TRPV4 inhibition downregulated neuronal damage. Even while CRC therapy reduces H-MRP-induced oxidative neurotoxicity and apoptosis, it may still trigger TRPV4-mediated caspases, ROS, mitochondrial dysfunction, and LPO, which in turn may produce H-MRP-induced oxidative damage and apoptosis.

***Ethics Committee Approval:*** The ethics committee accepted the study, which used cells cultivated using commercial cell culture. Ethics committee approval of this project is not required.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

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HÖO.

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# Assessment of the Presence of Infraorbital Foramen and Accessory Foramen in Adolescent and Adult Populations Using Cone Beam Computed Tomography

# Adölesan ve Yetişkin Popülasyonlarda İnfraorbital Foramen ve Aksesuar Foramen Varlığının Konik Işınlı Bilgisayarlı Tomografi Kullanılarak Değerlendirilmesi

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**ABSTRACT**

**Objectives**: This study aimed to evaluate the vertical and horizontal dimensions, shape, anatomical location of the infraorbital foramen (IOF) and the presence of accessory infraorbital foramen (AIOF) in adolescent and adult individuals using cone-beam computed tomography (CBCT). Additionally, it aimed to contribute to clinical applications and address the lack of data on the adolescent population in the literature.

**Materials and Methods**: CBCT images of 1,000 patients who presented to the Department of Oral and Maxillofacial Radiology between 2021 and 2023 were retrospectively reviewed. A total of 315 individuals (193 males, 122 females) who met the inclusion criteria were included in the study. The dimensions of the IOF, its distances to adjacent anatomical landmarks, its shape, and the presence of AIOF were evaluated.

**Results:** In this study, IOF dimensions were larger in males, with the horizontal width greater on the right and the vertical height greater on the left. The most common IOF shape was circular, and accessory foramina were present in 31.6% of individuals, more frequently in males on the right. A statistically significant variation in the distance between the IOF and the midline (IOF-ML) with respect to age was observed on the right.

**Conclusions**: Detailed knowledge of the IOF's location, shape, and variations is crucial for preventing complications during surgical procedures, particularly infraorbital nerve blocks. The dimensions of the infraorbital foramen and its distances to anatomical landmarks in adolescents are generally similar to those in the adult population.

**Keywords**: Adolescent, adult, anatomic variation, cone-beam computed tomography, foramen

**ÖZ**

**Amaç:** Bu çalışma, konik ışınlı bilgisayarlı tomografi (KIBT) kullanılarak adölesan ve yetişkin bireylerde infraorbital foramenin (IOF) dikey ve yatay boyutlarını, şeklini, anatomik konumunu ve aksesuar infraorbital foramen (AIOF) varlığını değerlendirmeyi amaçlamıştır. Ayrıca, literatürde adölesan popülasyona dair veri eksikliğini gidermeye ve klinik uygulamalara katkıda bulunmayı hedeflemiştir.

**Materyal ve Metot:** 2021-2023 yılları arasında Ağız, Diş ve Çene Radyolojisi Anabilim Dalı'na başvuran 1.000 hastanın KIBT görüntüleri retrospektif olarak incelenmiştir. Çalışma dahil kriterlerini karşılayan toplam 315 birey (193 erkek, 122 kadın) çalışmaya dahil edilmiştir. IOF'nin boyutları, çevre anatomik yapılara olan mesafeleri, şekli ve AIOF varlığı değerlendirilmiştir.

**Bulgular:** Bu çalışmada, erkeklerde IOF boyutlarının daha büyük olduğu, yatay genişliğin sağ tarafta, dikey yüksekliğin ise sol tarafta daha fazla olduğu bulunmuştur. En yaygın IOF şekli dairesel olup, aksesuar foramenler bireylerin %31,6'sında, daha çok erkeklerde ve sağ tarafta gözlemlenmiştir. IOF ile orta hat (IOF-ML) arasındaki mesafenin yaşa göre sağ tarafta istatistiksel olarak anlamlı farklılık gösterdiği saptanmıştır.

**Sonuç:** IOF'nin yeri, şekli ve varyasyonları hakkında detaylı bilgi, özellikle infraorbital sinir blokları olmak üzere cerrahi prosedürler sırasında komplikasyonları önlemek için çok önemlidir. Adölesanlarda infraorbital foramenin boyutları ve anatomik dönüm noktalarına olan mesafeleri genellikle yetişkin popülasyondakilere benzerdir.

**Anahtar Kelimeler:** Adölesan, açıklık, anatomik varyasyon, konik ışınlı bilgisayarlı tomografi, yetişkin

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## INTRODUCTION

The infraorbital foramen is an anatomical opening located in the maxillary bone through which the infraorbital nerve (ION), artery, and vein pass. The infraorbital nerve arised from the trigeminal ganglion and emerges through the IOF, providing sensory innervation to the upper cheek, lower eyelid, parts of the nasal region, upper lip, and maxillary sinus.[1,2]

One of the fundamental principles in surgical practice is to avoid injury to critical anatomical structures during any operative intervention. In this context, the IOF holds particular significance across various medical specialties, including otolaryngology, ophthalmology, plastic surgery, and dentistry, especially in oral and maxillofacial surgery. Additionally, it serves as a crucial landmark for accessing the maxillary sinus externally, as utilized in procedures like Caldwell-Luc surgery.[3-8]

ION block is crucial in performing these procedures. It also plays a significant role in postoperative pain management and the treatment of trigeminal neuralgia.[1-6]

An AIOF represents an anatomical variation characterized by a smaller aperture located near the primary IOF. This AIOF typically combines with either the infraorbital canal or the orbital floor. The ION is observed in four main branches: internal nasal, external nasal, lower palpebral and upper lip. The AIOF may transmit one or more of these branches.[3-7]

Consequently, precise knowledge of the IOF's anatomical location, its spatial relationships with adjacent structures, and its anatomical variations is of critical importance. Such knowledge is essential not only for the prevention of iatrogenic injury but also for improving the efficacy of regional nerve blocks in this area.[9]

Numerous studies have shown considerable changeability in the shape and location of the IOF among different populations and ethnic groups.[3,5,7,9,10]

This study aims to assess the vertical and horizontal dimensions, shape, and anatomical location of the IOF in adolescent and adult populations using CBCT, and to determine the prevalence of AIOF. The position, size, and variations of the IOF may change throughout the developmental process. Therefore, evaluating adolescent individuals—whose anatomical structures have not yet fully matured—is important for understanding age-related differences in IOF morphology. The data of our study will contribute to clinical practice by providing reference values for surgical procedures and will fill the data gap in the literature regarding the adolescent population.

## MATERIALS AND METHODS

***Ethics Committee Approval:*** Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Zonguldak Bülent Ecevit University (Date: 17.04.2024, decision no: 2024/07). This study was conducted in accordance with the World Medical Association's Declaration of Helsinki. All patients provided informed consent for the use of their radiographic data in scientific research.

***Samples:*** The sample size was calculated using G*Power 3.1 software, based on a significance level of 5% ($\alpha = 0.05$), 80% statistical power ($1-\beta = 0.80$), and a medium effect size (Cohen's $d = 0.5$). Power analysis revealed that a minimum of 128 participants (64 per group) was required to detect statistically significant differences between two independent groups. In this study, CBCT images of 1,000 patients referred to the Department of Oral and Maxillofacial Radiology, Faculty of Dentistry, Zonguldak Bülent Ecevit University, for diagnostic purposes between 2021 and 2023 were retrospectively reviewed. A total of 315 patients (193 males, 122 females) aged between 10 and 74 years meeting the inclusion and exclusion criteria were included in the study. Thus, the power of the study was further increased. CBCT images were obtained using the Veraviewepocs 3D R100 / F40 tomography device (J. Morita Mfg. Corp., Kyoto, Japan) with an 8x10 cm field of view (FOV), 90 kVp, 5 mA, and a voxel size of 0.125 $mm^3$. The CBCT images were analyzed using the i-Dixel 2.0 software (J. Morita Corporation, Osaka, Japan).

***Inclusion Criteria:*** In order for patients to be included in the study, the following criteria were met:

- Their CBCT images were free of artefacts and distortions,
- They gave consent for their radiographic images to be used in scientific studies,
- They were of Turkish nationality.

***Exclusion Criteria:*** Patients were excluded from the study if any of the following existed:

- They had cysts, tumors or craniofacial syndromes in the relevant anatomical region,
- They had prior orthodontic treatment or surgery in the area
- Their CBCT images contained artefacts that hindered evaluation.

In this study, the horizontal and vertical dimensions of the IOF were measured. To determine the anatomical location of the IOF, the distances between the IOF and the infraorbital margin (IOF-IOM), the lateral nasal wall (IOF-LNW), and the midline (IOF-ML) were measured. Additionally, the shape of the IOF was classified, and the presence of an AIOF was also evaluated. The images were evaluated once by consensus between a specialist in oral and maxil-

lofacial radiology with seven years of experience and a research assistant with two years of experience. To assess interobserver reliability, 10% of the images were randomly selected and independently reviewed by both observers. Interobserver agreement was assessed using Kappa statistics, which demonstrated excellent concordance ($\kappa$=0.957, $p<0.001$). In cases of uncertainty, a second evaluator [Assoc. Prof. (G.G.)] was consulted to perform the additional assessment, and the examiners then engaged in further evaluations to reach a final consensus.

***Statistical Analysis:*** Statistical analyses were performed using the SPSS software package, version 22.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics, independent samples t-tests, and Chi-square tests were used for data evaluation. Interventional studies involving animals or humans, as well as other studies requiring ethical approval, must specify the approving authority and provide the corresponding ethical approval code. A significance level of $p<0.05$ was accepted as significant.

## RESULTS

The mean age of the male participants was 47.6±14.1 years (range: 10–74 years), while the mean age for female participants was 44.87±16.2 years (range: 11–73 years). The horizontal dimension of the IOF was larger on the right side, whereas the vertical dimension was greater on the left side (Table 1).

Analysis of IOF shapes revealed that the most common shapes in both genders were circular, oblique oval, vertical oval, and horizontal oval, respectively (Table 2). A statistically significant difference was found between genders for both horizontal and vertical measurements bilaterally, with males having larger values in all parameters ($p=0.0001$) (Table 2). While significant differences favoring males were observed for the IOF-LNW and IOF-ML distances, no statistically significant difference between genders was found for the IOF-IOM distances (Table 3).

**Table 1**. Horizontal and vertical dimensions of the IOF and the mean age of the participants.

| Parameter | Left Horizontal | Left Vertical | Right Horizontal | Right Vertical | Age of male | Age of female |
|---|---|---|---|---|---|---|
| **n** | 315 | 315 | 315 | 315 | 193 | 122 |
| Mean ±SD (mm) | 3.86±0.59 | 4.24±0.65 | 3.87±0.55 | 4.20±0.56 | 47.6±14.1 | 44.87±16.2 |
| Min-Max (mm) | 2.39-6.11 | 2.56-7.32 | 1.96-5.61 | 1.87-6.00 | | |

IOF; infraorbital foramen.

**Table 2.** Horizontal and vertical dimensions of the IOF.

| | Horizontal Length Mean (mm) | Vertical Length Mean (mm) | Circular n (%) | Oblique Oval n (%) | Horizontal Oval n (%) | Vertical Oval n (%) | Total (n) |
|---|---|---|---|---|---|---|---|
| **Male (n=193)** | 4.07 | 4.40 | 166 (43) | 127 (32.9) | 34 (8.8) | 59 (15.3) | 386 |
| **Female (n=122)** | 3.67 | 4.06 | 104 (42.6) | 80 (32.5) | 15 (6.1) | 45 (18.8) | 244 |
| **Total** | 3.87 | 4.23 | 270 (42.8) | 207 (32.8) | 49 (7.9) | 104 (16.5) | 630 |
| **p-value** | **0.0001** | **0.0001** | 0.172 | 0.346 | 0.991 | 0.456 | |

IOF; infraorbital foramen.

**Table 3.** Relationship between IOF position and gender.

| Gender | Left Side IOF-IOM (mm) Mean ± SD | Left Side IOF-LNW (mm) Mean ± SD | Left Side IOF -ML (mm) Mean ± SD | Right Side IOF-IOM (mm) Mean ± SD | Right Side IOF-LNW (mm) Mean ± SD | Right Side IOF-ML (mm) Mean ± SD |
|---|---|---|---|---|---|---|
| **Male (n=193)** | 8.36 ± 1.75 | 12.76 ± 2.74 | 27.25 ± 2.86 | 8.57 ± 1.88 | 12.34 ± 2.83 | 26.97 ± 2.78 |
| **Female (n=122)** | 8.42 ± 1.70 | 11.86 ± 2.74 | 26.13 ± 2.11 | 8.22 ± 1.67 | 11.28 ± 2.70 | 25.79 ± 2.45 |
| **Total** | 8.39 ± 1.73 | 12.41 ± 2.77 | 26.82 ± 2.64 | 8.44 ± 1.81 | 11.93 ± 2.82 | 26.50 ± 2.71 |
| **p-value** | 0.734 | **0.004** | **0.0001** | 0.098 | **0.001** | **0.0001** |

IOF-IOM: infraorbital foramen-infraorbital margin; IOF-LNW: infraorbital foramen-lateral nasal wall; IOF-ML: infraorbital foramen-midline.

Evaluation of the presence of AIOF revealed a total of 199 AIOFs (31.6%) among 315 individuals. A statistically significant difference was observed, with males demonstrating higher rates on the right side. (p = 0.012) (Table 4).

An analysis of the relationship between age groups and distances to anatomical landmarks revealed a statistically significant difference was found only for the IOF-ML distance on the right side (p =0.08). This difference was attributed to the higher mean values observed in the 50–64 age group and the lower values recorded in the 15–19 and 20–34 age groups (Table 5).

**Table 4.** Presence of accessory infraorbital foramen.

| Gender | **Left Side,** n (%) | **Right Side,** n (%) | **Total,** n (%) |
|---|---|---|---|
| **Male (n=193)** | 69 (50.0) | 69 (50.0) | 138 (35.7) |
| **Female (n=122)** | 34 (55.7) | 27 (44.3) | 61 (25) |
| **Total** | 103 (51.7) | 96 (48.3) | 199 (31.6) |
| **p-value** | 0.178 | 0.012 | |

**Table 5.** Mean values of IOF dimensions and distances to anatomical landmarks by age groups.

| Parameter | Side | 10–14 years | 15–19 years | 20–34 years | 35–49 years | 50–64 years | 65–79 years | p-value |
|---|---|---|---|---|---|---|---|---|
| **Horizontal Length (mm)** | Left | 3.58±0.37 | 3.84±0.55 | 3.88±0.64 | 3.83±0.57 | 3.88±0.58 | 4.27±0.80 | 0.09 |
| | Right | 3.69±0.47 | 3.68±0.51 | 3.86±0.62 | 3.88±0.56 | 3.90±0.54 | 4.09±0.53 | 0.55 |
| **Vertical Length (mm)** | Left | 3.96±0.31 | 4.18±0.60 | 4.28±0.68 | 4.28±0.57 | 4.20±0.70 | 4.45±0.92 | 0.56 |
| | Right | 4.27±0.37 | 4.05±0.52 | 4.19±0.59 | 4.18±0.50 | 4.27±0.60 | 4.19±0.59 | 0.83 |
| **IOF-IOM Distance (mm)** | Left | 8.96±1.24 | 8.80±2.36 | 8.63±2.01 | 8.22±1.63 | 8.35±1.62 | 8.50±1.82 | 0.59 |
| | Right | 9.30±1.84 | 8.70±2.42 | 8.55±2.02 | 8.13±1.70 | 8.62±1.71 | 8.63±1.68 | 0.33 |
| **IOF-LNW Distance (mm)** | Left | 13.04±2.27 | 12.76±2.34 | 12.82±2.69 | 12.35± 2.73 | 12.27±2.93 | 12.07±3.02 | 0.65 |
| | Right | 12.70±2.76 | 12.31±2.61 | 12.48±2.74 | 11.76 ±2.70 | 11.75±2.98 | 12.40±3.28 | 0.22 |
| **IOF-ML Distance (mm)** | Left | 25.34±1.22 | 26.54±2.37 | 26.73±3.04 | 26.94 ±2.51 | 26.77±2.74 | 27.52±2.72 | 0.59 |
| | Right | 26.32±0.79 | 25.18±1.54 | 25.77±2.99 | 26.31 ±2.76 | 27.18±2.62 | 26.89±2.91 | **0.008** |

IOF-IOM: infraorbital foramen-infraorbital margin; IOF-LNW: infraorbital foramen-lateral nasal wall; IOF-ML: infraorbital foramen-midline.

## DISCUSSION AND CONCLUSION

The morphometric characteristics of the IOF play a significant role in the application of anesthesia techniques targeting the ION.[11,12] Accurate localization of the IOF and understanding the orientation of the infraorbital canal are essential for achieving effective nerve blockade.[13] During surgical procedures, the neurovascular structures passing through the IOF may be damaged, leading to complications such as paresthesia or anesthesia.[14]

The studies conducted by Sokhn et al.,[5] Dağıstan et al.,[8] and Nanayakkara et al.[10] also investigated the horizontal and vertical dimensions of the IOF, reporting results similar to those found in the present study. However, while the first two studies did not find a statistically significant association between IOF dimensions and gender,[5,8] Nanayakkara et al., in a study on the Sri Lankan population, reported that males exhibited larger dimensions compared to females.[10] Our findings are consistent with the results of the latter study.

Previous research has shown varied results regarding the shape of the IOF. In the Indian population, the most common shape was vertical oval (42.7%),[15] while in the Sri Lankan population, the oval form was most frequently observed.[11] In a separate study on the Lebanese population, the circular shape was predominant (52.4%), consistent with the findings of our study.[5] In a study conducted on the Turkish population,[8] the shapes were generally classified into circular and oval categories, with the oval form being the most frequent (58%). However, upon closer examination, the oval category was further subdivided into oblique, vertical, and horizontal forms. From this perspective, the results of our study align closely with those in the literature. Although the most common shape in our study was circular (42.8%), the overall prevalence of the oval form—when all oval

subtypes are combined—is comparable to the results of other studies conducted on the Turkish population.

Shape variations of the IOF may lead to significant differences in clinical practice. Since the shape affects the size of the foramen and the direction of the nerve's emergence, it can directly influence the success of local anesthesia procedures. It has been reported that small and round foramina may complicate needle positioning, while larger or oval foramina may hinder achieving complete nerve block due to branching of the ION.[16-21]. Moreover, the shape and orientation of the IOF play a critical role in surgical planning.

In the study performed by Dağıstan et al.,[8] no significant association was found between gender and the distances from the IOF to the infraorbital margin, lateral nasal wall, and midline. However, in the study by Sokhn et al.,[5] similar to our findings, a statistically significant relationship was reported between gender and the distances of IOF-LNW and IOF-ML, with greater distances observed in males. Aggarwal et al.[16] reported an average IOF-ML distance of 25.69 ± 2.37 mm, while Gupta[17] found this value to be 28.5 ± 2.6 mm. These studies also found the measured distances to be significantly greater in males. In our study, no significant difference was found between genders regarding the IOF-IOM distance. However, the distances between the IOF-LNW, as well as the IOF-ML, were significantly greater in males. The higher mean values reported may be attributed to ethnic differences among populations.

