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Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. I n: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93113.

### Journal article on the Internet

Abood S. Quality improvement initiative in nursing homes: The ANA acts in an advisory role. Am J Nurs [serial on the Internet] 2002 [cited 12 Aug 2002]; 102. Available from: www.nursingworld.org/AJN/2002/june/wawatch.htm

### Website

Cancer-pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources [updated 16 May 2002; cited 9 Jul 2002]. Available from: www.cancer-pain.org

### An organization as an author

The Intensive Care Society of Australia and New Zealand. Mechanical ventilation strategy in ARDS: Guidelines. Int Care J Aust 1996;164:282-4.

### Acknowledgements

The source of financial grants and the contribution of colleagues or institutions should be acknowledged.

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JOURNAL OF CONTEMPORARY MEDICINE

Formerly Çağdaş Tıp Dergisi

# CONTENTS

YEAR 2024 VOLUME 14 ISSUE 6 e-ISSN 2667-7180

## ORIGINAL ARTICLES

JOURNAL OF CONTEMPORARY MEDICINE

Formerly Çağdaş Tıp Dergisi

# CONTENTS

YEAR 2024 VOLUME 14 ISSUE 6 e-ISSN 2667-7180

## ORIGINAL ARTICLES



## REVIEW

JOURNAL OF
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Original Article / Orijinal Araştırma

# Congenital Heart Diseases Detected by Fetal Echocardiography and the Prevalence: A Single Center Experience

## Fetal Ekokardiyografi ile Tespit Edilen Doğumsal Kalp Hastalıkları ve Prevelansı: Tek Merkez Deneyimi

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## Abstract

**Aim**: Fetal echocardiography is an effective screening tool for the detection of cardiac anomalies. The aim of this study is to evaluate risk groups of pregnant women, to determine congenital heart diseases in each group and to find the prevalence of cardiac anomalies in our region.

**Material and Method**: Our study included all pregnant women who were referred for fetal echocardiography between January 2023 and September 2024.

**Results**: A total of 387 pregnant women underwent fetal echocardiography of which 136 were low-risk group and 251 were high-risk group. The mean ages of pregnant women were 27.43±1.37 and 28.54±5.45 years, respectively. Among the high-risk group, maternal diabetes (13.17%), dysrhythmia (5.42%) and history of extracardiac anomaly in previous child or fetus (8.53%) were the most common reasons for referral. While ventricular septal defect was the most detected congenital heart disease in low risk group; hypoplastic left heart syndrome (1.20%) and pulmonary atresia/hypoplasia (1.20%) were the most detected cardiac anomalies in high-risk group. The prevalence of cardiac anomalies in the low-risk and high-risk pregnancies was found to be 2.94% and 6.37% respectively while the overall prevalence was 5.16%.

**Conclusion**: Fetal echocardiography is a very useful technique when performed by experienced individuals with sufficient time. Dedicated cardiac screening should be part of the routine anomaly scan. Also, detailed fetal echocardiography should be performed in all pregnant women who were in low or high risk groups.

**Keywords**: Congenital heart diseases, fetal echocardiography, referral risk group, prevalence

## Öz

**Amaç**: Fetal ekokardiyografi, kardiyak anomalilerin tespiti için etkili bir tarama aracıdır. Bu çalışmanın amacı, gebe kadınların risk gruplarını değerlendirmek, her gruptaki konjenital kalp hastalıklarını belirlemek ve bölgemizde kardiyak anomalilerin prevalansını bulmaktır.

**Gereç ve Yöntem**: Çalışmamız Ocak 2023 ve Eylül 2024 tarihleri arasında fetal ekokardiyografi için sevk edilen tüm gebeleri içermektedir.

**Bulgular**: Toplam 387 gebe kadına fetal ekokardiyografi uygulandı, bunlardan 136'sı düşük risk grubunda ve 251'i yüksek risk grubundaydı. Gebelerin ortalama yaşları sırasıyla 27,43±1,37 ve 28,54±5,45 yıldı. Maternal diyabet (%13,17), disritmi (%5,42) ve ekstrakardiyak anomalisi olan önceki çocuk veya fetüs öyküsü (%8,53) yüksek risk grubunda en sık sevk nedenleriydi. Ventriküler septal defekt düşük risk grubunda en sık tespit edilen doğumsal kalp hastalığı iken; hipoplastik sol kalp sendromu (%1,20) ve pulmoner atrezi/hipoplazi (%1,20) yüksek risk grubunda en sık tespit edilen kardiyak anomalilerdi. Serimizde doğumsal kalp hastalıklarının prevalansı düşük riskli ve yüksek riskli gebeliklerde sırasıyla %2,94 ve %6,37 olarak bulunurken, genel prevalans %5,16 idi.

**Sonuç**: Fetal ekokardiyografi, yeterli zamana sahip deneyimli kişiler tarafından yapıldığında çok yararlı bir tekniktir. Özel kardiyak tarama rutin anomali taramasının bir parçası olmalıdır. Ayrıca, düşük veya yüksek risk grubunda olan tüm gebe kadınlara ayrıntılı fetal ekokardiyografi yapılmalıdır.

**Anahtar Kelimeler**: Doğumsal kalp hastalıkları, fetal ekokardiyografi, sevk risk grubu, prevelans

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## INTRODUCTION

Fetal cardiology represents one of the most exciting and rapidly evolving areas in the field of fetal medicine. Fetal echocardiography is completely noninvasive and harmless and is the best tool in this direction.[1] Congenital heart disease (CHD) is the most common congenital anomaly found in humans. In various studies, the incidence of CHD varies between approximately 4-50/1000 live births, of which 2.5-3/1000 live births present seriously ill in the neonatal period or early infancy and require specialist cardiac care.[2] Despite considerable advances in medical care, CHD is associated with substantial morbidity and death.[3] Accurate prenatal diagnosis of the CHD subtype is important to enable better clinical decision making, including prenatal management, recommendations for termination of the pregnancy, postnatal management of the patient, and for early referral to pediatric cardiology and cardiovascular surgery centers.[2,3] Also, prenatal diagnosis has been suggested to impart survival advantage in the great arteries (TGA), hypoplastic left heart syndrome (HLHS), and coarctation of aorta (CoA).[4-6] Additionally, fetal therapy can be offered for specific defects such as critical aortic stenosis and critical pulmonary stenosis, and various rhythm disturbances. Also, early termination can be offered if indicated which can help in reducing the incidence of complex CHDs.[2,7]

The sensitivity and specificity of fetal echocardiography have increased over time. A study of meta-analysis about first-trimester echocardiography in diagnosing CHDs, showed a sensitivity of 85% and specificity of 99%.[8] However, two meta-analyses of whole gestation fetal echocardiography also included first trimester echocardiography in diagnosing CHDs showed lower sensitivity values of 63.1% and 60.3%, respectively.[9,10] On the other hand, in a recent meta-analyses study of Yu et al. demonstrated that first trimester echocardiography is effective in diagnosing the CHDs, as a pooled sensitivity of 75% and a specificity of 99.9%.[11]

Although fetal echocardiography is established screening tool for the detection of cardiac anomalies, its utility and awareness remains less in most areas of the world. There is no data from our local region about the usage and outcome of fetal echocardiography. In this study, the distribution of pregnant women who underwent fetal echocardiography in our tertiary hospital according to low and high-risk factors, the reasons for admission and CHDs detected in fetal echocardiography were evaluated.

## MATERIAL AND METHOD

### Study population

The study was a retrospective research and was obtained from our University Medical Research Ethics Committee (Date: 23.09.2024, Decision No: 10-2024/02, Number: E-11095095-050.04-216395). It was in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients for the use of data from medical records.

This study is a retrospective research which was performed between January 2023 and September 2024. A total of 387 pregnant women who were in the 18th to 36th week of gestation were included in our study. The patients consisted of pregnant women who were referred by obstetricians due to various reasons which were classified as high-risk and low-risk groups.[12] The study population was analyzed in detail in terms of pregnancy history, reasons for applying to our clinic, use of any medication, presence of chromosomal or fetal anomalies, number and characteristics of previous pregnancies, presence of congenital or acquired heart diseases and family history. Also, all pregnant women were grouped as either high-risk or low-risk pregnancies according to these parameters.

### Fetal echocardiography

Fetal heart examinations were performed using Philips Affiniti 50 (Philips Healthcare, Andover, Netherlands) echocardiography device with 2.5-5 MHz transducers by the same echocardiographic scanner. All fetal echocardiographic examinations were performed using standard techniques that determined the fetal position and heart axis and provided Doppler and M-mode measurements.[13,14] In all the cases, four chamber view, outflow-tract views, three vessel view, aortic and ductal arch views were done. Fetal heart rate was noted and any arrhythmia was confirmed with M-mode imaging, color Doppler and pulse-wave Doppler were used whenever necessary. All the images were recorded.

## RESULTS

A total of 387 pregnant women were included in the study. **Table 1** shows low-risk and high-risk pregnancy groups according to referral criteria. Thus, 136 (35.13%) pregnant women were in the low-risk group and 251 (64.87%) were in the high-risk group. The most common reasons for referral in the high-risk group were maternal diabetes (13.17%), dysrhythmia (5.42%) and a previous history of a child or fetus with extracardiac anomalies (8.53%). However, in the low-risk pregnancies, lack of good image of the fetal heart by ultrasonography was the major reason for referral (20.93%).