The studies by Dağıstan et al.,[8] and Sokhn et al.[5] did not report any statistically significant relationship between age groups and the distances from the IOF to anatomical landmarks. In another study conducted by Lee et al., it was demonstrated that the location of the IOF varied between genders, and this variation primarily occurred during the early years of life, stabilizing after the age of 20.[6] In our study, no significant age-related changes in IOF location were observed, and the measured distances showed a similar distribution across all age groups. It is important to note that our sample consisted of individuals aged 10 years and older.

Studies analyzing the IOF and/or AIOF in the adolescent population (ages 10–19) using CBCT are limited.[6,18,19] In the study by Ali et al.,[18] an AIOF was detected in 29% of a patient population ranging in age from 16 to 85 years. In a study by Zdilla et al.,[19] which employed a completely different methodology, the location of the IOF was referenced relative to specific anatomical landmarks. It was reported that, regardless of age, the IOF is located approximately 2 mm from the midpoint between the nasospinale and jugale points. This finding may prove valuable in improving the accuracy of ION block procedures.

In adolescent individuals, the IOF may be positioned more superiorly or medially, which may necessitate adjustments in needle angulation during the administration of local anesthesia. Therefore, given the age-related variability in IOF morphology during adolescence, preoperative evaluation using CBCT is essential to enhance clinical success and minimize the risk of complications.[6,16-19]

It is evident from the literature that the reported prevalence of AIOF varies across different studies. Research conducted on Sri Lankan, Lebanese, Thai, and Iranian populations reported AIOF prevalence rates ranging from 7% to 9%.[5,10,20,21] In studies involving the Indian population, this prevalence was found to be between 20% and 29%.[18,22] Studies have reported highly variable rates in the Turkish population, ranging from 7% to as high as 56%.[7,8] In the present study, the prevalence of AIOF was determined to be 31%. Although these variations suggest that racial and ethnic factors may influence prevalence, the wide range of results reported within the Turkish population indicates that further studies with larger sample sizes are necessary to confirm the significance of ethnic factors in this regard. On the other hand, in our study, high-resolution images were obtained using a voxel size of 0.125 mm³. In the study by Çelebi et al.[7], images were acquired with a voxel size of 0.3 mm at 120 kVp and 5 mA. In the study by Dağıstan et al.,[8] the voxel size was not specified; however, the images were acquired at 110 kVp, up to 20 mA, and with a FOV of 16×18 cm. Differences in voxel size among the devices may lead to variations in detection sensitivity, particularly for small structures such as accessory foramina.

Measurements taken on dry skulls benefit from the absence of soft tissues, allowing clearer identification of bony landmarks, but they neglect soft tissue influence and in vivo artifacts On the other hand, CBCT provides high accuracy and reproducibility for 3D morphometric analysis, yet its precision is affected by soft-tissue attenuation, metal-induced artefacts, voxel resolution, and segmentation thresholding Moreover, CBCT-derived IOF measurements may differ from manual dry-skull measurements, potentially yielding higher mean values Recognizing these methodological differences is essential for interpreting morphometric data.[10,20,23]

This study also has certain limitations. Firstly, it has a retrospective design and is based solely on CBCT images obtained within a specific time frame at a single center, which may limit the generalizability of the results. Furthermore, only individuals of Turkish origin were included in the study; therefore, it is not possible to generalize the morphometric characteristics of the IOF to individuals of different ethnic

backgrounds. The selection of 10 years as the lower age limit in this study was primarily based on anatomical and developmental factors. This dynamic development may hinder the standardization of measurements and reduce the reliability of the findings. Therefore, only adolescent and adult age groups were included in the study.

In conclusion, this study revealed that the morphometric characteristics of IOF are largely similar in adolescent and adult individuals. The data obtained may contribute to the safe and accurate localization of the IOF in clinical practice. Additionally, considering the results of this study, the presence of AIOF should be taken into consideration during anesthesia practices and especially during surgical procedures.

***Ethics Committee Approval:*** Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Zonguldak Bülent Ecevit University (Date: 17.04.2024, decision no: 2024/07). This study was conducted in accordance with the World Medical Association's Declaration of Helsinki. All patients provided informed consent for the use of their radiographic data in scientific research.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

***Author Contributions:*** Concept – ÇŞ, İÇ; Supervision – ÇŞ, İÇ, GG; Materials – ÇŞ, İÇ; Data Collection and/or Processing – GG, EH; Analysis and/or Interpretation – GG, EH, ÇŞ; Writing –ÇŞ, İÇ, GG, EH.

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# Gynecologic Cancer Awareness Levels of Women and Influential Factors

# Kadınların Jinekolojik Kanser Farkındalık Düzeyleri ve Etkileyen Faktörler

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**ABSTRACT**

**Objective:** This study was carried out to determine the awareness levels of women regarding gynecologic cancers and the factors affecting these levels.

**Materials and Methods:** This descriptive study was conducted between November 2023 and May 2024 with the participation of 277 married women aged 20-65 years who presented to the obstetrics and gynecology outpatient clinics of a public hospital in Türkiye. A Descriptive Information Form and the Gynecologic Cancers Awareness Scale (GCAS) were used to collect data.

**Results:** The mean GCAS score of the participants was 146.28±27.27. The age, number of pregnancies, and number of deliveries variables were positively and significantly related to the total GCAS scores of the participants and their scores in some of the dimensions of GCAS ($p<0.05$). Some sociodemographic characteristics of the participants, including their education and income levels, as well as their gynecologic healthcare service experiences, were also associated with their levels of awareness regarding gynecologic cancers ($p<0.05$).

**Conclusions:** Based on the results of this study, it is important to increase the number of awareness-raising and education programs addressing gynecologic cancers and consider the factors that can affect the awareness levels of women while planning these services.

**Keywords:** Cancer awareness, gynaecological cancer, nursing, women's health

**ÖZ**

**Amaç:** Bu çalışma, kadınların jinekolojik kanserler konusundaki farkındalık düzeylerini ve bu farkındalığı etkileyen faktörleri belirlemek amacıyla gerçekleştirilmiştir.

**Materyal ve Metot:** Tanımlayıcı nitelikteki bu çalışma, Kasım 2023-Mayıs 2024 tarihleri arasında gerçekleştirilmiştir. Çalışma, Türkiye'de bir kamu hastanesinin kadın doğum polikliniklerine başvuran 20-65 yaş aralığındaki 277 evli kadın ile yürütülmüştür. Veriler, Tanıtıcı Özellikler Formu ve Jinekolojik Kanserler Farkındalık Ölçeği (JİKFÖ) kullanılarak toplanmıştır.

**Bulgular:** Kadınların JİKFÖ puan ortalamasının 146,28±27,27 olduğu saptandı. Yaş, gebelik ve doğum sayısı ile ölçek toplam puanları ve bazı alt boyut puanları arasında pozitif ve anlamlı ilişkiler belirlendi ($p<0,05$). Buna ek olarak, kadınların eğitim ve gelir durumu gibi bazı sosyodemografik özellikleri ile jinekolojik sağlık hizmeti deneyimlerinin de jinekolojik kanserlere ilişkin farkındalık düzeyleri ile ilişkili olduğu saptandı ($p<0,05$).

**Sonuç:** Elde edilen bulgular doğrultusunda, jinekolojik kanserlere yönelik farkındalık programların ve eğitimlerin arttırılması ve bu hizmetlerin planlanmasında kadınların farkındalık düzeylerini etkileyebilen faktörlerin göz önünde bulundurulması önemlidir.

**Anahtar Kelimeler:** Hemşirelik, jinekolojik kanser, kadın sağlığı, kanser farkındalığı

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## INTRODUCTION

Gynecologic cancers include all types of cancer originating in female reproductive organs (cervix, ovaries, uterus, vagina, vulva, and fallopian tubes).[1] According to the 2022 data provided by the Global Cancer Observatory (GLOBOCAN), among 9.66 million women who received a new diagnosis of cancer, 6.9% were diagnosed with cervical cancer, 4.3% were diagnosed with uterine cancer, 3.4% were diagnosed with ovarian cancer, and the incidence of cancer constinues increased.[2] As in the rest of the world, gynecologic cancers are among the leading causes of death in women in Türkiye.[3]

In addition to many severe physiological problems and mortality risks, gynecologic cancers affect women negatively in other areas such as quality of life, sexuality, and fertility.[4] Protection from gynecologic cancers becomes more important every day considering their increasing prevalence and negative effects on many aspects of women's lives.[5] Primary healthcare services have important duties in terms of protection from gynecologic cancers. Within the scope of these services, it is highly important to recognize the symptoms of gynecologic cancers, implement screening programs, conduct more research, and make faster decisions for referrals. The main purpose of these services is to raise awareness in women regarding gynecologic cancers to achieve these aims. Cancer awareness makes individuals more knowledgeable about the risk factors and symptoms of, as well as screening programs for, cancers and mobilizes them.[6] Cooper et al. (2011) emphasized that early diagnosis and survival rates could be increased through gynecologic cancer awareness.[7] Thus, it should be ensured that women develop awareness regarding gynecologic cancers, as well as positive health behaviors. In the literature, there is a limited number of studies examining the gynecologic cancer awareness levels of women. These studies have highlighted the need for women for information about gynecologic cancers.[8,9] To meet these needs, first, women need to have a consciousness and awareness of gynecologic cancers. It is thought that uncovering the awareness status of women regarding gynecologic cancers will provide guidance for education and counseling services about gynecologic cancers to be offered in primary care. It is important to plan and implement these education and counseling services by keeping the factors affecting the awareness levels of women in mind. In this context, this study aimed to determine the gynecologic cancer awareness levels of women and influential factors. The Research Questions: What is the level of women's awareness of gynaecological cancers?, and What are the factors influencing women's awareness of gynaecological cancers?

## MATERIALS AND METHODS

***Ethics Committee Approval:*** Before collecting data, ethical approval was obtained from Medical Research Ethics Committee of Kahramanmaras Sütçü İmam University (Date: 20.06.2023, decision no: 2023/07-02). Then, institutional permission was received from the chief physician's office of the hospital where the study would be conducted (Date: 30.10.2023, decision no: E-18649120-044-837499). Individuals who agreed to participate in the study were given detailed information about the purpose and scope of the study by the researcher in person, and their written consent was obtained using the Informed Consent Form. All procedures of the study followed the ethical principles of the Declaration of Helsinki.

***Study Design:*** This study was conducted with a descriptive design. This study made it possible to simultaneously reach women in the target audience and present the existing situation comprehensively. This design was also preferred as it provided the opportunity to prioritize women in the planning of awareness-raising services about gynecologic cancers or identify the areas that need interventions. In the reporting process of the study, the *STROBE* (*Strengthening the Reporting of Observational Studies in Epidemiology*) checklist, which aims to increase the methodological clarity and reporting quality of observational studies, was utilized.

***Population and Sample:*** The population of this study consisted of women who presented to obstetrics and gynecology outpatient clinics of a public hospital in Türkiye between November 2023 and May 2024. The inclusion criteria for the study were determined as being 20-65 years old, being married, being able to communicate in Turkish, and agreeing to participate in the study. Women who were diagnosed with a gynecologic cancer were excluded. Because no clear information about size of the population was available, a sample size calculation formula for an unknown population was used in the study. In this calculation, an incidence of 77.2% corresponding to the rate of women who had heard of gynecologic cancers in the study conducted by Akcan et al. (2024) was used.[10] Accordingly, the minimum required sample size of participants to represent the population was determined as 272. The data collection forms were administered using face-to-face interview method. Within the specified data collection period, 277 women were reached.

***Data Collection Instruments:*** A Descriptive Information Form and the Gynecologic Cancers Awareness Scale were used to collect data.

***Descriptive Information Form:*** This form, which was prepared by the researchers based on the literature review, includes sociodemographic, obstetric

and gynaecological characteristics of women.[7-9, 11,12]

***Gynecologic Cancers Awareness Scale (GCAS):*** GCAS was developed in 2017 by Alp Dal and Ertem to evaluate the awareness levels of married women aged 20-65 regarding gynecologic cancers. The scale consists of 41 items and four dimensions. The overall Cronbach's alpha internal consistency coefficient of the scale was reported as 0.94. GCAS is evaluated based on its total score, which varies in the range of 41 to 205. Higher scores indicate higher levels of awareness regarding gynecologic cancers.[13] In this study, the overall Cronbach's alpha coefficient of the scale was found to be 0.96, while the coefficients of its dimensions were 0.97 for "Awareness of Routine Follow-Up and Severe Illness Perceptions in Gynecologic Cancers", 0.91 for "Awareness of Gynecologic Cancer Risks", 0.77 for "Awareness of Protection from Gynecologic Cancers", and 0.88 for "Awareness of Early Diagnosis and Information in Gynecologic Cancers".

***Statistical Analysis:*** The IBM SPSS Statistics 22 program was used to analyze the collected data statistically. The Kolmogorov-Smirnov test was used to test the normality of the distribution of the data, and it was determined that the data had a non-normal distribution. Descriptive statistics are presented as frequency, percentage, mean, standard deviation, minimum, and maximum values. The Mann-Whitney U test was used for two-group comparisons, and the Kruskal-Wallis test for three or more groups. Bonferroni correction was applied post hoc when Kruskal-Wallis results were significant. Statistical significance was set at $p<0.05$.

## RESULTS

The mean age of the participants was 37.2±11.9. It was determined that 81.6% of the participants had university or higher degrees. While 21.7% of the participants were in menopause, 72.6% did not attend regular gynecologic examinations, and 22.4% had undergone a gynecologic operation before. Additionally, 43% of the participants had not had a pap smear test before, and 17.3% had a family history of gynecologic cancers. Other descriptive characteristics of the participants are presented in Table 1.

**Table 1.** Descriptive characteristics of the participants (n=277).

| **Characteristics** | | **Mean±SD (Min.-Max)** |
|---|---|---|
| **Age (years)** | | 37.2±11.9 (20-65) |
| **Age of first pregnancy** | | 18.3±13.0 (17-39) |
| **Number of pregnancies** | | 1.7±1.5 (0-6) |
| **Number of deliveries** | | 1.2±1.1 (0-4) |
| | | **n (%)** |
| **Education level** | Literate with no formal degree/primary school/middle school | 17 (6.1) |
| | High school | 34 (12.3) |
| | University or above | 226 (81.6) |
| **Income status** | Income < expenses | 93 (33.6) |
| | Income ~ expenses | 154 (55.6) |
| | Income > expenses | 30 (10.8) |
| **Smoking status** | Smoker | 91 (32.9) |
| | Non-smoker | 186 (67.1) |
| **History of miscarriage/ abortion/stillbirth (n=102)** | Yes, 1 time | 60 (58.8) |
| | Yes, 2 times | 30 (29.4) |
| | Yes, 3 or more times | 12 (11.8) |
| **Menopause** | Yes | 60 (21.7) |
| | No | 217 (78.3) |
| **Attends regular gynecologic examinations** | Yes | 76 (27.4) |
| | No | 201 (72.6) |
| **History of previous gynecologic operation** | Yes | 62 (22.4) |
| | No | 217 (78.3) |
| **Type of gynecologic operation (n=62)** | Endometrial myomectomy/polypectomy | 31 (50) |
| | LEEP & conization | 11 (17.7) |
| | Ovarian cystectomy | 8 (12.9) |
| | TAH-BSO | 8 (12.9) |
| | Aesthetic purposes (perineoplasty) | 3 (4.8) |
| | Uterine adhesions | 1 (1.7) |
| **History of previous pap smears** | Yes, with normal results | 129 (46.5) |
| | Yes, with abnormal results | 29 (10.5) |
| | No | 119 (43.0) |

SD: Standard deviation.

**Table 1.** Continue.

| | | |
|---|---|---|
| **Family history of gynecologic cancer** | Yes | 48 (17.3) |
| | No | 229 (82.7) |
| **Family member with a history of gynecologic cancer (n=48)** | Mother/sister | 20 (41.7) |
| | Other family members (e.g., grandmother, aunt, cousin) | 28 (58.3) |
| **Received information about gynecologic cancers** | Yes | 128 (46.2) |
| | No | 149 (53.8) |
| **Source of information about gynecologic cancers (n=128)** | Healthcare institution | 59 (46.1) |
| | Internet (e.g., social media) | 42 (32.8) |
| | Close circle | 17 (13.3) |
| | Television | 9 (7.0) |
| | Books/magazines/newspapers | 1 (0.8) |
| **Visit to healthcare institutions for reproductive health problems** | Yes | 235 (84.8) |
| | No | 42 (15.2) |
| **Barriers to visiting healthcare institutions for reproductive health problems** | No barriers | 171 (61.7) |
| | Fear of getting diagnosed with an important problem | 40 (14.4) |
| | Embarrassment | 34 (12.3) |
| | Being too busy/unable to find time | 16 (5.8) |
| | Privacy | 14 (5.1) |
| | Male physicians | 2 (0.7) |

SD: Standard deviation.

Participants' mean GCAS subscale scores were 84.25±17.26 for Awareness of Routine Follow-Up and Severe Illness Perceptions in Gynecologic Cancers, 34.25±7.46 for Awareness of Gynecologic Cancer Risks, 19.65±4.98 for Awareness of Protection from Gynecologic Cancers, and 16.80±3.48 for Awareness of Early Diagnosis and Information in Gynecologic Cancers. The mean total GCAS score was 146.28±27.27 (Table 2).

There were weak but significant positive correlations between age, number of pregnancies, and number of deliveries and the Awareness of Routine Follow-Up and Severe Illness Perceptions in Gynecologic Cancers subscale scores. A similar weak, positive, and significant correlation was found between age and total GCAS scores ($p<0.05$) (Table 3).

**Table 2.** GCAS total and subscale scores of the participants.

| | | Mean±SD | Minimum-Maximum |
|---|---|---|---|
| **GCAS Subscales** | Awareness of Routine Follow-Up and Severe Illness Perceptions in Gynecologic Cancers | 84.25±17.26 | 22-110 |
| | Awareness of Gynecologic Cancer Risks | 34.25±7.46 | 11-55 |
| | Awareness of Protection from Gynecologic Cancers | 19.65±4.98 | 6-30 |
| | Awareness of Early Diagnosis and Information in Gynecologic Cancers | 16.80±3.48 | 4-20 |
| **GCAS Total** | | 146.28±27.27 | 41-205 |

SD: Standard deviation.