The demographic data were summarized in **Table 2**. The comparison of the pregnant women included in the study according to their risk status revealed p=0.06. In the risk groups the mean ages were 27.43±1.37 and 28.54±5.45 years, respectively and no statistically significant difference was found between the groups (p>0.05). The mean gestational week was 22.73±2.25 and 23.61±1.61 weeks in the study population, respectively. Similarly, no statistical difference was detected for this parameter between the groups (p>0.05). The percentages of primiparas in low and high-risk groups were 65.44% and 58.56, respectively. Additionally, 2 and 5 pregnancies were multiple in the low-risk and high-risk groups, respectively.

**Table 1: Distribution of pregnant women according to low-risk and high-risk factors.**

| Risk groups and factors | N: 387 | % |
|---|---|---|
| **1. Low risk group** | | |
| Lack of good image of the fetal heart by ultrasound | 81 | 20.93 |
| Suspicion of CHD during 2nd trimester ultrasound | 41 | 10.59 |
| Self-referral | 14 | 3.61 |
| Total | 136 | 35.13 |
| **2. High risk group** | | |
| **2.a. Maternal factors** | | |
| Maternal diabetes | 51 | 13.17 |
| In vitro fertilization | 18 | 4.65 |
| Multiple pregnancy | 15 | 3.87 |
| Maternal use of medicine | 11 | 2.84 |
| Advanced maternal age | 13 | 3.35 |
| Maternal CHD | 7 | 1.81 |
| Maternal rheumatologic diseases | 5 | 1.29 |
| Maternal TORCH infections | 1 | 0.25 |
| **2.b. Fetal factors** | | |
| Dysrhythmia | 21 | 5.42 |
| Polyhydramniosis, oligohydramniosis | 13 | 3.35 |
| Fetal extracardiac anomaly | 12 | 3.10 |
| Chromosomal anomaly | 2 | 0.51 |
| Increased nuchal translucency | 3 | 0.77 |
| **2.c. Hereditary factors** | | |
| Previous child or fetus with CHD | 21 | 5.42 |
| Previous child or fetus with extracardiac anomaly | 33 | 8.53 |
| Familial CHD (excluding parents and siblings) | 25 | 6.45 |
| Total | 251 | 64.87 |

CHD; congenital heart diseases, TORCH; Toxoplasma, O (others), Rubella, Cytomegalovirus, Herpes simplex virus.

**Table 2: The demographic data of study population.**

| | Low risk group (N:136) | High risk group (N:251) | p value |
|---|---|---|---|
| Age (years) | 27.43±1.37 (19-44) | 28.54±5.45 (21-44) | >0.05 |
| Gestational week (weeks) | 22.73±2.25 (17-36 weeks) | 23.61±1.61 (17-36 weeks) | >0.05 |
| Primipara (N/%) | 89/65.44 | 147/58.56 | >0.05 |
| Multipara (N/%) | 45/34.56 | 99/41.44 | >0.05 |
| Multiple pregnancy (N/%) | 2/1.47 | 5/1.99 | >0.05 |

In the low-risk group; ventricular septal defect was detected in 4 cases (2.94%) (**Table 3**). However; ventricular septal defect was detected in 2 cases (0.79%), double outlet right ventricle in 2 cases (0.79%), hypoplastic left heart syndrome in 3 cases (1.20%), tricuspid atresia in 2 cases (0.79%), pulmonary atresia/hypoplasia in 3 cases (1.20%), tricuspid atresia and TGA in 1 case (0.40%), aortic coarctation/aortic arch hypoplasia in 1 case (0.40%), corrected TGA in 1 case (0.40%) and truncus arteriosus in 1 case (0.40%) were detected in the high-risk group (**Table 3**). So, the prevalence of CHD in low-risk and high-risk pregnancies were found as 2.94% and 6.37%, respectively. Also, we found the overall prevalence of CHD in our study population as 5.16%.

**Table 3: Distribution of congenital heart diseases according to low-high risk groups**

| Congenital heart disease | Low risk group (N:136) | High risk group (N:251) |
|---|---|---|
| Ventricular septal defect | 4 (2,94%) | 2 (0.79%) |
| Double outlet right ventricle | - | 2 (0.79%) |
| Hypoplastic left heart syndrome | - | 3 (1.20%) |
| Tricuspid atresia | - | 2 (0.79%) |
| Pulmonary atresia/hypoplasia | | 3(1.20%) |
| Tricuspid atresia and transposition of great arteries (TGA) | - | 1 (0.40%) |
| Aortic coarctation/aortic arch hypoplasia | - | 1 (0.40%) |
| Corrected TGA | - | 1(0.40%) |
| Truncus arteriosus | - | 1(0.40%) |
| Total | 4(2.94%) | 16(6.37%) |

TGA; Transposition of great arteries

Rhythm disturbances were also detected in our study. By this way, premature atrial extra systoles were detected in 3 fetuses in low-risk group while premature ventricular beats were detected in 5 pregnant women in high-risk groups.