**Table 3.** Relationships between age, number of pregnancies, number of deliveries and the scale and subscale scores of the participants.

| | Test p-value | Awareness of Routine Follow-Up and Severe Illness Perceptions in Gynecologic Cancers | Awareness of Gynecologic Cancer Risks | Awareness of Protection from Gynecologic Cancers | Awareness of Early Diagnosis and Information in Gynecologic Cancers | GCAS Total |
|---|---|---|---|---|---|---|
| **Age** | **r** | 0.241 | -0.042 | -0.024 | 0.087 | 0.136 |
| | **p** | **0.001** | 0.484 | 0.694 | 0.147 | **0.023** |
| **Number of pregnancies** | **r** | 0.166 | -0.016 | -0.039 | 0.016 | 0.104 |
| | **p** | **0.006** | 0.790 | 0.520 | 0.794 | 0.084 |
| **Number of deliveries** | **r** | 0.172 | -0.026 | -0.026 | 0.029 | 0.114 |
| | **p** | **0.005** | 0.667 | 0.670 | 0.637 | 0.061 |

r; Spearman correlation analysis *0.1-0.3: weak correlation, 0.3-0.7: moderate correlation, 0.7-1.0: strong correlation.

Significant differences were found in the Awareness of Routine Follow-Up and Severe Illness Perceptions in Gynecologic Cancers subscale based on income status. The median scores of the Awareness of Gynecologic Cancer Risks subscale differed significantly between participants who were in menopause and those who were not in menopause. The Awareness of Protection from Gynecologic Cancers subscale scores were significantly different between smokers and non-smokers. Significant differences in the Awareness of Early Diagnosis and Information in Gynecologic Cancers subscale were found according to education level. The median total GCAS scores of the participants showed significant differences based on income status ($p<0.05$) (Table 4).

**Table 4.** Comparisons of GCAS total and subscale scores of the participants based on their descriptive characteristics.

| Variables | | Awareness of Routine Follow-Up and Severe Illness Perceptions in Gynecologic Cancers | Awareness of Gynecologic Cancer Risks | Awareness of Protection from Gynecologic Cancers | Awareness of Early Diagnosis and Information in Gynecologic Cancers | GCAS |
|---|---|---|---|---|---|---|
| | | **Mean±SD Median (min-max)** | **Mean±SD Median (min-max)** | **Mean±SD Median (min-max)** | **Mean±SD Median (min-max)** | **Total** |
| **Education level** | Literate/primary school/middle school[1] | 80.41±25.24 85 (22-110) | 37.76±8.74 35 (16-55) | 19.58±6.42 18 (7-30) | 15.11±4.59[1] 16 (4-20) | 142.00±40.47 148 (49-205) |
| | High school[2] | 80.25±23.33 86 (23-110) | 31.52±8.22 3 (11-46) | 18.50±5.42 19 (6-28) | 15.50±4.59[2] 17.50 (4-20) | 137.73±36.57 144 (46-187) |
| | University or above[3] | 85.15±15.35 87 (22-110) | 34.62±7.18 35 (11-55) | 19.83±4.79 20 (6-30) | 17.12±3.11[3] 18 (4-20) | 147.88±24.18 150 (41-205) |
| | Test and p-value | KW=0.450 p=0.799 | KW=4.534 p=0.104 | KW=1.369 p=0.504 | KW=7.508 **p=0.023** **3>1*** | KW=1.976 p=0.372 |
| **Income status** | Income < expenses[1] | 81.12±18.94 84 (22-110) | 33.34±7.20 35 (11-46) | 18.83±5.13 19 (6-29) | 18.83±5.13 17 (4-20) | 141.04±30.07[1] 146 (41-190) |
| | Income ~ expenses[2] | 86.59±15.55±87 (23-10) | 34.99±7.39 35 (11-55) | 20.01±4.63 20 (6-30) | 20.01±4.63 18 (4-20) | 149.92±24.15[2] 152 (54-205) |
| | Income > expenses[3] | 81.93±18.82 87.50 (25-110) | 33.26±8.37 35 (14-55) | 20.33±6.01 21 (6-30) | 20.33±6.01 18 (4-20) | 143.80±31.08[3] 149 (52-205) |
| | Test and p-value | KW=6.175 **p=0.046** **2>1*** | KW=2.407 p=0.300 | KW=3.165 p=0.205 | KW=5.437 p=0.066 | KW=7.164 **p=0.028** **2>1*** |
| **Smoking status** | Smoker | 84.48±16.86 87 (23-110) | 33.50±6.96 34 (11-55) | 17.78±4.56 17 (6-30) | 17.20±3.36 18 (4-20) | 143.46±27.31 147 (49-205) |
| | Non-smoker | 83.78±18.12 86.50 (22-110) | 34.61±7.68 35 (11-55) | 20.57±4.93 21 (6-30) | 16.60±3.52 17 (4-20) | 147.66±27.21 150 (41-205) |
| | Test and p-value | MU=8332.000 p=0.833 | MU=7543.5 p=0.141 | **MU=5252.500 p<0.001** | MU=7304.000 p=0.060 | MU=7550.500 p=0.145 |
| **Menopause** | Yes | 87.31±16.30 88 (23-110) | 33.33±7.00 33.50 (13-55) | 19.21±4.54 18.50 (8-30) | 16.98±2.91 18 (4-20) | 148.23±25.74 150 (49-205) |
| | No | 83.40±17.45 86 (22-110) | 34.50±7.57 36 (11-55) | 19.77±5.10 20 (6-30) | 16.75±2.62 18 (4-20) | 145.74±27.71 149 (41-205) |
| | Test and p-value | MU=5444.500 p=0.052 | MU=5410.500 **p=0.045** | MU=5875.000 p=0.246 | MU=6243.000 p=0.246 | MU=6243.000 p=0.627 |

KW=Kruskal Wallis H test, *corrected Bonferroni test, MU=Mann-Whitney U test, X=Mean, SD=Standard deviation.

Significant differences were found in the Awareness of Routine Follow-Up and Severe Illness Perceptions in Gynecologic Cancers subscale based on regular gynecologic examination, history of gynecologic operations, and pap smear history. Significant differences in the Awareness of Early Diagnosis and Information in Gynecologic Cancers subscale were found according to regular gynecologic examination, and pap smear history. The median total GCAS scores of the participants showed significant differences based on regular gynecologic examination, history of gynecologic operations, and pap smear history ($p<0.05$) (Table 5).

**Table 5.** Comparison of GCAS total and subscale scores of the participants based on their gynaecological history.

| Variables | | Awareness of Routine Follow-Up and Severe Illness Perceptions in Gynecologic Cancers | Awareness of Gynecologic Cancer Risks | Awareness of Protection from Gynecologic Cancers | Awareness of Early Diagnosis and Information in Gynecologic Cancers | GCAS Total |
|---|---|---|---|---|---|---|
| | | **Mean±SD Median (min-max)** | **Mean±SD Median (min-max)** | **Mean±SD Median (min-max)** | **Mean±SD Median (min-max)** | **Mean±SD Median (min-max)** |
| **Attendance to regular gynecologic examinations** | Yes | 89.67±17.27<br>89 (22-110) | 34.38±8.74<br>35 (11-55) | 22.02±5.54<br>22 (6-30) | 17.14±3.74<br>18 (4-20) | 154.59±29.45<br>157 (51-205) |
| | No | 82.67±16.85<br>85 (22-110) | 34.20±6.93<br>35 (11-55) | 18.76±4.45<br>19 (6-30) | 16.67±3.37<br>18 (4-20) | 143.13±25.78<br>148 (41-205) |
| | Test and p-value | MU=5091.500<br>**p<0.001** | MU=7491.000<br>p=0.804 | MU=4512.500<br>p<0.001 | MU=6348.000<br>**p<0.028** | MU=5151.000<br>**p<0.001** |
| **History of previous gynecologic operation** | Yes | 90.90±11.85<br>88 (55-110) | 35.46±6.95<br>35 (11-55) | 20.20±4.22<br>20 (6-30) | 17.46±2.40<br>18 (4-20) | 155.13±17.74<br>154 (121-203) |
| | No | 82.41±18.07<br>86 (22-110) | 33.91±7.57<br>35 (11-55) | 19.50±5.17<br>20 (6-30) | 16.62±3.70<br>18 (4-20) | 143.83±28.92<br>148 (41-205) |
| | Test and p-value | MU=4694.00<br>**p<0.001** | MU=6124.500<br>p=0.482 | MU=6125.00<br>p=0.482 | MU=6050.500<br>p=0.396 | MU=5100.500<br>**p=0.010** |
| **History of previous pap smears** | Yes, with normal results[1] | 88.03±15.33[1]<br>87 (22-110) | 34.31±7.11<br>35 (11-55) | 20.20±5.08<br>20 (6-30) | 17.42±2.97[1]<br>18 (4-20) | 151.00±24.67[1]<br>151 (46-205) |
| | Yes, with abnormal results[2] | 85.41±16.91[2]<br>88 (23-110) | 35.62±8.62<br>35 (15-55) | 19.31±4.64<br>20 (6-30) | 16.24±3.82[2]<br>17 (4-20) | 148.24±28.57[2]<br>152 (49-203) |
| | No[3] | 79.87±18.40[3]<br>84 (22-110) | 33.85±7.55<br>35 (11-49) | 19.15±4.93<br>20 (8-28) | 16.27±3.81[3]<br>17 (4-20) | 140.68±28.78[3]<br>146 (41-190) |
| | Test and p-value | KW= 12.582<br>**p=0.002**<br>**1>3*** | KW= 0.660<br>p=0.719 | KW= 1.918<br>p=0.383 | KW= 8.218<br>**p=0.016**<br>**1>3*** | KW= 8.342<br>**p=0.015**<br>**1>3*** |
| **Family history of gynecologic cancer** | Yes | 88.87±12.96<br>88 (44-110) | 34.89±7.05<br>35 (15-55) | 20.25±4.89<br>19.50 (9-30) | 17.58±2.40<br>18 (8-20) | 152.56±21.13<br>150 (72-203) |
| | No | 83.28±17.90<br>86 (22-110) | 34.11±7.55<br>35 (11-55) | 19.53±5.00<br>20 (6-30) | 16.64±3.65<br>18 (4-20) | 144.96±28.25<br>149 (41-205) |
| | Test and p-value | MU=4575.00<br>p=0.068 | MU=5351.00<br>p=0.773 | MU=5161.000<br>p=0.506 | MU=480.000<br>p=0.161 | MU=4823.500<br>p=0.183 |

**Table 5.** Continue.

| | | | | | | |
|---|---|---|---|---|---|---|
| **Received information about gynecologic cancers** | Yes | 84.78±18.11<br>87 (22-110) | 34.17±8.19<br>35 (11-55) | 19.93±5.25<br>20.50 (6-30) | 16.94±4.77<br>18 (4-20) | 147.15±29.89<br>150.500 (41-205) |
| | No | 83.79±16.53±1.35<br>86 (22-110) | 34.31±6.79<br>35 (11-55) | 19.41±4.75<br>19 (6-30) | 16.68±3.21<br>18 (4-20) | 145.53±24.88<br>148 (51-205) |
| | Test and p-value | MU=8729.000<br>p=0.224 | MU=9290.000<br>p=0.711 | MU=8749.000<br>p=0.235 | MU=8369.000<br>p=0.075 | MU=8386.500<br>p=0.084 |
| **Visit to healthcare institutions for reproductive health problems** | Yes | 85.45±16.47<br>87 (22-110) | 34.38±7.29<br>35 (11-55) | 19.95±4.94<br>20 (6-30) | 16.89±3.30<br>18 (4-20) | 147.95±26.32<br>150 (41-205) |
| | No | 77.50±20.03<br>83.50 (23-107) | 33.50±8.40<br>35.50 (11-49) | 18.00±4.93<br>18 (6-27) | 16.28±4.33<br>18 (4-20) | 136.90±30.76<br>145.50 (46-182) |
| | Test and p-value | MU=8729.000<br>p=0.224 | MU=9290.000<br>p=0.711 | MU=8749.000<br>p=0.235 | MU=8369.000<br>p=0.075 | MU=8386.500<br>p=0.084 |

## DISCUSSION AND CONCLUSION

Raising awareness and knowledge about gynecologic cancers is crucial for early diagnosis and timely treatment. In this study, the mean GCAS score was 146.28±27.27, indicating a moderate awareness level, given the scale range of 41–205. Similar GCAS scores have been reported in previous studies with different populations.[10-12,14-16] In some others, the GCAS scores of women have been reported to be higher than those in our study.[8,17-21] Differences in results may be associated with various factors, including differences in the education and income levels, previous healthcare experiences, and healthcare service access opportunities of the samples. The result of this study showed the necessity to take into account both the individual and health-related characteristics of women while evaluating their gynecologic cancer awareness levels.

The participants of this study who were older had higher levels of gynecologic cancer awareness in general and in the context of routine follow-ups and severe illness perceptions. Similarly, Kıyak and Burucu found a weak and positive relationship between age and gynecologic cancer awareness.[18] Karakuş Selçuk et al. reported that women over the age of 42 had higher levels of gynecologic cancer awareness.[20] These results may be related to the increased levels of women's health-related experience and frequency of attending medical follow-ups and examinations among older women.

In this study, the number of pregnancies and deliveries was not significantly associated with total GCAS scores but showed a correlation with the Awareness of Routine Follow-Up and Severe Illness Perceptions in Gynecologic Cancers subscale. Similar variables have been explored in previous studies examining their effects on GCAS scores. According to Gökşin et al., women who had children had lower levels of gynecologic cancer awareness in comparison to those without children.[19] Similarly, Atlas and Er Güneri stated that women who experienced 1-2 pregnancies had higher levels of awareness than those who experienced 3 or more pregnancies.[17] These findings suggest that the impact of pregnancy and delivery numbers on gynecologic cancer awareness should be evaluated through more comprehensive, multivariate analyses. In this context, our results underline the need for a deeper examination of obstetric factors influencing awareness levels.

The participants of our study who had university or higher degrees had higher levels of awareness of early diagnosis and information on gynecologic cancers. This result was similar to those in previous studies, indicating that higher education levels affect information and awareness related to gynecologic cancers positively.[9,10,12,17,22] This may be explained by the increase in the health literacy of individuals or their access to health-related information as their education levels increase.

In this study, the participants who had lower levels of income also had lower levels of gynecologic cancer awareness in general and in the context of routine follow-up and severe illness perceptions. Karakuş Selçuk et al. also found higher levels of gynecologic cancer awareness among women with higher income levels.[20] It was emphasized that socioeconomic inequalities had a significant effect on gynecologic cancer awareness.[23,24] Adequate income may facilitate women's access to health information, increasing their awareness. Our findings highlight the need to prioritize women with lower income and education levels when planning healthcare services and educational programs related to gynecologic cancers.

Non-smoking participants in this study demonstrated higher awareness regarding protection from gynecologic cancers compared to smokers. This finding is supported by previous studies, which often show that non-smoking women are more likely to engage in protective health behaviors.[18,20] The result may reflect a tendency among some participants to avoid harmful habits in an effort to reduce their cancer risk.

The participants of this study who were not in menopause had higher levels of awareness regarding gynecologic cancer risks compared to those who were in menopause. Previous studies showed that the cancer-related awareness levels of women of reproductive age were higher than those of postmenopausal women, and it was considered that the reason for this could be the openness of younger women to health-related information.[9,25] The gynecologic cancer awareness levels of postmenopausal women may also be influenced by their belief that they do not have the same risks associated with reproductive health.

Participants who attended regular gynecologic examinations and had a history of gynecologic operations showed higher gynecologic cancer awareness. Similarly, Dulkara et al. reported greater awareness among women undergoing gynecologic exams at least once a year.[26] In contrast, Teskereci et al. found no significant association between gynecologic examination or operation status and gynecologic cancer awareness.[27] These conflicting results of different studies may be attributed to various factors like sociodemographic characteristics and health literacy. Furthermore, the gynecologic cancer awareness levels of women may have been influenced by how they experienced processes such as gynecologic examinations and operations, as well as the counseling services that they received in this context.

In this study, participants who had undergone pap smear tests with normal results showed higher

awareness levels overall, particularly in the Routine Follow-Up and Severe Illness Perceptions and Early Diagnosis and Information subscales, compared to those with no pap smear history. Similarly, Gökşin et al. reported higher total GCAS scores among women with a history of pap smears.[19] This finding is expected, as limited awareness is a known barrier to participation in pap smear screening programs.[28,29]

This study has some limitations. It was conducted in a single hospital, limiting the generalizability of the findings. Additionally, its descriptive design prevents causal interpretations. Future longitudinal studies with larger and more diverse samples are needed to explore changes in gynecologic cancer awareness over time. In addition, some factors that may influence gynecologic cancers and awareness levels, such as contraceptive methods, diet, and systemic diseases, were not assessed in this study. This represents an important limitation that may restrict the generalizability of the findings.

In conclusion, this study showed that women's awareness levels regarding gynecologic cancers are associated with various sociodemographic, obstetric, and gynecologic healthcare-related factors. Identifying these awareness levels and the factors influencing them is crucial for effective screening and early diagnosis. Based on the findings, it is essential to ensure that education and awareness programs about gynecologic cancers are accessible, especially for women with lower education and income levels, who may face barriers in accessing healthcare. Additionally, increasing community-based awareness and information efforts is necessary to protect women at all stages of life, including menopause. Strengthening collaboration with Cancer Early Diagnosis, Screening and Education Centres to implement targeted awareness strategies in Türkiye could help reach underserved populations more effectively. Encouraging regular gynecologic follow-ups and screenings, and supporting women's health literacy should be prioritized to improve preventive care. Supporting and scaling up these public health initiatives is essential for reducing gynaecological cancers nationwide.

***Ethics Committee Approval:*** Before collecting data, ethical approval was obtained from the Medical Research Ethics Committee of Kahramanmaraş Sütçü İmam University (Date: 20.06.2023, decision no: 2023/07-02). Then, institutional permission was received from the chief physician's office of the hospital where the study would be conducted (Date: 30.10.2023, decision no: E-18649120-044-837499). Individuals who agreed to participate in the study were given detailed information about the purpose and scope of the study by the researcher in person, and their written consent was obtained using the Informed Consent Form. All procedures of the study followed the ethical principles of the Declaration of Helsinki.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

***Author Contributions:*** Concept – AA, ÇÇD, DVY; Supervision – AA, DVY; Materials – AA, ÇÇD; Data Collection and/or Processing – ÇÇD, FKT; Analysis and/or Interpretation – AA, FKT; Writing – AA, ÇÇD, FKT, DVY.

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# Psychological Factors in Chronic Sore Throat

# Kronik Boğaz Ağrısında Psikolojik Faktörler

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**ABSTRACT**

**Objective:** Chronic sore throat is one of the common causes of presentation to otolaryngology outpatient clinics. Although non-infectious causes are usually blamed, it is thought to be related to many etiologic factors. In this study, psychological factors associated with chronic sore throats, especially anxiety, depression, somatosensory amplification, and somatization, were examined.

**Materials and Methods:** The study was conducted with 77 participants, including 41 patients with chronic sore throat and 36 healthy controls. Sociodemographic data and psychological assessments using the Hospital Anxiety and Depression Scale (HAD), Somatization Scale, and Somatosensory Amplification Scale (SAS) were collected.