## DISCUSSION

Today, fetal echocardiography has become increasingly used. The sensitivity of fetal echocardiography performed by experienced hands is also high.[9,10] With fetal echocardiography, not only simple CHDs but also complex CHDs and situs anomalies can be detected prenatally.[15] Also, fetal echocardiography helps to improve the pregnancy outcome of fetuses with selected CHD, and there is a clinical benefit with regard to infant outcomes.[13-16] The diagnosis of CHDs from fetal echocardiography is dependent on several factors including the skill of the operator, indications for referral, makeup of the population and the ultrasonographic skill of the referring obstetricians.

The reported incidence of CHD in different studies varies from 4 to 50/1000 live births,[2] with the generally the accepted incidence being 8/1000 live births.[17] Geographic and ethnic differences in the incidence of CHD subtypes have been reported.[18,19] The variations in particular congenital heart lesions could have a biological basis and may be related to different genetic/epigenetic susceptibility.[20,21]

The mean ages of our patients were 27.43±1.37 and 28.54±5.45 years in each risk groups, respectively. Also, these results are comparable to other studies.[22] The main indications for referral were lack of good image of the fetal heart by ultrasonography in low-risk group and maternal diabetes in high-risk group. There were also high prevalence of dysrhythmia (5.42%) and history of previous child or fetus with extracardiac anomaly (8.53%) in our high-risk population. These results were also similar with the studies which have shown fetal extracardiac anomaly

scan to be the most common indication for referral.[23,24] Our tertiary center is being the apex center of surrounding countries which especially gets referrals of high-risk pregnancies. Additionally, these results were the first reports of our tertiary center.

Various studies have reported different frequencies of CHD in pregnant women at different risk groups. In a study conducted by Özbarlas et al. in high- and low-risk pregnant women, the frequency of CHD was found to be 7.8% and 2.7%, respectively.[25] Also, in a recent study of Altın these frequencies were found as 15.2% in the high-risk group and 9% in the low-risk group (p=0.008).[26] Similarly, in our series, the prevalence of CHD was found to be 2.94% in low-risk pregnancies and 6.37% in high-risk pregnancies, while the overall prevalence was found to be 5.16%. On the other hand, in the studies conducted by Özkutlu et al.[27] and Özbarlas et al.[25] ventricular septal defect was the most frequently detected congenital heart disease. Similarly, in our study, ventricular septal defect was the most frequently detected CHD in both the high-risk and low-risk groups.

The fact that some heart anomalies are seen in the baby at a rate much higher than expected if the mother has a disease suggests the possibility of cytoplasmic (mitochondrial) transmission in these cases.[18,19] When the mother's metabolic diseases and the drugs she uses are considered as environmental factors for the fetus; diabetes mellitus, phenylketonuria, lupus, rubella, alcohol, lithium, amphetamines and antiepileptic drugs significantly increase the incidence of CHD.[13,16,25,27] There is also a relationship between chromosome structural disorders and congenital heart anomalies.[18,19]

In the study of Özkutlu et al., the risk factors such as maternal metabolic diseases, fetal arrhythmias and previous CHD in fetuses or children were found to be the most common risk factors in high-risk pregnant women.[27] In the study of Özbarlas et al., the most common risk factors were found to be maternal metabolic diseases, previous CHD in fetuses or children and non-cardiac fetal malformations.[25] In our study, the most common risk factors were diabetes due to maternal causes, dysryhtmia due to fetal causes and fetal anomalies in previous pregnancies due to hereditary causes. In addition, in our study, the most common reason for application in the low-risk group was found to be lack of good image of the fetal heart by ultrasound, in accordance with the literature. In the light of our results, we suggest that pregnancies with diabetes should be evaluated by fetal echocardiography regularly in certain gestational weeks.

### Limitation

This study was limited by its retrospective nature at a single academic center and relatively small sample size. Also, information such as maternal and familial hereditary factors was lacking and was not evidence based.

## CONCLUSION

Fetal echocardiography is a very useful technique when performed by experienced individuals with sufficient time. In the presence of CHD detected by fetal echocardiography, the family can be given the necessary counseling and precautions can be taken in advance for postnatal cardiac procedures. Fetal echocardiography should definitely be performed especially in high-risk pregnant women. However, the low prevalence of CHD in low-risk group, both in our study and in most studies in the literature, makes fetal echocardiography a priority for this group. However, it is necessary to properly identify selected cases in this patient group.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was obtained from Karamanoğlu Mehmetbey University Medical Research Ethics Committee (Date: 23.09.2024, Decision No: 10-2024/02, Number: E-11095095-050.04-216395).