**Results:** No significant differences were found between groups in terms of age, gender, smoking habits, psychiatric history, or ongoing psychiatric treatment. Somatization Scale and SAS scores were significantly higher in the patient group (p=0.001 and p=0.005). No significant differences were found in HAD-A and HAD-D scores between the patient and control groups. However, a significant positive correlation was observed between HAD-A and SAS scores.

**Conclusions:** Psychological factors, particularly somatosensory amplification, may contribute to the persistence of chronic sore throat. These findings highlight the importance of incorporating psychological assessments in the management of such cases to improve diagnostic accuracy and treatment outcomes.

**Keywords:** Anxiety, chronic sore throat, depression, somatization, somatosensory amplification

**ÖZ**

**Amaç:** Kronik boğaz ağrısı, kulak burun boğaz polikliniklerine başvuruların yaygın nedenlerinden biridir. Genellikle enfeksiyöz olmayan nedenler suçlansa da, birçok etiyolojik faktörle ilişkili olduğu düşünülmektedir. Bu çalışmada, kronik boğaz ağrısıyla ilişkili psikolojik faktörler, özellikle anksiyete, depresyon, somatosensoriyel amplifikasyon ve somatizasyon incelenmiştir.

**Materyal ve Metot:** Çalışma, kronik boğaz ağrısı olan 41 hasta ve 36 sağlıklı kontrol olmak üzere 77 katılımcıyla yürütülmüştür. Sosyodemografik veriler ve Hastane Anksiyete ve Depresyon Ölçeği (HAD), Somatizasyon Ölçeği ve Somatosensoriyel Amplifikasyon Ölçeği (SAS) kullanılarak psikolojik değerlendirmeler toplandı.

**Bulgular:** Gruplar arasında yaş, cinsiyet, sigara içme alışkanlıkları, psikiyatrik öykü veya devam eden psikiyatrik tedavi açısından anlamlı bir fark bulunmamıştır. Somatizasyon ölçeği ve SAS puanları hasta grubunda anlamlı şekilde daha yüksekti (p=0,001 ve p=0,005). Hasta ve kontrol grupları arasında HAD-A ve HAD-D skorlarında anlamlı bir fark bulunmamıştır. Ancak HAD-A ve SAS skorları arasında anlamlı pozitif korelasyon gözlenmiştir.

**Sonuç:** Psikolojik faktörler, özellikle somatosensoriyel amplifikasyon, kronik boğaz ağrısının devam etmesine katkıda bulunabilir. Bu bulgular, tanı doğruluğunu ve tedavi sonuçlarını iyileştirmek için bu tür vakaların yönetiminde psikolojik değerlendirmelerin dahil edilmesinin önemini vurgulamaktadır.

**Anahtar Kelimeler:** Anksiyete, depresyon, kronik boğaz ağrısı, somatizasyon, somatosensoriyel amplifikasyon

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## INTRODUCTION

Sore throats are a common reason for visits to otolaryngology clinics and are most often caused by infections. A sore throat lasting longer than 14 days is defined as a chronic sore throat. Guidelines recommend evaluation by a specialist if symptoms persist for more than 3-4 weeks. The cause of chronic sore throat is usually non-infectious, and many etiological factors have been reported in the literature, including physicochemical factors (smoking, snoring, postoperative pain, medications, reflux), environmental factors such as air pollution, excessive or improper use of the voice, accompanying diseases, and side effects of drugs. The treatment of patients with chronic sore throat is recommended to be etiology-specific due to the variability of etiological factors.[1,2]

Many factors causing sore throats have been investigated, especially the relationship between laryngopharyngeal reflux (LFR) patients and psychiatric disorders, and it has been found that anxiety and depressive symptoms affect the occurrence, development, and treatment efficacy of resistant LFR.[3] It has been reported that employees who experience higher work stress experience multiple health problems such as sore throat, eye strain, tinnitus, hoarseness, chronic cough with phlegm, chest tightness, sensitive stomach, or peptic ulcer.[4] Patients with chronic pharyngitis have more anxiety and depression symptoms than the general population.[5]

Somatization, somatosensory amplification (SA), anxiety, and depression are considered psychological conditions that frequently accompany chronic illnesses, including medically unexplained symptoms. Studies have shown that about 80% of people see an otolaryngologist after having vague, medically unexplained symptoms like tinnitus, dizziness, and headaches.[6] In patients with long-standing sinonasal issues, elevated levels of psychological distress- particularly depression, anxiety, and somatization-are linked to greater symptom intensity and poorer surgical outcomes.[7]

This research aimed to quantify anxiety, depression, SA, and somatization levels among individuals reporting chronic sore throat symptoms without any identifiable organic pathology. A unifying hypothesis that adequately explains the emergence of such symptoms in the absence of an identifiable disease has not yet been proposed.

## MATERIALS AND METHODS

***Ethics Committee Approval:*** The data collection process was conducted according to the Declaration of Helsinki. Approval for the study was obtained from the Van Yuzuncu Yil University Non-Interventional Ethics Committee (Date: 12/05/2023, decision no: 2023/05-23).

***Study Design:*** This study, which was conducted in a cross-sectional case-control design between January 2024 and July 2024, included a total of 77 people, including 41 patients with chronic sore throat and 36 controls, who applied to the Ear Nose Throat (ENT) outpatient clinic. The inclusion criteria were as follows; patients between the ages of 18 and 65 years who volunteered to participate in the study, who complained of chronic sore throat lasting at least four weeks, who applied to the ENT outpatient clinic for this reason, who were not associated with infective or organic causes, and who did not have chronic changes (mucosal hypertrophy, erythema, edema, mucosal atrophy, granuloma) in the oropharynx and laryngopharynx on examination were included. All patients who met the inclusion criteria were first evaluated by two experienced ENT physicians, and patients with disagreement in the degree of pachydermia (thickening and edema of the mucosa between the arytenoid cartilages are typically observed as posterior laryngeal hypertrophy during endoscopic examination) were excluded from the study. The exclusion criteria were as follows; neck mass and malignancy, history of neck and throat surgery, presence/history of gastrointestinal diseases, glossopharyngeal neuralgia, chronic changes in the oropharynx and laryngopharynx on examination, intense pachydermia, significant nasal obstruction, chronic rhinosinusitis, presence of active psychiatric disease, chronic diseases such as diabetes mellitus, uncontrolled hypertension, patients with low literacy skills who could not fill out the forms, patients with cognitive defects such as mental retardation or neurodegenerative diseases. Age- and gender-matched healthy individuals without any complaints were included in the control group.

***Data Collection Tools***

*Sociodemographic Data Form*: This form collects various sociodemographic details, including age, gender, marital status, education level, income level, smoking habits, and medical and psychiatric history of both patients and control participants.

*Hospital Anxiety and Depression Scale (HAD)*: Designed to assess anxiety (HAD-A) and depression (HAD-D) in individuals with physical illnesses and those seeking primary healthcare services, this self-report scale consists of 14 items.[8] Seven items assess depressive symptoms, while the remaining seven evaluate anxiety symptoms. Responses are recorded on a 4-point Likert scale (0-3), with possible subscale scores ranging from 0 to 21. Scores of 0-7 are considered within the normal range, whereas scores of 8 or above indicate a significant presence of anxiety or depression. The scale has been validated for use in the Turkish population.[9]

*Somatization Scale*: This subscale of the Minnesota Multiphasic Personality Inventory (MMPI), developed by McKinley and Hathaway, consists of 33 items answered in a true/false format.[10] Among these, 17 are reverse-scored. Each incorrect response to a reverse-scored item and each correct response to the remaining items receives one point. The total score ranges from 0 to 33. The Turkish adaptation of the scale demonstrated an internal reliability coefficient of 0.83.[11]

*Somatosensory Amplification Scale (SAS)*: Developed by Barsky et al. to evaluate the tendency to amplify normal bodily sensations, this self-report instrument consists of 10 items rated on a 5-point Likert scale.[12] The total score reflects the degree of somatosensory amplification. The Turkish adaptation and reliability study was conducted by Güleç et al.[13]

***Statistical Analysis:*** Descriptive analyses were performed to summarize the general characteristics of the study sample. Continuous variables were presented as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages (n, %). The chi-square test was employed to assess associations between categorical sociodemographic variables. To compare scale scores between the two groups, the Independent Samples t-test and Pearson Correlation Analysis were utilized. A significance threshold of $p<0.05$ was applied. All statistical analyses were conducted using the SPSS software package. The reliability of all scales was confirmed, with Cronbach's alpha coefficients exceeding 0.70.

## RESULTS

The study included 77 participants, comprising 41 patients and 36 healthy control subjects. The mean age of the patient group was 39.29 ± 14.58 years, while the control group had a mean age of 35.53 ± 12.87 years. No statistically significant differences were found between the groups concerning age and gender ($p>0.05$). Additionally, no significant differences were observed regarding smoking habits, psychiatric history, or ongoing psychiatric treatment. However, the patient group exhibited significantly higher use of stomach medication and a greater prevalence of mild pachydermia (Table 1).

**Table 1.** Results of the relationship between categorical measures and the group.

| | | **Patient (41)** n (%) | **Control (36)** n (%) | **p*** |
|---|---|---|---|---|
| **Gender** | Male | 9 (22) | 13 (36.1) | 0.170 |
| | Female | 32 (78.0) | 23 (63.9) | |
| **Marital status** | Married | 27 (65.9) | 16 (44.4) | **0.003** |
| | Single | 9 (22.0) | 20 (55.6) | |
| | Widow | 5 (12.2) | 0 (0.0) | |
| | Divorced | 0 (0.0) | 0 (0.0) | |
| **Education** | Primary school | 23 (56.1) | 5 (13.9) | **0.001** |
| | Secondary school | 4 (9.8) | 4 (11.1) | |
| | High school | 7 (17.1) | 12 (33.3) | |
| | College/ University | 7 (17.1) | 15 (41.7) | |
| **Income** | Income less than expenditure | 19 (46.3) | 17 (47.2) | **0.002** |
| | Income and expenditure equal | 21 (51.2) | 9 (25.0) | |
| | Income more than expenditure | 1 (2.4) | 10 (27.8) | |
| **Smoking** | Yes | 4 (9.8) | 8 (22.2) | 0.132 |
| | No | 37 (90.2) | 28 (77.8) | |
| **Occupation** | Unemployed | 8 (19.5) | 11 (30.6) | 0.**013** |
| | Housewife | 22 (53.7) | 5 (13.9) | |
| | Worker | 4 (9.8) | 4 (11.1) | |
| | Employee-Civil servant | 5 (12.2) | 12 (33.3) | |
| | Retired | 1 (2.4) | 2 (5.6) | |
| | Employer | 1 (2.4) | 2 (5.6) | |
| **Psychotherapy** | No | 36 (87.8) | 35 (97.2) | 0.124 |
| | Yes | 5 (12.2) | 1 (2.8) | |

*: The relationship is significant at $p<0.05$.

**Table 1.** Continue.

| | | | | |
|---|---|---|---|---|
| **Comorbidity** | No | 32 (78.0) | 32 (88.9) | 0.205 |
| | Yes | 9 (22.0) | 4 (11.1) | |
| **Any medication** | No | 25 (61.0) | 31 (86.1) | **0.013** |
| | Yes | 16 (39.0) | 5 (13.9) | |
| **Psychiatric medication** | No | 37 (90.2) | 35 (97.2) | 0.215 |
| | Yes | 4 (9.8) | 1 (2.8) | |
| **Pachydermia** | No | 16 (39.0) | 35 (97.2) | **0.001** |
| | Mild | 25 (61.0) | 1 (2.8) | |
| | Intense | 0 (0.0) | 0 (0.0) | |
| **Stomach medication** | Yes | 9 (22.0) | 1 (2.8) | **0.013** |
| | No | 32 (78.0) | 35 (97.2) | |
| **Age**, Mean ± SD | | 39.29 ± 14.58 | 35.53 ± 12.87 | 0.05 |

*: The relationship is significant at p<0.05.

Regarding the administered scales, SAS scores were significantly elevated in the patient group (p=0.001 and p=0.005, respectively). In contrast, HAD-A and HAD-D scores did not show significant differences between the two groups (Table 2).

Correlation analyses identified a positive association between HAD-A and HAD-D scores. Furthermore, a strong positive correlation was detected between HAD-A and SAS scores (Table 3).

**Table 2.** Comparison of scales according to groups.

| | **Patient** | | **Control** | | | |
|---|---|---|---|---|---|---|
| | **(Mean±SD)** | **Range** | **(Mean±SD)** | **Range** | **t** | ***p** |
| HAD-A | 7.46 ± 5.27 | 19.00 | 7.69 ± 3.90 | 17.00 | -0.216 | 0.830 |
| HAD-D | 6.95 ± 3.97 | 15.00 | 7.03 ± 4.27 | 15.00 | -0.081 | 0.935 |
| Somatization | 19.90 ± 5.90 | 22.00 | 16.83 ± 4.41 | 19.00 | -2.557 | **0.001** |
| Somatosensorial amplification | 31.76 ± 7.25 | 36.00 | 26.44 ± 9.12 | 33.00 | -2.849 | **0.005** |

*: The relationship is significant at p<0.05; * HAD-A: Hospital Anxiety and Depression Scale- Anxiety; HAD-D: Hospital Anxiety and Depression Scale-Depression.

**Table 3.** Results of correlation analysis between measurements.

| | | **Age** | **HAD-A** | **HAD-D** | **Somatization** | **Somatosensorial amplification** |
|---|---|---|---|---|---|---|
| **Age** | r | 1 | | | | |
| | p | | | | | |
| **HAD-A** | r | -0.119 | 1 | | | |
| | p | 0.304 | | | | |
| **HAD-D** | r | -0.211 | 0.330 | 1 | | |
| | p | 0.066 | **0.003** | | | |
| **Somatization** | r | 0.086 | -0.126 | -0.177 | 1 | |
| | p | 0.454 | 0.273 | 0.125 | | |
| **Somatosensorial amplification** | r | -0.057 | 0.390 | 0.106 | -0.039 | 1 |
| | p | 0.623 | **0.001** | 0.360 | 0.736 | |

*: The relationship is significant at p<0.05; *: HAD-A: Hospital Anxiety and Depression Scale- Anxiety; HAD-D: Hospital Anxiety and Depression Scale-Depression.

## DISCUSSION AND CONCLUSION

The study examined the levels of somatization and SA in patients with chronic sore throat, excluding possible medical conditions. Our findings suggest that these two psychological states may be important factors. To our knowledge, this issue has not been addressed in previous research.

Sore throat is a common symptom in otorhinolaryngology practice, and psychological evaluation may be required in addition to physical examination in patients presenting with sore throat in cases where there is no response to treatment and the etiology is not clearly defined.[2,14] Patients' reactions to sore throats may differ; while some patients get used to their long-lasting pain and do not care, some want to seek medical support immediately. The associations between psychological factors and many similar disorders associated with pain have been investigated in the literature. In this research, we examined the relationship between patients presenting with sore throats and psychological disorders such as anxiety, depression, somatization, and SA.

The high scores of somatization and SA in the patient group may indicate that these patients associate their physical symptoms with emotional or psychological stress. It has been frequently emphasized in the literature that somatization is associated with chronic pain syndromes. Somatization is defined as the expression of psychological stress through physical symptoms and is particularly common in cases of chronic pain. In these individuals, pain and somatization are thought to be shaped by common biological and psychological mechanisms.[15] Various mechanisms underlie the persistent stimulation of the pain system in chronic pain conditions, including continuously active nociceptive nerves (visceral sensitivity, neurogenic inflammation), ongoing neuronal excitation (central sensitization, neuroinflammation), and sustained pain processing within the central nervous system (central sensitization, neuroinflammatory responses).[16] Recent studies have shown that there are important links between emotion regulation mechanisms and pain, and that they share common brain circuits.[17,18] This suggests that somatization may contribute to the chronicity of pain. For example, in other types of chronic pain, such as low back pain, somatization has been shown to influence the disease course significantly.[19]

It has been reported that psychiatric factors such as anxiety and depression, as well as somatization mechanisms, may be effective in atypical chronic sore throat. In particular, it has been stated that sore throat symptoms may be related to stress and anxiety, and this should be taken into consideration when a physical cause cannot be found.[20] It has been reported that anxiety may trigger throat disorders through physiologic effects such as muscle tension, respiratory changes, and autonomic nervous system responses. Moreover, chronic anxiety and stress may lead to the weakening of the immune system and increase susceptibility to viral and bacterial infections.[21] It should also be kept in mind that symptoms such as globus hysteria and dysphagia are common in chronic throat disorders and anxiety states. In addition, complaints such as headaches, gastrointestinal system disorders, muscle aches, and sore throats can be commonly observed in somatization disorders. In a study investigating psychological factors in patients with chronic pharyngitis, somatization disorder was found most frequently.[22] In a study involving 883 consecutive patients with medically unexplained symptoms who visited an ENT clinic, it was found that somatic symptoms were common, one or more symptoms were present, depression and anxiety levels were higher, and patients made more visits to the doctor.[23] Some studies suggest that emotional disorders such as anxiety and depression may trigger pain, such as a sore throat, especially during stressful periods. Although no significant difference was found between the patient and control groups in terms of anxiety and depression scores in our study, the strong positive correlation between HAD-A and SAS suggests that anxiety, especially at the individual level, may be closely related to somatosensory sensitivity. This suggests that as the level of anxiety increases in individuals with a sore throat, sensitivity to internal bodily sensations may also increase, and this may affect symptom severity. The fact that there was no difference at the group level suggests that interindividual variability may be important in this relationship. Therefore, it is important to focus not only on group averages but also on individual-level psychophysiological interactions in terms of clinical evaluation. Further research may reveal important results in this regard. However, fewer somatization studies focus on sore throat compared to other types of pain, and the gap in this field requires more multidisciplinary studies.

SA is frequently viewed as a behavior linked to psychological distress, and it is characterized by the tendency to perceive bodily sensations as intense, dangerous, and disturbing. In the circuit model of SA, the middle insula plays a central role, where emotional and motivational information comes from the anterior cingulate cortex, amygdala, and orbitofrontal cortex, and integrates with sensory processing mediated by the posterior insula. This is recognized as an important area for processing pain and sensory experiences.[24]

A positive correlation between anxiety (especially health anxiety) and SA has been reported.[25] SA is ubiquitous in psychological conditions such as somatization disorder and health anxiety.[26] This condition, which can be explained by the person's percep-

tion of bodily sensations with excessive sensitivity and misinterpretation of these sensations, may occur with many different symptoms. SA was first described in hypochondriac patients. However, the results of studies show that these symptoms are not specific to hypochondriacs. The relationship between SA and pain has been particularly investigated in pain conditions such as fibromyalgia, osteoarthritis, headaches, temporomandibular disorders, and chronic low back pain. Indeed, several cross-sectional studies have shown high levels of bodily sensation exaggeration in individuals with high symptom reporting.[27] There have been significant reported relationships between an increased number of somatic symptoms and somatosensory amplification in individuals with persistent physical symptoms.[15] Another recent study demonstrated the effect of both symptom focusing and SA on symptom persistence and reduced mental and physical functioning in individuals with persistent physical complaints.[28]

The findings of our study demonstrate the need to consider psychological factors in individuals with atypical sore throat. Previous research indicates that at least one-third of the general population experiences "medically unexplained symptoms" (MUS) at least once in their lifetime. Moreover, persistent MUS is observed in approximately 3 to 10% of the general population, and nearly half of primary care patients visit a general practitioner due to such symptoms.[15,29] A focus on somatic symptoms and bodily sensations may be misinterpreted in clinical assessments and may lead to unnecessary medical tests or treatments. It is known that cultural and social factors may increase the exaggeration of somatic symptoms, especially when the expression of psychological distress is limited in one's environment. It should also be recognized that health professionals risk inadvertently reinforcing somatic complaints by focusing on such symptoms.

Our study has some limitations. First, the number of people included in the study was relatively small. Secondly, although patients with extensive pachydermia were excluded from the study, the number of gastric medication and mild pachydermia was higher in the patient group. This may be considered a limitation regarding the relationship between pachydermia and pain. However, it has also been reported in the literature that there is no correlation between the degree of pachydermia and LFR symptoms.[30] Additionally, indices that could assess reflux were not used in the study, but it was excluded based on medical history and examination. Although patients with evident laryngopharyngeal reflux (LPR) symptoms or endoscopic findings such as intense pachydermia were excluded, it is possible that mild or subclinical forms of LPR and other subtle organic pathologies may not have been fully ruled out due to the lack of standardized reflux scoring systems in our protocol. Thirdly, with the use of self-report scales and a cross-sectional design, causal inferences cannot be made in this respect. Finally, future studies with larger samples may yield additional data by examining the potential confounding effects of sociodemographic variables such as education level, marital status, and age.

In conclusion, a sore throat may present as a symptom of discomfort that may not be due to a physical cause. It should be kept in mind that it may be associated with psychological factors such as somatization disorder and SA. A holistic perspective should be developed by considering psychological disorders in treatment. In this way, the quality of life of individuals can be enhanced, and unnecessary medical interventions can be prevented.

***Ethics Committee Approval:*** Our study was approved by the Van Yuzuncu Yil University Non-Interventional Ethics Committee (Date: 12/05/2023, decision no: 2023/05-23). The data collection process was conducted according to the Declaration of Helsinki.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

***Author Contributions:*** Concept – AY, MI; Supervision – MI, MZE, SA; Materials – MA, SA; Data Collection and/or Processing – MA, MZE, SA; Analysis and/or Interpretation –AY, MI; Writing – AY,MI.

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# Epidemiological and Clinical Predictors of Mortality in Firearm Injuries: A Retrospective Study from a Level-1 Trauma Center

# Ateşli Silah Yaralanmalarında Mortaliteyi Öngören Epidemiyolojik ve Klinik Faktörler: Seviye-1 Travma Merkezinden Retrospektif Bir Çalışma

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## ABSTRACT

**Objective**: Firearm-related injuries remain a significant cause of trauma morbidity and mortality worldwide. This study aimed to evaluate the epidemiological and clinical characteristics of firearm injuries and identify predictors of in-hospital mortality.

**Materials and Methods:** This retrospective cohort study included patients presenting with firearm injuries to Marmara University Pendik Training and Research Hospital during the period spanning from January 1 to December 31, 2024. Data on demographics, injury mechanism, anatomical injury sites, trauma scores, vital signs, laboratory findings, interventions, and outcomes were collected. Univariate logistic regression analyses were performed to identify factors associated with mortality, along with their odds ratios (OR).

**Results**: A total of 119 patients were included (mean age: 33.3 ± 12.8 years; 89.1% male). The overall in-hospital mortality rate was 9.2%. Non-survivors were more likely to be female and have suicide-related injuries. Univariate analysis revealed that female gender (OR: 6.286), suicide intent (OR: 40.125), lower Glasgow Coma Scale (OR: 0.490), lower Revised Trauma Score (OR: 0.113), and higher Injury Severity Score (OR: 1.323) were independent predictors of mortality. Head/neck and chest injuries were associated with higher mortality and increased need for surgery and blood transfusion.

**Conclusions**: Early assessment of vital signs, trauma scores, and anatomical injury sites can provide valuable prognostic information in firearm-related trauma. Beyond mortality, the high rates of hospitalization and surgical intervention highlight the broader burden of firearm injuries on healthcare systems.

**Keywords:** Emergency care, firearm injuries, injury severity, mortality, trauma score

## ÖZ

**Amaç:** Ateşli silah yaralanmaları dünya genelinde önemli bir travma morbidite ve mortalite nedenidir. Bu çalışmanın amacı, ateşli silah yaralanmalarının epidemiyolojik ve klinik özelliklerini değerlendirmek ve hastane içi mortaliteyi öngören faktörleri belirlemektir.

**Materyal ve Metot:** Bu retrospektif kohort çalışmaya, Marmara Üniversitesi Pendik Eğitim ve Araştırma Hastanesi'ne 1 Ocak–31 Aralık 2024 tarihleri arasında ateşli silah yaralanması nedeniyle başvuran hastalar dahil edildi. Hastaların demografik verileri, yaralanma mekanizması, anatomik yaralanma bölgeleri, travma skorları, vital bulguları, laboratuvar değerleri, uygulanan girişimler ve klinik sonuçları değerlendirildi. Hastane içi mortalite ile ilişkili faktörleri belirlemek amacıyla univaryant lojistik regresyon analizleri yapıldı ve olasılık oranları (OR) hesaplandı.

**Bulgular:** Toplam 119 hasta çalışmaya dahil edildi (ortalama yaş: 33,3 ± 12,8 yıl; %89,1 erkek). Genel hastane içi mortalite oranı %9,2 idi. Hayatını kaybeden hastalar arasında kadın cinsiyet ve intihar girişimi daha yaygındı. Univaryant analizlerde kadın cinsiyet (OR: 6,286), intihar girişimi (OR: 40,125), düşük Glasgow Koma Skoru (OR: 0,490), düşük Revize Travma Skoru (OR: 0,113) ve yüksek Travma Şiddet Skoru (OR: 1,323) mortalite ile ilişkili bulundu. Baş-boyun ve göğüs yaralanmaları daha yüksek mortalite, cerrahi girişim ihtiyacı ve kan transfüzyonu ihtiyacı ile ilişkiliydi.

**Sonuç:** Ateşli silah yaralanmalarında vital bulgular, travma skorları ve anatomik yaralanma bölgelerinin erken değerlendirilmesi prognostik açıdan önemli bilgiler sağlayabilir. Mortalitenin ötesinde, bu hastalardaki yüksek yatış ve cerrahi müdahale oranları, ateşli silah yaralanmalarının sağlık sistemine olan ciddi yükünü de ortaya koymaktadır.

**Anahtar Kelimeler:** Acil bakım, ateşli silah yaralanmaları, mortalite, travma skoru, yaralanma şiddeti

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## INTRODUCTION

Firearm-related injuries have emerged as one of the more persistent contributors to trauma care burden across the globe.[1] In the United States, these incidents lead to over 48,000 deaths each year, yet the toll is not limited to fatalities.[2] While many patients survive firearm injuries, the aftermath often includes lasting impairments, including mobility issues, disrupted cognitive function, and psychological disturbances that may persist for years.[3] The complexity of these outcomes underscores the importance of a prompt and well-coordinated clinical response, beginning most critically at the point of entry: the emergency department (ED). Early evaluation, stabilization, and appropriate triage play a crucial role in determining outcomes.[4]

Both globally and in Türkiye, the increasing availability of firearms and the rising incidence of interpersonal violence have led to a growing clinical and forensic burden.[5,6] Despite the increasing frequency of these injuries, a need remains for region-specific data that captures their evolving epidemiological and clinical characteristics and informs strategies for effective trauma care delivery.[7]

By evaluating vital signs, injury locations, trauma scores, patient demographics, and injury intent, early predictors of poor outcomes can be identified to optimize acute management strategies. In this context, this study aims to address that need by examining firearm injury cases in a level-1 trauma center in Türkiye, with a focus on identifying the key factors associated with in-hospital mortality, thereby providing insights that may support early risk stratification and guide improvements in trauma management practices.

## MATERIALS AND METHODS

***Ethics Committee Approval:*** The study protocol received approval from the Marmara University Clinical Research Ethics Committee (Date: 31.01.2025, decision no: 09.2025-25-0053). Given its retrospective design, the requirement for informed consent was waived by the ethics committee. The study was conducted in alignment with the Declaration of Helsinki and complies with the STROBE guidelines for reporting observational studies.[8]

***Study Design and Settings:*** A single-center retrospective cohort study was carried out at Marmara University Pendik Training and Research Hospital, which is a level-1 trauma center with advanced diagnostic and surgical capabilities.

***Study Participants:*** We retrospectively analyzed all patients who presented with firearm-related injuries to Marmara University Pendik Training and Research Hospital between January 1 and December 31, 2024. Patients with missing critical data (e.g., outcome status) were excluded from the study.

***Variables and Data Sources:*** Data were obtained from the hospital's electronic health records and patient files. For each patient, demographic information (age and sex) and the mechanism of injury (homicide or suicide) were recorded. Clinical variables included the anatomical location of the injury (head/neck, chest, abdomen, upper extremity, lower extremity), initial Glasgow Coma Scale (GCS), Revised Trauma Score (RTS),[9] and Injury Severity Score (ISS),[10] as well as initial laboratory values (complete blood count, biochemistry and blood gas results). During treatment, the need for blood transfusions and surgical interventions was recorded. Additionally, hospital length of stay and clinical outcomes (discharge, admission, or in-hospital mortality) were also recorded.

***Outcomes:*** The primary outcome of the study was in -hospital mortality. Secondary outcomes included surgical intervention, hospitalization, and duration of hospitalization.

***Statistical Analysis:*** All statistical analyses were carried out using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). The distribution characteristics of the continuous variables were assessed visually through histograms. Categorical variables were summarized as frequencies with percentages. For numeric data, normally distributed variables were expressed as means with standard deviations, whereas non-normally distributed variables were described using medians and interquartile ranges. Group comparisons were made using the Chi-square test for categorical variables. Depending on the distribution pattern, continuous variables were compared using either the Student's t-test or the Mann–Whitney U test. To explore potential predictors of in-hospital mortality, univariate logistic regression analysis was performed. A p-value of $<0.05$ was considered statistically significant.

## RESULTS

A total of 124 patients with firearm injuries presented to the emergency department during the study period. Five patients who left the hospital against medical advice and without completing treatment were excluded from the final analysis. Thus, a total of 119 patients were included in the study. The majority were male (89.1%), with a mean age of 33.3 ± 12.8 years. Among these, 63 patients (52.9%) were discharged from the ED, while 48 (40.3%) required hospitalization. Specifically, 39 were admitted to inpatient wards, and 9 to intensive care units (ICUs). In-hospital mortality occurred in 11 patients (9.2%), including deaths in the ED (n = 5), operating room (n = 3), and ICU (n = 3) (Figure 1).

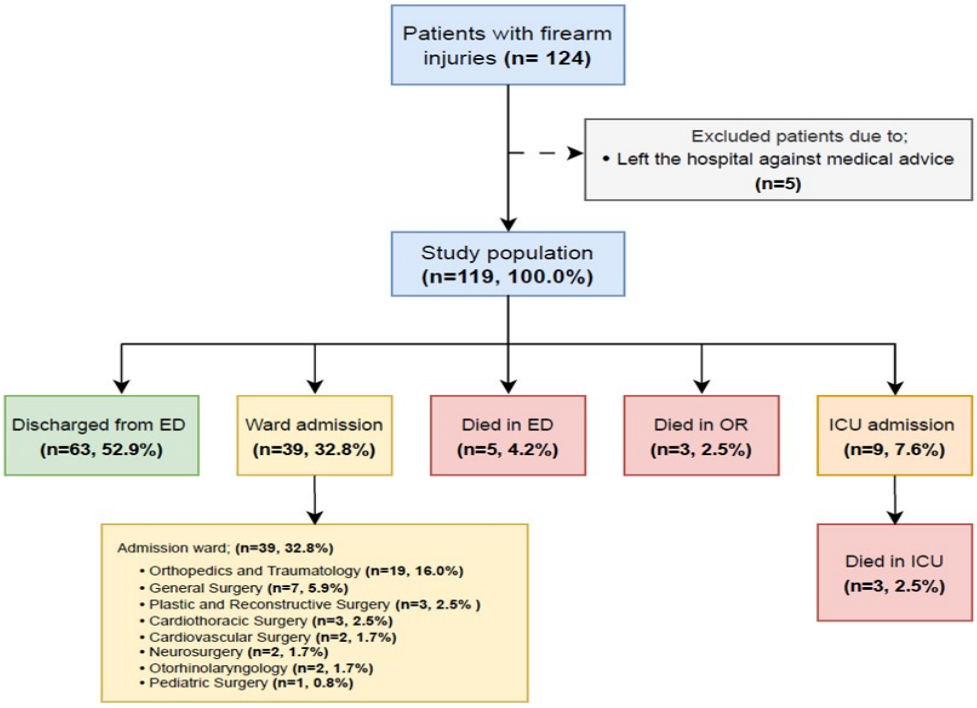


**Figure 1:** Flow chart of the study. ED: Emergency department; ICU: Intensive care unit; OR: Operating room.

When comparing survivors and non-survivors, the mean age was 32.9 ± 12.9 years and 37.1 ± 11.9 years, respectively, with no statistically significant difference between the groups (p=0.303). Several other parameters demonstrated significant differences. Female sex and suicide-related injuries were more prevalent among non-survivors (p=0.019 and p<0.001, respectively). Non-survivors also presented with markedly compromised physiological parameters, including lower systolic and diastolic blood pressures, decreased respiratory rate, and significantly reduced Glasgow Coma Scale scores (all p<0.001). Laboratory findings showed lower hemoglobin, hematocrit, and pH levels, as well as a significantly elevated base deficit (all p<0.001), suggesting greater physiological derangement. Trauma severity was also notably worse in this group, with lower Revised Trauma Scores and higher Injury Severity Scores (both p<0.001). In terms of interventions, all non-survivors received blood transfusions (p<0.001), and none underwent basic medical treatment alone (p=0.003). Additionally, non-survivors had a significantly shorter median length of hospital stay compared to survivors (1 hour vs. 9 hours, p=0.014). These findings are detailed in Table 1.

In terms of anatomical injury distribution, the most frequently affected region was the lower extremities (61.3%), followed by the upper extremities (23.5%), abdomen (22.7%), head/neck (17.6%), and chest (14.3%). As some patients sustained injuries involving more than one anatomical region, the total number of injury sites exceeds the total number of patients. While this limits direct comparisons, several meaningful differences were observed. Patients with chest and head/neck injuries had notably higher in-hospital mortality rates (41.2% and 19.0%, respectively), compared to other anatomical groups. These regions also demonstrated lower Revised Trauma Scores (RTS) and higher Injury Severity Scores (ISS), reflecting more severe trauma. Specifically, the median ISS reached 16 (IQR: 10–75) for chest injuries and 9 (IQR: 4–23) for head/neck injuries. Blood transfusion was required in 64.7% of chest injury cases and 33.3% of head/neck injuries, further highlighting their clinical severity. Surgical interventions were most frequent among patients with abdominal injuries (55.6%) and chest injuries (58.8%), while also elevated in upper extremity trauma (46.4%). Lower extremity injuries, although common, were associated with the lowest mortality (2.7%), highest discharge rate from the ED (64.4%), and shortest median hospital stay (6 hours, IQR: 3–78). These findings suggest that the anatomical site of injury plays a critical role in predicting clinical outcomes and resource utilization in firearm-related trauma (Table 2).

**Table 1.** Comparison of baseline demographic, clinical, laboratory, and outcome characteristics between survivors and non-survivors among patients with firearm injuries.

| Variables | Subcategory | All patients (n=119) | Survivors (n=108) | Non-survivors (n=11) | p |
|---|---|---|---|---|---|
| **Age (year),** mean ± SD | | 33.3 ± 12.8 | 32.9 ± 12.9 | 37.1 ± 11.9 | 0.303 |
| **Gender,** n (%) | Male | 106 (89.1) | 99 (91.7) | 7 (63.6) | **0.019** |
| | Female | 13 (10.9) | 9 (8.3) | 4 (36.4) | |
| **Intent of injury,** n (%) | Homicide | 101 (84.8) | 93 (86.1) | 8 (72.7) | |
| | Unintentional | 14 (11.8) | 14 (12.9) | 0 (0.0) | **0.001** |
| | Suicide | 4 (3.4) | 1 (0.9) | 3 (27.2) | |
| **Vitals,** median (IQR) | Systolic BP (mmHg) | 125 (110-135) | 127 (113-136) | 60 (0-84) | **0.001** |
| | Diastolic BP (mmHg) | 78 (65-88) | 80 (70-89) | 40 (0-56) | **0.001** |
| | Pulse rate (beats per min) | 82 (75-89) | 82 (76-89) | 45 (0-95) | **0.007** |
| | Respiratory rate (/min) | 24 (18-34) | 25 (18-34) | 8 (0-12) | **0.001** |
| **Glasgow Coma Scale,** median (IQR) | | 15 (15-15) | 15 (15-15) | 3 (3-8) | **0.001** |
| **Laboratory parameters,** median (IQR) | Hemoglobin (g/dL) | 14.7 (13.3-15.7) | 14.8 (13.7-15.8) | 11.6 (7.0-12.8) | **0.001** |
| | Hematocrit (%) | 42.5 (39.4-45.8) | 42.9 (40.3-46.2) | 33.7 (22.2-36.7) | **0.001** |
| | ALT (U/L) | 24.0 (17.0-33.8) | 23.5 (17.0-33.0) | 40.0 (14.5-403.8) | 0.296 |
| | AST (U/L) | 33.0 (27.0-42.8) | 33.0 (27.0-41.8) | 40.5 (29.8-327.5) | **0.040** |
| | Creatinine (mg/dL) | 0.9 (0.8-1.1) | 0.91 (0.8-1.07) | 0.81 (0.71-1.16) | 0.413 |
| | pH | 7.33 (7.28-7.37) | 7.34 (7.31-7.38) | 7.18 (7.02-7.3) | **0.001** |
| | Base deficit (mmol/L) | 3.5 (1.6-5.6) | 2.6 (1.5-4.6) | 9.8 (4.8-14.5) | **0.001** |
| | Lactate (mmol/L) | 3.4 (2.3-5.3) | 3.3 (2.3-5.0) | 5.4 (2.6-17.0) | 0.081 |
| **Trauma score,** median (IQR) | Revised Trauma Score | 7.55 (7.55-7.84) | 7.55 (7.55-7.84) | 2.33 (0.00-3.51) | **0.001** |
| | Injury Severity Score | 5 (4-13) | 5 (4-9) | 75 (25-75) | **0.001** |
| **Intervention,** n (%) | Basic medical intervention | 48 (40.3) | 48 (43.6) | 0 (0.0) | **0.003** |
| | Blood transfusion | 31 (26.1) | 20 (18.5) | 11 (100.0) | **0.001** |
| | Surgery | 46 (38.7) | 39 (36.1) | 7 (63.6) | 0.074 |
| **Length of stay** (hours), median (IQR) | | 7 (3-112) | 9 (4-116) | 1 (1-14) | **0.014** |

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BP: Blood pressure; IQR: Interquartile range; SD: Standard deviation.