**Informed Consent:** Signed written informed consent was taken from all participants.

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Original Article / Orijinal Araştırma


# Long-term Effectiveness of Amoxicillin Prophylaxis for Children with Primary Vesicoureteral Reflux

## Primer Vezikoüreteral Reflü Profilaksisinde Amoksisilinin Uzun Dönem Etkinliğinin Değerlendirilmesi

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## Abstract

**Aim**: The use of antibiotic prophylaxis in the conservative treatment of vesicoureteral reflux (VUR) has a long historical precedent. In this study, we investigated the long-term efficacy of amoxicillin as antibiotic prophylaxis.

**Material and Method**: A retrospective investigation was conducted to examine the clinical characteristics and follow-up results of patients with VUR who received amoxicillin prophylaxis for at least of six months.

**Results**: A total of 44 patients were included in the study, comprising 13 girls (29.5%) and 31 boys (70.5%), with a mean age of 2.9±1.3 months. During a mean follow-up period of 27.4±19.4 months, nine patients (20.5%) experienced one urinary tract infection (UTI), while two patients (4.5%) had a febrile UTI. Antibiotic revision was performed in a total of four patients (9%), including two patients with a febrile UTI and two patients with gastrointestinal side effects.

**Conclusion**: The long-term follow-up of patients with VUR who have been treated with amoxicillin prophylaxis has demonstrated that this is an effective and safe treatment option.

**Keywords**: Vesicoureteral reflux, urinary tract infection, amoxicillin

## Öz

**Amaç**: Vezikoüreteral reflü (VUR)'un konservatif tedavisinde antibiyotik profilaksisi uzun zamandan beri kullanılmaktadır. Bu çalışmada antibiyotik profilaksisi olarak amoksisilinin uzun dönem etkinliği araştırıldı.

**Gereç ve Yöntem**: VUR tanısı ile takip edilen ve en az 6 ay ve daha uzun süre amoksisilin profilaksisi alan hastaların klinik özellikleri ve izlem sonuçları retrospektif olarak araştırıldı.

**Bulgular**: Çalışmaya 13'ü kız (%29.5), 31'i erkek (%70.5) olmak üzere 44 hasta alındı ve yaş ortalaması 2.9±1.3 aydı. Ortalama 27.4±19.4 ay takipte 9 hastada (%20.5) bir kez idrar yolu enfeksiyonu (İYE) ve 2 hastada (%4.5) ateşli İYE tespit edildi. İki hasta ateşli İYE, 2 hastada ise gastrointestinal yan etkiler olmak üzere toplam 4 hastada (%9) antibiyotik revizyonu yapıldı.

**Sonuç**: VUR'lu hastaların amoksisilin profilaksisi ile uzun dönem takibi etkili ve güvenilir bir tedavi seçeneğidir.

**Anahtar Kelimeler**: vezikoüreteral reflü, idrar yolu enfeksiyonu, amoksisilin

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## INTRODUCTION

Vesicoureteral reflux (VUR) is one of the most prevalent congenital urologic anomaly of the urinary tract, occurring in 1% of newborns and serving as a substantial risk factor for renal scarring. The prevalence of renal scarring has been documented to range from 36% to 56% in children with a history of urinary tract infection (UTI) and VUR.[1] VUR is present in 30 to 40 percent of children investigated for UTI.[2] The primary objective in the management of VUR is to prevent the patient from developing a febrile UTI and renal parenchymal scarring. Over the past 20 to 30 years, there has been a notable shift in approach from more aggressive surgical intervention to a more conservative management strategy. Studies have demonstrated that there is no notable discrepancy between the surgically and conservatively treated groups in terms of new renal scar formation or scar progression.[35] The initial preference for all degrees of reflux is to assess the potential for spontaneous resolution with conservative treatment. In the conservative approach, follow-up or antimicrobial prophylaxis is applied in accordance with the degree of VUR and the patient's clinical status.

The most commonly utilized agents in prophylaxis are trimethoprim-sulfamethoxazole, amoxicillin, and nitrofurantoin. Trimethoprim-sulfamethoxazole is the preferred antibiotic for prophylaxis, but its primary disadvantage is its high rate of antibiotic resistance and contraindication in infants under two months of age.[6] In infants under two months of age, amoxicillin is frequently the initial agent of choice for antibiotic prophylaxis. However, in the subsequent period, it is often replaced with trimethoprim-sulfamethoxazole, despite the absence of definitive clinical evidence to support this practice. The optimal duration of amoxicillin prophylaxis remains uncertain. Consequently, this study aimed to assess the efficacy of amoxicillin prophylaxis and to determine the safest duration for its use in patients with primary VUR.