**Table 2.** Comparison of clinical characteristics, interventions, and outcomes by injury site among patients with firearm injuries (n = 119).

| Injury Site | All patients | Head/ neck | Chest | Abdomen | Upper extremity | Lower extremity |
|---|---|---|---|---|---|---|
| **n** (%) | 119 (100.0) | 21 (17.6) | 17 (14.3) | 27 (22.7) | 28 (23.5) | 73 (61.3) |
| **RTS**, median (IQR) | 7.55 (7.55-7.84) | 7.55 (5.14-7.84) | 5.14 (0.65-7.55) | 7.55 (7.10-7.84) | 7.69 (7.55 - 7.84) | 7.55 (7.55-7.84) |
| **ISS,** median (IQR) | 5 (4-13) | 9 (4-23) | 16 (10-75) | 9 (4-16) | 7 (4-14) | 4 (4-9) |
| **X-ray**, n (%) | 90 (75.6) | 12 (57.1) | 6 (35.3) | 14 (51.9) | 26 (92.9) | 71 (97.3) |
| **Computed Tomography**, n (%) | 104 (87.4) | 19 (90.5) | 11 (64.7) | 24 (88.9) | 23 (82.1) | 67 (91.8) |
| **Blood Transfusion**, n (%) | 31 (26.1) | 7 (33.3) | 11 (64.7) | 9 (33.3) | 6 (21.4) | 13 (17.8) |
| **Surgery**, n (%) | 46 (38.7) | 7 (33.3) | 10 (58.8) | 15 (55.6) | 13 (46.4) | 24 (32.9) |
| **LOS** (hour), median (IQR) | 7 (3-112) | 9 (4-118) | 5 (1-97) | 29 (4-140) | 17 (4-115) | 6 (3-78) |
| **Discharge from ED**, n (%) | 63 (52.9) | 10 (47.6) | 2 (11.8) | 11 (40.7) | 13 (46.4) | 47 (64.4) |
| **In-hospital mortality**, n (%) | 11 (9.2) | 4 (19.0) | 7 (41.2) | 4 (14.8) | 3 (10.7) | 2 (2.7) |

ED: Emergency department; ISS: Injury Severity Score; IQR: Interquartile range; LOS: Length of stay; RTS: Revised Trauma Score.

Table 3 presents the results of univariate logistic regression analyses evaluating predictors of in-hospital mortality among patients with firearm injuries. Several variables were found to be significantly associated with mortality. Female patients exhibited a significantly higher risk of death compared to males (OR 6.29, 95% CI: 1.54–25.62, p=0.01). Suicide-related injuries were strongly associated with mortality, demonstrating a markedly increased risk compared to other injury intents (OR 40.13, 95% CI: 3.73–431.15, p=0.002). Among physiological parameters, lower systolic and diastolic blood pressures were both significantly associated with increased mortality risk (SBP: OR 0.959, 95% CI: 0.940–0.979, p<0.001; DBP: OR 0.943, 95% CI: 0.916–0.970, p<0.001), as were lower respiratory rate (OR 0.791, 95% CI: 0.700–0.893, p<0.001) and lower GCS score (OR 0.490, 95% CI: 0.345–0.696, p<0.001). Trauma severity measures also showed strong associations with mortality. A lower RTS was associated with a significantly increased risk of death (OR 0.113, 95% CI: 0.026–0.487, p=0.003), while a higher ISS was similarly predictive of mortality (OR 1.323, 95% CI: 1.091–1.603, p=0.004).

**Table 3.** Logistic regression analysis shows the factors affecting survival.

| Variable | **Odds Ratio** (95%CI) | p |
|---|---|---|
| **Female gender** | 6.286 (1.542-25.624) | **0.01** |
| **Age, years** | 1.003 (0.991-1.016) | 0.63 |
| **Suicide intent** | 40.125 (3.734-431.149) | **0.002** |
| **Systolic blood pressure** | 0.959 (0.940-0.979) | **0.001** |
| **Diastolic blood pressure** | 0.943 (0.916-0.970) | **0.001** |
| **Respiratory rate** | 0.791 (0.700-0.893) | **0.001** |
| **Glasgow Coma Scale** | 0.490 (0.345-0.696) | **0.001** |
| **Revised Trauma Score** | 0.113 (0.026-0.487) | **0.003** |
| **Injury Severity Score** | 1.323 (1.091-1.603) | **0.004** |

CI: Confidence interval.

## DISCUSSION AND CONCLUSION

This study investigated firearm-related injuries at a level 1 trauma center, aiming to examine epidemiological trends while also identifying the key clinical determinants of mortality. The analysis revealed that certain physiological parameters and trauma scores were consistently associated with poor outcomes, emphasizing their importance in early risk assessment. Of particular note is the prognostic impact of injury intent and anatomical location. Furthermore, our study has shown that findings such as unstable vital signs and impaired consciousness are associated with mortality. Rapid intervention and aggressive treatment approaches are required for these patients.

There are many different results in the literature regarding the effect of gender on mortality.[4,7,11,12] While many studies show no differences,[4,7,11] some studies, like ours, indicate that mortality is higher in women.[12] These differences suggest that major factors such as sociodemographic variables may influence trauma outcomes. In particular, suicide attempts involving firearms are associated with particularly high mortality.[11] The lethality of such injuries stems from the mechanism of harm, which often results in extensive and irreversible damage, leaving limited opportunity for medical intervention.[11] These findings underscore the importance of identifying individuals at risk of self-harm involving firearms and implementing preventive strategies, including mental health interventions and restrictions on access to firearms, to reduce the likelihood of fatal outcomes in this vulnerable population.[13]

Abnormal vital signs are associated with mortality in firearm injuries, as in many other diseases.[14,15] Low systolic and diastolic blood pressure, high heart and respiratory rates, and low GCS scores were more common in those who did not survive, suggesting possible involvement of early physiological deterioration and central nervous system damage. Many scoring systems have been developed to assist physicians in making decisions and predicting prognosis.[16,17] These models attempt to guide clinicians by combining important predictors.[9,10,13] In this regard, the RTS, which integrates GCS, blood pressure, and respiratory rate in a structured manner, is widely used in trauma patients.[9] In our study, it was observed that RTS was significantly lower in patients who died. While trauma scores alone may not be decisive, their ability to integrate multiple clinical dimensions into a single risk estimate makes them valuable tools in high-pressure emergency care settings.[16]

In addition, several laboratory findings demonstrated strong associations with in-hospital mortality, warranting closer clinical attention. Lower hemoglobin and hematocrit levels observed in non-survivors likely reflect significant blood loss or hemodilution due to aggressive fluid resuscitation, both of which are indicative of physiological compromise.[1,4] More notably, markedly elevated base deficit and decreased pH levels were found in fatal cases, underscoring the prognostic importance of metabolic aci-

dosis in trauma.[1] Base deficit has been widely validated as a sensitive marker of tissue hypoperfusion and shock severity, with established correlations to transfusion needs and adverse outcomes in trauma patients.[7,19] Similarly, systemic acidemia, as reflected by low pH values, may indicate impaired perfusion and ongoing anaerobic metabolism.[1] Incorporating these laboratory markers into early triage and decision-making protocols may enhance the timely identification of critically ill patients and guide the intensity of resuscitative efforts in firearm-related trauma.

Another critical determinant of prognosis in firearm injury patients is the anatomical location of the injury.[3] Multiple injuries are common in firearm trauma, which limits direct comparisons of these injuries, but certain areas (head/neck and chest) have been consistently associated with higher mortality rates. High -velocity ballistic injuries to these areas cause rapid deterioration of vital organ function (e.g., heart, lungs, brain) due to the cavitation and blast effects of the bullet, which can lead to irreversible damage within minutes if not treated immediately.[18] In a retrospective study by Karaca et al.,[4] the highest mortality rate was observed in patients with head and neck injuries (41%), followed by abdominal (25%) and chest (5.5%) injuries. The ISS is widely used to help clinicians assess the severity of such injuries.[10,19] This anatomy-based scoring system quantitatively determines the trauma load by assigning weighted values to the most severely injured body regions.[10] In our study, a high ISS score was also found to be associated with mortality. Thus, the ISS serves as a practical and validated prognostic tool in the management of firearm-related injuries.[4,20]

Lastly, the rates of diagnostic imaging use in our study were higher than those typically reported in general trauma populations.[21] This trend may reflect a combination of increased clinical caution and the growing influence of defensive medicine, particularly in high-risk scenarios such as firearm injuries.[22] The fear of missing life-threatening injuries has led to a lowering of the threshold for using advanced imaging methods even in hemodynamically stable patients.[23] While this approach may improve diagnostic accuracy, it also raises important questions regarding resource utilization, radiation exposure, and the necessity of evidence-based imaging protocols in the treatment of penetrating trauma.[24,25]

This study has several limitations that should be acknowledged. First, the single-center design may affect the generalizability of the findings, as local social determinants of health could differ substantially from those in other regions. Second, the retrospective nature of the study introduces inherent risks of incomplete or inaccurately recorded data. Nevertheless, because all cases involved medicolegal firearm injuries, institutional documentation was likely more thorough than in standard clinical practice. This enhanced data fidelity likely improved the completeness and reliability of the dataset despite the retrospective design. Furthermore, several subgroup analyses—including those related to female gender and suicide intent—should be interpreted with caution due to small sample sizes, which may have contributed to wide confidence intervals and increased statistical variability in the regression estimates. Finally, although logistic regression was used to identify potential predictors of mortality, the limited number of mortality cases (n = 11) precluded the application of multivariate analysis. This constraint limited our ability to control for potential confounding factors between variables.

In conclusion, firearm injuries present complex clinical and public health challenges. Our study emphasizes the prognostic value of early vital sign assessment, anatomical injury location, and trauma scoring systems in predicting outcomes. High mortality rates in head, neck, and chest injuries highlight the need for rapid identification and aggressive interventions. Beyond mortality, the high rates of hospitalization and surgical intervention underscore the broader morbidity burden and resource demands these injuries impose on healthcare systems.

***Ethics Committee Approval:*** The study protocol received approval from the Marmara University Clinical Research Ethics Committee (Date: 31.01.2025, decision no: 09.2025-25-0053). Given its retrospective design, the requirement for informed consent was waived by the ethics committee.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

***Author Contributions:*** Concept – EK, MBK, MA; Supervision – EK, EA; Materials – EK, MBK, MA, AT, OÖ; Data Collection and/or Processing – EK, AT, OÖ; Analysis and/or Interpretation – EK, EA; Writing –EK, MBK, MA, AT, OÖ, EA.

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# Factors Affecting Pregnant Women's Fear of Birth Levels during Labour and Effects of the Fear of Birth on Birth Pain, Birth Trauma Perception and Mood: An Analytical-Cross-Sectional Study

# Doğum Eylemindeki Gebelerin Doğum Korkusu Düzeyini Etkileyen Faktörler ve Doğum Korkusunun, Doğum Ağrısı, Doğum Travması Algısı ve Duygulanım Düzeyine Etkisi: Analitik Kesitsel Çalışma

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**ABSTRACT**

**Objective:** This study aimed to investigate the factors influencing pregnant women's fear of childbirth during labour when they arrived at the hospital for delivery.

**Materials and Methods:** This was an analytical, cross-sectional study conducted with 244 pregnant women admitted to the Obstetrics Clinic of Sakarya Training and Research Hospital. Data were collected using a Descriptive Information Form, the Delivery Fear Scale, the Visual Analogue Scale, the City Birth Trauma Scale and the Labour Agentry Scale.

**Results:** Participants' mean childbirth fear scale scores were found to be below the moderate level. Fear levels were significantly correlated with participation in childbirth education and delivery method ($p<0.05$), but not with birth interventions or pain perception ($p>0.05$).
Fear was negatively correlated with perceived control and positively correlated with birth trauma scores ($p<0.05$).

**Conclusions:** Fear of childbirth can be alleviated by providing holistic and supportive care during the antenatal period. Reducing this fear may lead to improved birth outcomes. It is recommended that future research involve larger, multicenter samples and focus on identifying psychological, social and cultural variables, as well as evaluating interventions that effectively reduce childbirth fear.

**Keywords**: Fear of birth, midwifery, mood, pain, trauma

**ÖZ**

**Amaç:** Bu çalışmanın amacı, gebe kadınların doğum için hastaneye geldiklerinde, doğum sırasında yaşadıkları korkuyu etkileyen faktörleri araştırmaktır.

**Materyal ve Metot:** Bu çalışma, Sakarya Eğitim ve Araştırma Hastanesi Kadın Doğum Kliniği'ne başvuran 244 gebe ile yapılan analitik, kesitsel bir araştırmadır. Veriler Tanımlayıcı Bilgi Formu, Doğum Korkusu Ölçeği, Görsel Analog Ölçeği, City Doğum Travması Ölçeği ve Doğum Duygulanım Ölçeği kullanılarak toplanmıştır. Araştırma SPPS 25.0 programı kullanılarak analiz edilmiştir.

**Bulgular:** Katılımcıların doğum korkusu ölçek puan ortalaması orta düzeyin altında bulunmuştur. Korku düzeyleri, doğuma hazırlık eğitimine katılım ve doğum şekliyle önemli ölçüde ilişkili bulunurken ($p<0,05$), doğum müdahaleleri veya ağrı algısıyla ilişkili bulunmamıştır ($p>0,05$). Korku, algılanan kontrol ile negatif, doğum travması puanlarıyla pozitif korelasyon göstermiştir ($p<0,05$).

**Sonuç:** Doğum korkusu, doğum öncesi dönemde bütünsel ve destekleyici bakım sağlanarak hafifletilebilir. Bu korkunun azaltılması, doğum sonuçlarının iyileştirilmesine yol açacaktır. Gelecekteki araştırmaların, daha büyük, çok merkezli örnekleri içermesi ve psikolojik, sosyal ve kültürel değişkenleri belirlemeye odaklanması ve doğum korkusunu etkili bir şekilde azaltan müdahaleleri değerlendirmesi önerilir.

**Anahtar Kelimeler:** Ağrı, doğum korkusu, duygulanım, ebelik, travma

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## INTRODUCTION

Birth is inherently an uncertain and unpredictable process. If this uncertainty is not effectively managed, it may create difficulties in psychological adaptation and trigger fear among women.[1,2] Concerns about potential harm to themselves or their babies, as well as expectations or previous experiences of labour pain, trauma, and loss of control, can lead to intense fear and anxiety. These emotional responses are associated with various complications, including excessive bleeding, increased medical interventions, higher cesarean section rates, fetal distress, post-traumatic stress disorder, mood disorders, difficulty adapting to the maternal role, and breastfeeding problems in the postpartum period.[3-7] Collectively, such outcomes may discourage women from becoming pregnant or choosing to give birth again.[6,8]

The prevalence of fear of childbirth varies globally and is reported to range between 4% and 20%.[9] In Türkiye, studies indicate that approximately 20% of women report fear related to childbirth, while 6% to 13% experience a level of fear severe enough to impact the birthing process.[10]

Numerous studies have identified obstetric factors that contribute to childbirth-related fear. Variables such as parity,[11] mode of previous delivery, and prior birth experiences[3] have been shown to significantly influence the intensity of fear. These factors shape women's expectations of birth and affect their emotional and physiological responses during labour.[3,11]

This study aimed to identify the factors associated with fear of childbirth among pregnant women admitted to the hospital during labour. In addition, it sought to examine the relationship between childbirth fear and labour pain intensity, perception of birth as a traumatic event, and emotional state during labour. Understanding these interrelated factors can inform the development of targeted interventions to reduce childbirth fear, improve the birth experience, and support maternal mental health.

## MATERIALS AND METHODS

***Ethics Committee Approval:*** Prior to the commencement of the study, ethical approval was obtained from the Non-Interventional Ethics Committee of the Sakarya University Faculty of Medicine (Date: 15.11.2022, decision no: 324), along with permission from the hospital administration where the study was conducted. All participants provided verbal consent, permitting the use of their anonymized data for academic purposes. The study was conducted in accordance with the Declaration of Helsinki.

This analytical and cross-sectional study was conducted with pregnant women admitted to the delivery room of a training and research hospital. Inclusion criteria were being at least 37 weeks pregnant, having effective communication skills, and not having a high-risk pregnancy. Participants were informed about the purpose and procedures of the study, and data were collected through face-to-face interviews following verbal consent (Figure 1).

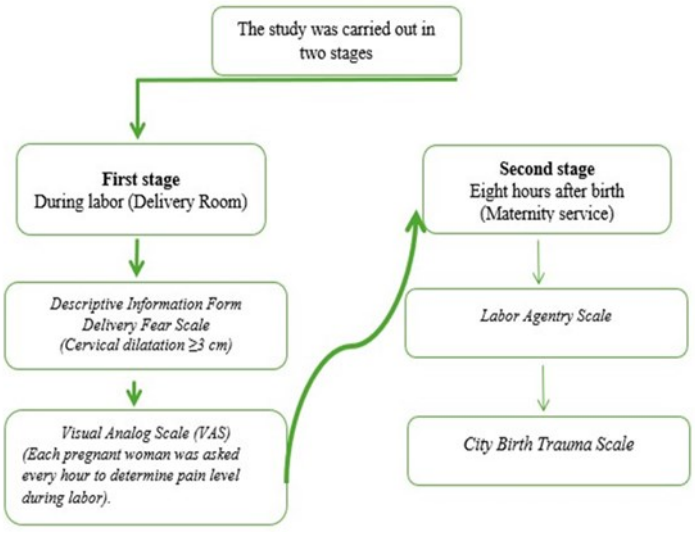


**Figure 1.** Data collection method.

The study took place in the obstetrics clinic of a high-capacity hospital where 6437 women gave birth in 2021. This number constituted the study population. Previous studies in Türkiye have reported varying prevalence rates of fear of childbirth. According to Bıyık and Aslan, 20% of women experience this fear, and 6-13% report fear significant enough to affect the birth process.[10] İsbir et al. found the rate to be as high as 42.4%.[3] These findings highlight the need to better understand and address childbirth-related fear in pregnant women. Using the EpiInfo 2022 program for known populations (95% confidence interval, α=0.05), the required sample size was calculated as 237. To account for possible drop-outs or incomplete data, the sample size was increased, and data collection was completed with 244 participants, thereby ensuring robust results. The study design aimed to minimize bias by focusing on full-term, low-risk pregnancies, thereby enhancing the validity and generalizability of findings. The goal was to explore childbirth experiences and associated psychological factors, particularly fear of childbirth, in a representative sample.

***Dependent Variable:*** Fear of birth

***Independent Variables:*** City Birth Trauma Scale and Labour Agentry Scale scores, birth pain, women's knowledge about pregnancy and birth and interventions performed during labour

***Forms and Scales Used in the Research:***

**Descriptive Information Form:** This form, prepared by researchers in line with the literature, consists of two parts.[1] The first includes eight, addressing participants' socio-demographic characteristics, while the second comprises 14 on pregnancy and birth-related variables, totaling 22 questions. Data were collected through verbal interviews, and additional clinical information, including hospitalization duration, labor stage, and medical interventions, was retrieved from medical records.

**Delivery Fear Scale (DFS):** Developed by Wijma et al., the DFS measures childbirth-related fear.[12] Its Turkish validity and reliability were established by Serçekuş et al.[1] The unidimensional scale includes 10 items, each rated on a 10-point Likert scale ranging from 1 (strongly disagree) to 10 (strongly agree). The total score can range from 10 to 100, with higher scores indicating a greater level of fear. Five of the items are positively worded, while the other five are negatively worded. The Cronbach alpha value of the scale was reported as 0.88 by Wijma et al., 0.90 by Serçekuş et al., and was found to be 0.92 in the study. The scale was administered during the first stage of labour, after women were admitted with a cervical dilation of 3 cm or more. The mean DFS score was 32.93±17.45.

**Visual Analog Scale (VAS):** VAS was used to assess labour pain. It consists of a 10 cm horizontal line anchored by "no pain" and "severe pain." Participants marked the point that best reflected their pain. The distance from the "no pain" end indicated the pain intensity.[13] VAS was administered hourly during labour, and the average pain score was calculated.

**City Birth Trauma Scale (CBTS):** Developed by Ayers et al., CBTS assesses postpartum trauma based on DSM-5 criteria.[14] The Turkish version has been validated.[15] Items 3-22 assess core PTSD symptoms across four domains: re-experiencing, avoidance, negative mood/cognitions, and hyperarousal. Dissociative symptoms (items 23-24) were used for screening only; participants with such symptoms were excluded. The original scale had a Cronbach's alpha of 0.71; the Turkish version, 0.76. In the current study, internal consistency was high (α=0.87). CBTS was administered postpartum during the second stage. The mean score was 40.4±1.89.

**Labour Agentry Scale (LAS):** The LAS, developed by Hodnett et al., measures perceived control during labour and has been used in various countries.[16] The Turkish validation was conducted by Gençalp.[17] The scale includes 29 items scored on a 5-point Likert scale (total range: 29-145), with higher scores indicating greater perceived control and a more positive birth experience. Cronbach's alpha was 0.86 in the original and 0.87 in the Turkish version; in the current study, it was 0.70. The LAS was administered in the second stage. The mean score was 113.14±19.71.

**Statistical Analysis:** Data were analyzed using SPSS 25.0. Descriptive statistics were presented as frequencies, percentages, and means. The Kolmogorov-Smirnov test assessed normality. Non-parametric tests were used due to the non-normal distribution. The Mann-Whitney U test compared two independent groups; Kruskal-Wallis was used for more than two. Bonferroni correction identified significant differences. Spearman's rank correlation evaluated relationships between variables. Statistical significance was set at $p<0.05$.

## RESULTS

Analysis of the socio-demographic characteristics of the pregnant women revealed that the majority of participants were aged 19-24, were high school or higher education graduates, and were homemakers. A statistically significant difference was found in DFS scores based on the variable of spouses' profession ($p<0.05$) (Table 1).

**Table 1.** Comparison of the mean scores obtained from the scales in terms of the participants' socio-demographic characteristics.

| Socio-Demographic Characteristics | | n (%) | Delivery Fear Scale Mean ± SD | Tests |
|---|---|---|---|---|
| **Age Groups (years)** | 19-24 | 107 (43.9) | 31.92±15.79 | KW= 0.014 |
| | 25-30 | 99 (40.6) | 33.65±18.22 | p=1.000 |
| | 31-36 | 30 (12.3) | 32.63±16.95 | |
| | 37-42 | 8 (3.2) | 38.75±29.88 | |
| **Educational Status** | Illiterate | 13 (5.3) | 36.23±24.57 | KW=1.616 |
| | Primary school | 85 (34.8) | 33.57±15.98 | p=0.446 |
| | High school and above | 146 (59.9) | 32.27±17.63 | |
| **Profession** | Homemaker | 200 (82.0) | 32.43±17.05 | **KW=6.188** |
| | Worker | 37 (15.2) | 37.32±19.31 | **p=0.045** |
| | Government Official | 7 (2.8) | 24.28±15.57 | |
| **Husband's Age groups (years)** | 20-24 | 14 (5.8) | 31.14±16.67 | KW=1.545 |
| | 25-29 | 66 (27.0) | 33.34±16.37 | P=0.672 |
| | 30-34 | 91 (37.3) | 32.97±19.77 | |
| | ≥35 | 73 (29.9) | 32.86±19.57 | |
| **Spouse's Educational Status** | Illiterate | 5 (2.0) | 29.80±8.58 | KW=0.130 |
| | Primary school | 56 (23.0) | 31.33±14.96 | P=0.937 |
| | High school and above | 183 (75.0) | 33.51±18.33 | |
| **Spouse's Profession** | Worker | 181 (74.2) | 34.98±18.51 | KW=9.823 |
| | Self-employed | 44 (18.0) | 27.13±10.89 | **p=0.007** |
| | Government official | 19 (7.8) | 26.84±15.41 | |
| **Total** | | **244 (100)** | | |

KW: Kruskal Wallis.

As shown in Table 2, multiparous women, those with planned pregnancies, and those admitted during the latent phase had higher DFS scores compared to others. Significant differences were also found in DFS mean scores according to variables such as participation in birth preparation training and type of delivery ($p<0.05$). It was observed that women who had not received childbirth preparation training and who delivered by cesarean section exhibited higher levels of fear of childbirth. Moreover, interventions during labour had no significant effect on fear of childbirth ($p>0.05$) (Table 2).

**Table 2.** Comparison of the mean scores obtained from the delivery fear scale in terms of the participants' pregnancy- and birth-related characteristics and in terms of the interventions undergone.

| | | n (%) | Delivery Fear Scale Mean ± SD | Tests |
|---|---|---|---|---|
| **Participants' Pregnancy and Birth-Related Characteristics** | | | | |
| **Parity** | Primiparae | 104 (42.6) | 35.72+18.65 | U=6285.000 |
| | Multiparae | 140 (57.4) | 30.87+16.26 | p=0.064 |
| **Is the pregnancy an intended pregnancy?** | Yes | 116 (47.5) | 33.10±18.01 | U=7214.000 |
| | No | 128 (52.5) | 32.78±16.99 | p=0.703 |
| **Receiving birth preparation training** | Yes | 8 (3.3) | 23.00±9.41 | U=552.000 |
| | No | 236 (96.7) | 33.27±17.57 | **p=0.046** |
| **Phase of labour when the pregnant woman was admitted to the delivery room** | Latent phase | 75 (30.7) | 37.10±20.35 | KW=4.683 |
| | Active phase | 143 (58.6) | 31.20±16.19 | p=0.096 |
| | Transition phase (cervical dilatation of 3 cm or more) | 26 (10.7) | 30.46±12.96 | |
| **Types of delivery** | Vaginal delivery without an intervention | 121 (49.6) | 28.53±13.02 | KW=10.689 |
| | Vaginal delivery with an intervention | 40 (16.4) | 35.00±20.26 | **p=0.005** |
| | Cesarean section | 83 (34.0) | 38.36±19.96 | |
| **Interventions undergone by the participants during labour** | | | | |
| **Electronic Fetal Monitoring (EFM)** | Yes | 239 (98.0) | 32.68±17.16 | U=419.000 p=0.253 |
| | No | 5 (2.0) | 45.20±27.83 | |
| **Undergoing Amniotomy** | Yes | 51 (20.9) | 32.09±17.95 | U=4684.500 |
| | No | 193 (79.1) | 33.16±17.35 | p=0.597 |
| **Enema Administration** | Yes | 3 (1.2) | 39.66±21.96 | U=274.000 |
| | No | 241 (98.8) | 32.85±17.43 | p=0.471 |
| **Undergoing Labour Induction** | Yes | 145 (59.4) | 33.88±17.76 | U=6634.500 |
| | No | 99 (40.6) | 31.55±16.98 | p=0.316 |

U: Mann-Whitney U Test; KW: Kruskal-Wallis.

The relationship between participants' mean DFS and VAS scores is illustrated in Figure 2. No statistically significant correlation was found between the two ($p>0.05$) (Figure 2).

Figure 3 shows the relationships among DFS, CBTS, and LAS scores. There was a statistically significant negative correlation between DFS and LAS scores, a positive correlation between DFS and CBTS scores, and a negative correlation between CBTS and LAS scores (Figure 3).

## DISCUSSION AND CONCLUSION

In this study, participants' mean score on the Delivery Fear Scale (DFS) was 32.93±17.45, indicating that fear of childbirth was below moderate levels. Higher DFS scores were observed among primiparous women, those with planned pregnancies, women who had not received childbirth preparation training, those admitted during the latent phase of labour, and those who gave birth via caesarean section. Fear levels were also higher in participants who did not undergo amniotomy or electronic fetal monitoring (EFM), who received enemas, or who experienced labour induction. Conversely, lower fear levels were reported among multiparous women, those with unplanned pregnancies, women who had received training, were admitted in the active or transition phases of labour, or gave birth vaginally.

Fear of childbirth is influenced by personality traits,[18] gestational age, pregnancy intention, and spousal support.[19] Fear of childbirth is more prevalent among nulliparous women[3] and homemakers.[3,20] While some studies associate fear of childbirth with work schedules,[21] childbirth preparation training has been shown to reduce this fear,[21,22] and higher fear levels are associated with cesarean preference.[23,24] Interestingly, participants who did not undergo EFM or amniotomy had higher fear levels, whereas those

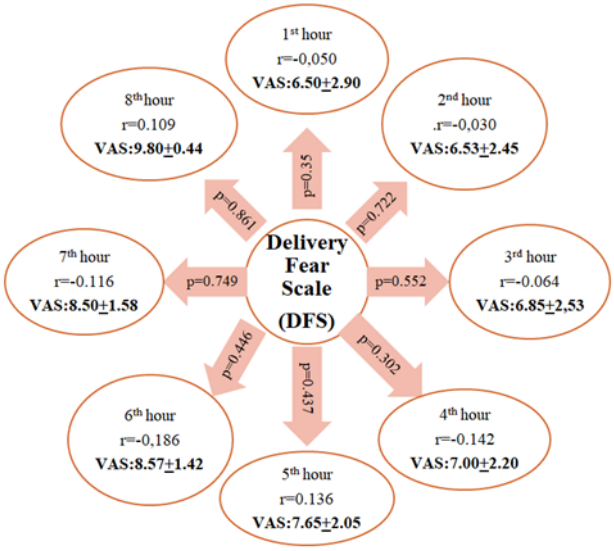


**Figure 2.** Relationship between the scores obtained from the DFS and VAS administered every hour during labour.

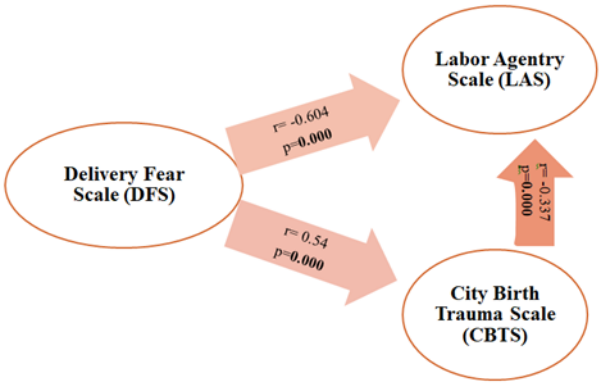


**Figure 3.** Relationship between the mean scores obtained from the overall delivery fear scale, city birth trauma scale and labour agentry scale.

who did often viewed these procedures as routine monitoring, which offered reassurance. Pregnant women perceive EFM not as an intervention but as checking the well-being of the fetus; thus, EFM gives women confidence during labor. Hourly Visual Analog Scale (VAS) pain scores during labor were not significantly correlated with DFS scores ($p>0.05$). In line with our findings, Simpson and Catling also reported that fear does not influence pain.[26] However, Place et al. noted that fear increases pain perception.[27] This suggests that labor pain and fear are influenced by multiple individual and contextual factors.

A significant positive correlation was found between DFS and City Birth Trauma Scale (CBTS) scores ($p<0.05$), indicating that higher fear is associated with more severe birth-related trauma symptoms. This aligns with literature showing that fear of childbirth increases the risk of postpartum PTSD and negatively impacts maternal-infant bonding and family dynamics.[28,29] Additionally, a negative correlation was found between DFS and the Labour Agentry Scale (LAS), which measures perceived control and emotional experience during birth. Higher fear was associated with a reduced sense of control and less positive mood during labour, supporting findings that women with lower fear report greater birth satisfaction.[30]

Fear of childbirth can intensify perceived pain, prolong labour, increase interventions, and lead to dissatisfaction. Holistic care that includes prenatal education, emotional support, and psychoeducation has been shown to reduce fear and its consequences.

In conclusion, this study found that fear of childbirth was, on average, below a moderate level, yet it was significantly influenced by factors such as childbirth preparation, type of delivery, and specific labour practices. While perceived pain was not directly associated with fear, a strong relationship was identified between childbirth fear, birth trauma, and negative emotional experiences. These findings highlight the need for targeted, supportive interventions to alleviate fear and foster positive birth experiences. In this study, we suggest conducting a multi-center study with more samples to explore the psychological and sociocultural aspects of fear related to childbirth in future research. The study provides important insights into the prevalence and influencing factors of childbirth fear among women in Türkiye. These findings contribute to the literature on maternal mental health and underline the importance of psychological support in perinatal care. Further large -scale, multi-centered studies are recommended to deepen understanding and inform the development of effective, targeted interventions to reduce childbirth fear and promote positive birth experiences.

***Ethics Committee Approval:*** Our study was approved by the Sakarya University Rectorate, Faculty of Medicine Dean's Office, Non-Interventional Ethics Committee" (Date: 15.11.2022, decision no: 324). The study was conducted in accordance with the Declaration of Helsinki.

***Conflict of Interest:*** No conflict of interest was declared by the authors.

***Author Contributions:*** Concept – MBC, HÖC, SCK; Supervision – MBC, HÖC; Materials – MBC, HÖC, BY, SCK; Data Collection and/or Processing – MBC, BY, SCK; Analysis and/or Interpretation – MBC, HÖC, BY, NUB; Writing – MBC, HÖC, BY, SCK, NUB.

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# The Role of Micronutrients and Thyroid Function Tests in Pediatric Hair Loss

# Çocuklarda Saç Dökülmesinde Mikrobesinlerin ve Tiroid Fonksiyon Testlerinin Rolü

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**ABSTRACT**

**Objective:** Hair loss is a common complaint among pediatric patients. This study aims to evaluate the potential associations between serum concentrations of ferritin, hemoglobin, iron, folate, 25-hydroxyvitamin D, free thyroxine, thyroid-stimulating hormone (TSH), zinc, and vitamin B12 in pediatric patients presenting with diffuse, non-scarring alopecia.

**Materials and Methods:** In this study, 75 children aged between 6 and 18 years who presented to the pediatric outpatient clinic with diffuse, non-scarring hair loss were included, along with 75 age and sex matched healthy children without hair loss who presented for routine check -ups as the control group. Children with a history of systemic disease, medication use, or dietary supplement use were excluded from both groups. The serum levels of the relevant parameters were statistically compared between the two groups.

**Results:** Children with hair loss had lower mean levels of zinc, folate, iron, vitamin B12, and TSH compared to the control group; however, only the decreases in zinc and folate levels were found to be statistically significant ($p<0.001$). Furthermore, when compared in terms of micronutrient deficiencies, only the folate level was significantly lower in the group with hair loss ($p=0.016$).

**Conclusions:** Our study is one of the first to suggest a potential role of folate deficiency in pediatric hair loss. In addition, micronutrient deficiencies were common in both groups. Therefore, we recommend that serum micronutrient levels, including folate, be assessed in children presenting with hair loss.

**Keywords:** Alopecia, child, folate, hair loss, micronutrient

**ÖZ**

**Amaç:** Saç dökülmesi, çocuk hastalarda sık karşılaşılan bir yakınmadır. Bu çalışmanın amacı, diffüz, skar bırakmayan saç dökülmesi olan çocuklarda serum ferritin, hemoglobin, demir konsantrasyonu, 25-hidroksivitamin D, folat, Tiroid sitümülan hormon (TSH), serbest tiroksin, çinko, ve B12 vitamini düzeylerinin rolünü araştırmaktır.

**Materyal ve Metot:** Bu çalışmada çocuk polikliniğine diffüz, skar bırakmayan saç dökülmesi ile başvuran 6-18 yaş arasında 75 çocuk ile cinsiyet ve yaş olarak eşleştirilmiş rutin tetkik için başvuran ve saç dökülmesi olmayan 75 sağlıklı çocuk (kontrol grubu) incelendi. İki grupta da kronik hastalığı olan ve herhangi bir takviye kullanımı olan hastalar çalışma dışı bırakıldı. Her iki grubun kan değerleri istatistiksel olarak karşılaştırıldı.

**Bulgular:** Saç dökülmesi olan çocuklarda çinko, folat, demir, vitamin B12 ve TSH düzeylerinin ortalama değerlerinin kontrol grubuna göre daha düşük olduğu saptandı; ancak istatistiksel olarak yalnızca çinko ve folat düzeylerindeki düşüklük anlamlı bulundu ($p<0,001$). Ayrıca, mikrobesin eksiklikleri açısından karşılaştırıldığında saç dökülmesi olan grupta yalnızca folat düzeyinde anlamlı düşüklük saptandı ($p=0,016$).

**Sonuç:** Çalışmamız çocuklarda saç dökülmesinde folat eksikliğinin rol oynayabileceğini gösteren ilk çalışmalardan biri olması nedeniyle önemlidir. Ayrıca her iki grupta da mikrobesin eksiklikleri sık görülmüştür. Bu nedenle saç dökülmesi ile başvuran çocuklardan folat düzeyi de dahil olmak üzere serum mikrobesin düzeylerinin değerlendirilmesini öneriyoruz.