## MATERIAL AND METHOD

In this study, the medical records of 285 patients with primary VUR who were followed up at pediatric nephrology clinic were retrospectively analyzed. The study included patients who had received amoxicillin prophylaxis for at least of six months. In order to be eligible for antibiotic prophylaxis, patients were required to have either dilated VUR or low-grade VUR, in addition to a history of UTI. Patients with other concomitant urologic abnormalities (obstructive uropathy, neurogenic bladder) and those receiving amoxicillin prophylaxis for less than six months were excluded from the study. The demographic characteristics, grade of VUR, scintigraphy findings, duration of follow-up, and UTIs during follow-up were recorded from the files. The diagnosis of UTI was made in cases with pyuria (>5 white blood cells per high power field) and/or nitrite positivity in urinalysis by urine culture using the catheter or clean catch method. Positive urine culture was defined as 10.000 colonies in a catheterized sample or >50.000 colonies in a clean catch sample.[7,8]

The diagnosis of VUR was made via voiding cystourethrogram, and grading was conducted in accordance with the international reflux grading system. In cases where the reflux was bilateral, the grade was determined by averaging. A grade III or above was defined as dilated VUR. Renal parenchymal abnormalities were evaluated using dimercaptosuccinic acid (DMSA) scintigraphy. The study was approved by the local ethics committee (2023/11).

Statistical Method; Descriptive analyses included means and standard deviations (SD) of continuous variables and distributions of categorical variables. Chi-square test was used to compare categorical variables. The overall level of significance was set at 0.05. Statistical analyses were done using the SPSS 24.0 (IBM Inc.) statistical package.

## RESULTS

A total of 44 patients who met the established criteria were included in the study. The cohort consisted of 13 female (29.5%) and 31 male (70.5%) patients, with a mean age of 2.9±1.3 months (**Table 1**). A history of previous UTI was present in 24 patients (54.5%), while 20 patients (45.5%) had a history of febrile UTI. Among the patients with a history of UTI, 10 were female (76.9%) and 14 were male (45.2%), and no statistically significant difference was observed between the two groups (p=0.053). The prevalence of dilated VUR was 77.3% (n=34), with a statistically significant higher incidence in males (p=0.025). Among these patients, 7 (53.8%) were female and 27 (87.1%) were male. During the follow-up period, nine patients (20.5%) experienced one episode of UTI, and two patients (4.5%) had a febrile UTI. A total of four patients (9%) underwent antibiotic revision, including two patients with febrile UTI and two patients with diarrhea. The mean duration of amoxicillin use was 15.9±10.1 months (range: 6-48 months), with a mean follow-up period of 27.4±19.4 months (range: 6-69 months).

**Table 1. Clinical and demographic characteristics of the patients**

| | |
|---|---|
| Age (month) | 2.9±1.3 |
| Gender (Male:Female) | 13:31 |
| Antenatal Hydronephrosis | 22 (50%) |
| Dilated VUR | 34 (77.3%) |
| Bilateral VUR | 25 (56.8%) |
| Renal Scarring | 7 (7.3%) |

## DISCUSSION

A review of recent studies indicates that there is no significant difference between conservative and surgical treatment of VUR in terms of the formation of scar tissue. In all cases of reflux, the initial approach should be to assess the potential

for spontaneous resolution through conservative treatment.[2] In the conservative approach, follow-up or antimicrobial prophylaxis is applied according to the degree of VUR and the patient's clinical status. In the European Urological Association guidelines, follow-up with prophylaxis is recommended as the initial treatment for children aged 1-5 years with grade III-V VUR.[5,7] In our study, 77% of the patients had dilated VUR and were followed up with antibiotic prophylaxis from the outset.

The randomized intervention for children with VUR (RIVUR) study demonstrated that the incidence of recurrent UTIs was 50% lower in the group that received prophylaxis compared to the placebo group.[8] In the Swedish Reflux study, antibiotic prophylaxis was compared with endoscopic injection and observation in children with VUR, and it was found that the incidence of recurrent UTI was significantly lower in girls who received antibiotic prophylaxis than in those who received observation.[9] Furthermore, these studies demonstrated that delayed treatment of UTIs was associated with an increased risk of renal scarring. In our study, 45.5% of patients had a history of febrile UTI prior to prophylaxis, whereas only 4.5% had febrile UTI at follow-up.

Advantage of antibiotics used in prophylaxis is that their active form or metabolites are excreted in the urine, thus keeping the urine free of bacteria. Trimethoprim-sulfamethoxazole is contraindicated in infants under 2 months of age and in newborns due to liver toxicity. Amino penicillins are the drugs of choice for the treatment of enterococcal urinary tract infection and can be used for prophylaxis in infants younger than 2 months of age. The bioavailability of amoxicillin is better than ampicillin.[12] There is insufficient information in the literature about the long-term use of amoxicillin prophylaxis and its effects. In our study, prophylactic amoxicillin use for a mean of 15.9 months was largely successful in preventing UTI and was generally well tolerated. During follow-up, amoxicillin was discontinued and trimethoprim-sulfomethoxazole was switched to amoxicillin in a total of 4 patients (9%), including 2 patients with febrile UTI and 2 patients with gastrointestinal side effects. Based on these results, long-term amoxicillin prophylaxis seems to be an effective and safe treatment option. In addition, it is an advantage to start treatment with a narrower spectrum agent in terms of possible resistance development.

There are some limitations in our study. First, there may be bias due to the retrospective nature of the study. Second, the number of patients is relatively small. Nevertheless, considering the mean follow-up and treatment times, it can be considered that the study may make a significant contribution to the treatment of VUR.

## CONCLUSION

In patients diagnosed with VUR in the infantile period who have been initiated on prophylaxis with amoxicillin, the continuation of this treatment option in the future has been demonstrated to be effective and safe.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was obtained from Karamanoğlu Mehmetbey University Clinical Researches Ethics Committee (Date: 27.02.2023, Decision No: 01-2023/11).

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article / Orijinal Araştırma

# A Comparison of Healthy Lifestyle Behaviors and Depression in Pre-Eclampsy Pregnancy

## Preeklampsi Gebelerde Sağlıklı Yaşam Biçimi Davranışları ve Depresyonun Karşılaştırılması

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## Abstract

**Aim**: It is thought that there is a relationship between healthy lifestyle behaviors and depression in preeclampsia, which is frequently encountered during pregnancy.

**Material and Method**: This is a descriptive design study. The sample comprised 168 pregnant women, including pregnant women with preeclampsia and healthy pregnant women. The data were collected with the Descriptive Information Form, the Healthy Lifestyle Behavior Scale-II, and the Beck Depression Scale. Appropriate statistical methods were utilized in the evaluation of the study.

**Results**: According to the results, the healthy lifestyle behaviors scale mean scores of pregnant women with preeclampsia were higher than those of healthy pregnant women (p=.03). No statistically significant difference was seen between preeclampsia and healthy pregnant women in terms of the mean Beck depression scores (p=.278). A negative, weak, linear relationship was found between Beck scores and healthy lifestyle behaviors scale total scores in pregnant women with preeclampsia (r=.243; p=.026). As Beck scale scores increased, healthy lifestyle behaviors scale total scores decreased.

**Conclusion**: The mean scores of health responsibility, spiritual development, and stress management sub-scales of healthy lifestyle behaviors were higher in preeclamptic pregnant women than healthy pregnant women. It is recommended to determine women's pre-pregnancy health behaviors and explore their negative behaviors for maternal and infant health.

**Keywords**: Depression, health behaviors, preeclampsia, pregnancy

## Öz

**Amaç**: Araştırmanın amacı preeklampsi gebelerde sağlıklı yaşam biçimi davranışları ve depresyon bulgularının değerlendirilmesidir.

**Gereç ve Yöntem**: Çalışma tanımlayıcı niteliktedir. Araştırma örneklemini preeklampsi tanısını alan gebeler ile sağlıklı gebeler olmak üzere toplam 168 gebe oluşturmaktadır. Veriler; Tanıtıcı Bilgi Formu, Sağlıklı Yaşam Biçimi Davranışları Ölçeği II ve Beck Depresyon Ölçeği ile toplandı. Çalışmanın değerlendirilmesinde uygun istatistiki yöntemler yapıldı.

**Bulgular**: Çalışmada preeklampsi gebelerin sağlıklı yaşam biçimi davranışları ölçek puan ortalamalarının sağlıklı gebelere oranla daha yüksek olduğu tespit edildi (p=.03). Preeklampsi ve sağlıklı gebeler arasında BECK depresyon puan ortalamaları arasında istatistiksel olarak anlamlı bir fark tespit edilmedi (p=.278). Preeklampsi gebelerde BECK puanlarıyla sağlıklı yaşam biçimi davranışları ölçek toplam puanları arasında; negatif yönlü, zayıf derecede, doğrusal bir ilişki saptandı (r=.243; p=.026). BECK puanları arttıkça sağlıklı yaşam biçimi davranışları ölçek toplam puanları azalmaktadır.