**Anahtar Kelimeler**: Alopesi, çocuk, folat, saç dökülmesi, mikrobesin

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## INTRODUCTION

Alopecia or hair loss is a common complaint among pediatric patients. Although diffuse non-scarring hair loss in childhood typically tends to resolve spontaneously, it is frequently associated with emotional stress, previous infections, endocrine disorders, and deficiencies in essential micronutrients. Micronutrient deficiencies may disrupt the hair follicle cycle, leading to increased hair shedding and reduced hair growth.[1] Additionally, thyroid dysfunctions have also been linked to diffuse hair loss.[2]

In clinical practice, hematological and biochemical parameters such as ferritin, hemoglobin, serum iron, zinc, folate, vitamin B12, thyroid-stimulating hormone (TSH) and fT4 are frequently evaluated in children presenting with diffuse hair loss to identify potential underlying causes affecting the hair cycle. However, the diagnostic and clinical significance of these laboratory abnormalities in the pediatric population remains controversial; current evidence is limited, and findings across studies are often inconsistent.

This study aims to evaluate the relationship between laboratory parameters and hair loss in children presenting to a tertiary pediatric outpatient clinic. By comparing these values with sex and age-matched healthy controls, the study seeks to elucidate key biochemical markers involved in pediatric hair loss and to contribute to more rational clinical decisions.

## MATERIALS AND METHODS

***Ethics Committee Approval:*** Approval for this study has been obtained from the Ethics Committee of Düzce University. (Date: 02.06.2025, decision no: 160). The ethical principles of the Helsinki Declaration were applied in the implementation of the study protocol.

***Study Design and Participants:*** In this retrospective case-control study, pediatric patients admitted to Düzce University Faculty of Medicine Pediatric Outpatient Clinic with the complaint of diffuse hair loss were included. Participants were categorized into two groups: a study group comprising 75 children who presented with complaints of hair loss, and a control group consisting of sex and age matched 75 children who were evaluated in the same clinic for routine laboratory assessments without any hair-related symptoms. Children aged 6 to 18 years presenting with diffuse non-scarring hair loss, without underlying dermatologic disorders such as tinea capitis, alopecia areata, or trichotillomania, were included in the study group. Children with a history of systemic disease, medication use, or dietary supplement use were excluded from both groups.

For both groups, relevant laboratory parameters were extracted from electronic medical records, including hemoglobin concentration, serum iron, ferritin, folate, 25(OH)D, TSH, fT4, zinc, and vitamin B12 levels. Specific reference intervals were used to interpret hemoglobin, iron, ferritin, and zinc values. Serum 25(OH)D levels of 20 ng/mL and above were considered normal vitamin D levels.[3] Normal reference values were defined as vitamin B12 $\geq$ 300 pg/mL[4], folate $\geq$ 4 ng/mL[5], zinc $\geq$ 70 µg/dL[6], and ferritin $\geq$ 15 ng/mL.[7] Hemoglobin levels < 11.5 g/dL in children aged 6 to 16 years, < 12 g/dL in females aged 17 to 18 years, and < 13 g/dL in males aged 17 to 18 years were classified as anemia.[8]

All laboratory results were compared between the two groups using appropriate statistical methods to determine the potential relationship between micronutrient status, thyroid function, and hair loss in children.

***Statistical Analysis:*** Descriptive statistics for continuous variables were presented as mean ± standard deviation, median (interquartile range, IQR: 25th–75th percentile), maximum and minimum values. Frequency and percentage were used to express categorical variables. The Shapiro-Wilk test was used to assess the normality of distribution for continuous variables. Comparisons of continuous variables between the hair loss group and the control group were performed using the Mann–Whitney U test. The chi-square test or Fisher's exact test was used to compare categorical variables between groups, whichever was appropriate. To evaluate whether folate level constituted a risk factor for hair loss, a univariate logistic regression analysis was conducted. All statistical analyses were performed using IBM SPSS Statistics version 20.0 (Chicago, IL, USA), and a p-value of <0.05 was considered statistically significant.

## RESULTS

A total of 75 patients were enrolled in the study. Among them, 63 (84%) were female. The mean age of patients was 13.24±3.81 years (min:6- max:17 years). Seventy-five healthy children whose age and gender matched the patient group were selected as the control group. Of 75 healthy individuals, 63 (84%) were female. The mean age of the control group was 13.13±3.80 years (min:6–max:17 years). The mean serum levels in the patient group were as follows: ferritin, 38.18 ± 27.73 ng/mL; 25(OH)D, 21.15 ± 9.93 ng/mL; folate, 6.92 ± 3.45 ng/mL; zinc, 86.74 ± 10.60 µg/dL; and vitamin B12, 406.33 ± 138.47 pg/mL. In the control group, the corresponding mean serum levels were: ferritin, 36.82 ± 20.78 ng/mL; 25(OH)D, 18.99 ± 8.86 ng/mL; folate, 10.47 ± 5.51 ng/mL; zinc, 98.66 ± 18.45 µg/dL and vitamin B12, 479.24 ± 225.55 pg/mL. The mean serum levels of zinc, folate, iron, vitamin

B12, and TSH were lower in the hair loss group. However, the differences in serum iron, vitamin B12, and TSH levels between groups were not statistically significant ($p = 0.81$, 0.096, and 0.604, respectively). In contrast, zinc and folate levels were significantly lower in the hair loss group ($p < 0.001$). Although the mean serum levels of 25(OH)D, ferritin, hemoglobin, and free T4 were higher in the hair loss group, these differences were not statistically significant ($p > 0.05$). A detailed comparison of the laboratory findings between groups is presented in Table 1.

In the hair loss group, low serum levels were observed in the following proportions of patients: zinc in 2 (2.7%), ferritin in 11 (14.7%), vitamin B12 in 19 (25.3%), 25(OH)D in 52 (69.3%), hemoglobin in 14 (18.7%), and folate in 15 (20%). In the control group, no patients had low serum zinc levels; however, low levels were detected for ferritin in 6 (8.0%), vitamin B12 in 22 (29.3%), 25(OH)D in 41 (54.7%), hemoglobin in 13 (17.3%), and folate in 5 (6.7%). There was no difference between groups in the ratio of patients with zinc, ferritin, vitamin B12, 25(OH)D, or hemoglobin levels below normal ($p > 0.05$). However, the ratio of patients with low folate levels was higher in the hair loss group compared to the control group ($p = 0.016$). Hypothyroidism was detected in only one patient from the hair loss group, and appropriate treatment was initiated. A detailed comparison of the distribution of laboratory abnormalities between groups is presented in Table 2.

Univariate logistic regression analysis was performed to evaluate whether folate and zinc levels, which showed significance in univariate comparisons, were associated with an increased risk of hair loss. Although the mean serum zinc level was lower in the hair loss group, no significant difference was found in the distribution of subnormal zinc levels between the groups; therefore, zinc was not included in the regression analysis. However, low folate levels were found to be significantly associated with hair loss. According to the univariate logistic regression analysis, children with low folate levels had a 3.5-fold increased risk of hair loss compared to those with normal folate levels ($p = 0.022$) (Table 3).

**Table 1.** Comparison of laboratory parameters between children with hair loss and healthy controls.

| Parameters | Total (n=150) | Patients group (n=75) | Control group (n=75) | p-value |
|---|---|---|---|---|
| | Mean±SD<br>Median (Min-Max)<br>(IQR) | Mean±SD<br>Median (Min-Max)<br>(IQR) | Mean±SD<br>Median (Min-Max)<br>(IQR) | |
| **Zinc**<br>(µg/dL) | 92.70±16.15<br>89.5 (60.9-148.0)<br>(82.0-99.7) | 86.74±10.60<br>86.0 (60.9-112.0)<br>(80.0-93.0) | 98.66±18.45<br>95.8 (72.0-148.0)<br>(85.3-105.0) | **0.001**[b] |
| **Iron**<br>(µg/dL) | 70.50±37.25<br>60 (13-190)<br>(44.0-94.2) | 68.14±31.48<br>60 (14-143)<br>(48.0-88.0) | 72.85±42.33<br>62 (13-190)<br>(39.0-112.0) | 0.810[b] |
| **Ferritin**<br>(ng/mL) | 37.50±24.43<br>33.0 (3.9-1390)<br>(19.4-48.0) | 38.18±27.73<br>33.0 (6.4-139.0)<br>(19.0-48.0) | 36.82±20.78<br>33.0 (3.9-109.0)<br>(21.0-49.0) | 0.766[b] |
| **Vitamin B12**<br>(pg/mL) | 442.78±190.07<br>425 (178-1360)<br>(287-533) | 406.33±138.47<br>419 (178-758)<br>(292-478) | 479.24±225.55<br>465 (180-1360)<br>(287-600) | 0.096[b] |
| **25(OH)D**<br>(ng/mL) | 20.07±9.32<br>16.8 (4.0-47.0)<br>(12-23) | 21.15±9.93<br>16.6 (4.0-47.0)<br>(11.8-22.0) | 18.99±8.86<br>17.0 (5.7-46.0)<br>(12.0-24.0) | 0.403[b] |
| **Hemoglobin**<br>(g/dL) | 13.05±1.35<br>13 (9.6-17.0)<br>(12.2-13.8) | 13.26±1.30<br>13.0 (11.4-17.0)<br>(12.3-14.0) | 12.85±1.37<br>12.8 (9.6-16.4)<br>(12.2-13.5) | 0.078[b] |
| **Folate**<br>(ng/mL) | 8.69±4.92<br>7.4 (1.3-23.0)<br>5.6-11.0) | 6.92±3.45<br>6.0 (1.3-15.5)<br>(4.3-9.1) | 10.47±5.51<br>8.2 (3.0-23.0)<br>(6.5-13.4) | **0.001**[b] |
| **TSH**<br>(mIU/L) | 1.90±0.86<br>1.5 (0.4-5.8)<br>(1.5-2.1) | 1.88±0.77<br>1.8 (0.4-5.5)<br>(1.5-2.2) | 1.92±0.94<br>1.5 (0.6-5.8)<br>(1.5-2.0) | 0.604[b] |
| **fT4**<br>(ng/dL) | 1.15±0.11<br>1.1 (1.0-1.9)<br>(1.1-1.2) | 1.16±0.12<br>1.2 (1.0-1.9)<br>(1.1-1.2) | 1.15±0.09<br>1.1 (1.0-1.5)<br>(1.1-1.2) | 0.368[b] |

b: Mann-Whitney U test.

**Table 2.** Comparison of the distribution of laboratory abnormalities between children with hair loss and healthy controls

| Parameters | | Total (n=150) | Patients group (n=75) | Control group (n=75) | p-value |
|---|---|---|---|---|---|
| **Zinc** | ≥70 µg/dL | 148 (98.7) | 73 (97.3 | 75 (100) | 0.497[c] |
| | <70 µg/dL | 2 (1.3) | 2 (2.7) | 0 (0) | |
| **Ferritin** | ≥15 ng/mL | 133 (88.7) | 64 (85.3) | 69 (92.0) | 0.198[c] |
| | <15 ng/mL | 17 (11.3) | 11 (14.7) | 6 (8.0) | |
| **Vitamin B12** | ≥300 pg/mL | 109 (72.7) | 55 (74.7) | 53 (70.7) | 0.198[c] |
| | <300 pg/mL | 41 (27.3) | 19 (25.3) | 22 (29.3) | |
| **25(OH)D** | ≥20 ng/mL | 57 (38.0) | 23 (30.7) | 34 (45.3) | 0.064[c] |
| | <20 ng/mL | 93 (62.0) | 52 (69.3) | 41 (54.7) | |
| **Hemoglobin** | Normal | 123 (82.0) | 61 (81.3) | 62 (82.7) | 0.832[c] |
| | Anemia | 27 (18.0) | 14 (18.7) | 13 (17.3) | |
| **Folate** | ≥4 ng/mL | 130 (86.7) | 60 (80.0) | 70 (93.3) | **0.016[c]** |
| | <4 ng/mL | 20 (13.3) | 15 (20.0) | 5 (6.7) | |

c: Chi-Square Test/Fisher's Exact test

**Table 3.** Univariate logistic regression analysis for folate values in hair loss.

| Parameters | | B (SE) | OR | 95 % CI | | p-value |
|---|---|---|---|---|---|---|
| **Folate** | ≥4 ng/mL | 1 | | | | |
| | <4 ng/mL | 1.253 (0.546) | 3.500 | 1.201 | 10.196 | **0.022** |

SE: Standard Error; OR: Odds Ratio; CI: Confidence Interval.

## DISCUSSION AND CONCLUSION

Hair loss is a common complaint among children and can lead to significant anxiety for both patients and their families. However, the existing literature on diffuse hair loss in the pediatric population is limited, with most studies focusing primarily on telogen effluvium, the most prevalent form of diffuse hair loss. In this study, we aimed to evaluate serum levels of vitamin D, vitamin B12, folate, zinc, ferritin, iron, and hemoglobin, as well as thyroid function tests, in children presenting with diffuse hair loss. Low ferritin levels, anemia, iron, vitamin B12, folate, and 25(OH)D deficiency, and thyroid dysfunction are considered potential factors causing hair loss.[9] Despite being investigated in previous research, the effects of these parameters on hair health remain controversial, with findings differing widely among studies.

Micronutrients play an integral role in maintaining the hair follicle cycle by supporting the dynamic proliferation of matrix cells within the follicular bulb, where cellular turnover is particularly high. At the molecular level, several vitamins and minerals, including vitamin D, ferritin, vitamin B12, folate, and zinc, have been implicated in the regulation of hair follicle cycling and growth. Folate acts as a coenzyme essential for the synthesis of nucleic acids and the metabolism of amino acids. Vitamin B12 functions as a cofactor for methionine synthase and participates in the synthesis of approximately 100 different compounds, such as DNA, RNA, and proteins. Given their essential roles in nucleic acid production and cellular proliferation, both folate and vitamin B12 are thought to be important for the maintenance of rapidly dividing cells, such as those found in the hair follicle.[10] Iron is a cofactor of the ribonucleotide reductase enzyme and is therefore an essential component of DNA synthesis. Rapidly proliferating hair matrix cells have a high iron requirement.[10,11] Zinc, serving as a cofactor for numerous enzymes, contributes to maintaining physiological homeostasis and plays an essential role in hair follicle cycling.[12] Additionally, the vitamin D receptor participates in key signaling pathways such as Wnt/β-catenin and Hedgehog, which are crucial for the initiation and maintenance of the anagen phase in hair follicles.[13] Thyroid hormones are essential for the normal development and upkeep of hair follicles, and therefore, hair loss may indicate an underlying thyroid dysfunction.[14]

Research on the relationship between iron and ferritin levels and hair loss has yielded conflicting results. However, iron deficiency and low ferritin levels are frequently observed in individuals experiencing hair loss.[15] Several studies have indicated that diffuse hair loss is more likely to develop when serum ferritin concentrations drop below a critical level, typically around 50 µg/L.[16] However, this association has not been supported by other studies.[10,17]

In a study conducted in Türkiye investigating the relationship between micronutrient levels and hair loss across all age groups, a positive correlation was observed between hemoglobin levels and hair loss exclusively in female patients. However, no signifi-

cant associations were found between hair loss and serum levels of vitamin B12, ferritin, folate, or zinc.[18] In another study conducted in Türkiye, no significant differences were found between patients with and without hair loss in terms of iron, hemoglobin, ferritin, selenium, vitamin B12, vitamin D levels, or thyroid function tests. Notably, individuals experiencing hair loss exhibited markedly reduced zinc levels.[19]

Among Egyptian children with diffuse non-scarring alopecia, anemia, low ferritin, and zinc levels were commonly observed, and a positive correlation was found between the severity of micronutrient deficiency and the extent of hair loss.[20] Cheung et al.[21] reported that ferritin deficiency was present in 45.2% of patients with hair loss, followed by vitamin D deficiency in 33.9% and zinc deficiency in 9.6%. Vitamin B12 deficiency was rare, observed in only 2.6% of cases, and no folate deficiency was detected. However, since this study lacked a control group, comparisons with healthy individuals could not be performed.

A study conducted in the USA demonstrated that children with hair loss had a significantly higher prevalence of iron deficiency compared to controls, while no differences were observed in vitamin D or zinc levels. Moreover, thyroid function tests (TFTs) were similar to those of healthy children.[1] Wu et al.[12] demonstrated that individuals experiencing hair loss had significantly reduced mean serum zinc levels compared to healthy controls, implying a potential role of zinc deficiency in the underlying pathophysiology of hair loss. However, another study reported no significant difference in zinc levels between the patient and control groups.[22]

One of the main reasons for the inconsistent findings regarding the relationship between micronutrient levels and hair loss in the literature is the absence of appropriate control groups in many studies. Since micronutrient deficiencies are also prevalent in the general population across many societies, the deficiencies observed in individuals with hair loss may not be distinguishable from this widespread condition. Moreover, the inclusion of study populations from diverse geographical and cultural backgrounds contributes to heterogeneity in results, due to variations in socioeconomic status and access to healthcare services. For instance, in less developed countries, hair loss is often not prioritized as a reason for medical consultation, whereas families with higher socioeconomic status are more likely to seek medical care for such complaints. The limited number of studies focusing specifically on diffuse hair loss in children, as well as the nutritional differences between children and adults, may further explain the conflicting findings reported in the literature.

In our study, zinc, folate, iron, vitamin B12, and TSH levels were found to be lower in children with hair loss compared to the control group; however, only zinc and folate levels reached statistical significance. No significant differences were observed in the other parameters. Within the hair loss group, the prevalence of deficiencies was 2.7% for zinc, 14.7% for ferritin, 25.3% for vitamin B12, 69.3% for (25 (OH)D, 18.7% for hemoglobin, and 20% for folate. Although micronutrient deficiencies were generally common among children with hair loss, only folate deficiency demonstrated a significant difference between groups when comparing rates of micronutrient levels below the normal reference range; the rates for other parameters were similar between groups. Given the high prevalence of micronutrient deficiencies in our population, we recommend that micronutrient levels be assessed in children presenting with hair loss.

An important strength of this study is the inclusion of an age- and sex-matched control group, which enables the isolation of the effect of micronutrient levels on hair loss from other confounding factors. However, the study has several limitations, including its retrospective design, single-center data collection, and the lack of detailed evaluation of other potential contributing factors such as psychosocial stressors, recent infections, use of cosmetic hair care products, and dietary habits.

In conclusion, this study aimed to highlight the importance of micronutrients and TFTs in the management of children with hair loss. Although these parameters did not reach statistical significance in association with hair loss, their deficiencies were notably prevalent in the general population, as evidenced by the control group. Our study is significant as one of the first to suggest that folate deficiency may play a role in pediatric hair loss. Therefore, we recommend that serum micronutrient levels, including folate, be routinely evaluated in children presenting with hair loss. Further clarification of folate's role in pediatric hair growth and the hair loss cycle requires well-designed prospective studies conducted across multiple centers with larger participant cohorts.

***Ethics Committee Approval:*** Our study was approved by the Düzce University Ethics Committee (Date: 02.06.2025, decision no: 160). The study was conducted in accordance with the principles of the Declaration of Helsinki

***Conflict of Interest:*** No conflict of interest was declared by the authors.

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