**Sonuç**: Preeklampsi gebelerde sağlıklı yaşam biçimi davranışlarının alt boyutlarından sağlık sorumluluğu, manevi gelişim, stres yönetimi puan ortalamaları sağlıklı gebelere göre daha yüksektir. Kadınların gebelik öncesi sağlık davranışlarının belirlenmesinin, olumsuz davranışlarının sorgulanmasının, anne ve bebek sağlığı için önemli olduğu düşünülmektedir.

**Anahtar Kelimeler**: Depresyon, gebelik, sağlık davranışları, preeklampsi

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## INTRODUCTION

Hypertensive diseases are among the major causes of morbidity and mortality for mothers, fetuses, and newborns in developed and developing countries.[1] It is reported that 14% of all maternal deaths worldwide are due to hypertensive diseases during pregnancy.[2] Diseases accompanied by hypertension in pregnancy adversely influence the health of both the mother and the baby.[3,4] Preeclampsia is a pregnancy hypertensive disease and is one of the three common causes of maternal death worldwide.[5] It is the second leading cause of maternal death in our country.[6]

Preeclampsia, which develops in the second half of pregnancy accompanied by urinary proteinuria and hypertension, affects 3-5% of pregnancies[7,8] and causes the death of approximately 500.000 infants and 70.000 mothers each year.[9]

The etiopathogenesis of pregnancy-associated preeclampsia is not known precisely, but it is thought to develop as a result of vasospasm, endothelial cell destruction, immunological factors, and secondary decreased organ perfusion.[10,11] Pathology in preeclampsia exists even from the onset of pregnancy, but clinical findings appear in the later stages of pregnancy. The early onset of clinical findings occurs with the aggravation of the pathology.[12]

Health promotion is defined as the individuals' gaining the power to improve their health and increase control over it. The use of health-promoting behaviors is essential to prevent diseases, early diagnosis, and maintenance of health. According to Pender, healthy lifestyle behaviors are classified as spiritual development, health responsibility, exercise, nutrition, interpersonal relationships, and stress management.[13]

It is pivotal for individuals to acquire and maintain healthy lifestyle behaviors at all stages of their lives.[14] During a critical period, such as pregnancy, it is expected that women develop healthy lifestyle behaviors before, during, and after pregnancy.

The healthy lifestyle behaviors of the mother during pregnancy affect the current pregnancy and its outcomes, and the development of the fetus/newborn in the short and long term. Therefore, there are many healthy lifestyle behaviors that the mother is expected to exhibit for a healthy pregnancy.[15]

When a risky situation is detected during pregnancy, not only the physical health of the mother but also her mental health is affected. Antenatal and postnatal anxiety and depression are observed in high-risk pregnant women diagnosed with preeclampsia.[16] Worrying about the baby due to preeclampsia, the threat of premature birth, anomaly birth, and the loss of the baby cause high levels of stress and, thus, depression in women.

Depression, which is a significant mental health problem frequently seen throughout the world, prevents people's functionality, creativity, happiness, and satisfaction, resulting in a reduction in the quality of life and workforce losses.[17] International studies indicate that depression is mostly seen in women aged 18-44, including fertility processes like pregnancy, childbirth, and the puerperium.[18,19] The prevalence of depression is reported to be 13-20% worldwide and 10% in Turkey.[20]

Depression is a significant individual and social health problem due to its high prevalence, chronicity, and recurrence rates, increasing the loss of workforce, maternal and fetal morbidity, mortality, and the risk of suicide. Therefore, early diagnosis and treatment of pregnancy depression are of vital importance.[21]

In this study, the researcher aimed to evaluate healthy lifestyle behaviors and depression findings in pregnant women with preeclampsia.

### Research Questions

- What are the healthy lifestyle behaviors in pregnant women with preeclampsia?
- What are the healthy lifestyle behaviors of normal pregnant women?
- Are there symptoms of depression in pregnant women with preeclampsia?
- Do normal pregnant women have symptoms of depression?
- Between healthy lifestyle behaviors in preeclampsia and normal pregnancies is there any difference?
- There is a difference between depression symptoms in preeclampsia and normal pregnancies is it?

## MATERIAL AND METHOD

### Study Design

This study is in a descriptive design.

### Participant and The Universe and Sampling of the Study

The universe of the study included pregnant women attending the Istanbul Kanuni Sultan Süleyman Training and Research Hospital Gynecology Polyclinics. There are two groups in the study: preeclamptic pregnant women and healthy pregnant women. To apply the Healthy Lifestyle Behaviors Scale and Beck Depression Scale with four scales, 286 pregnant women with preeclampsia admitted to the Istanbul Kanuni Sultan Süleyman Training and Research Hospital in 1 year was calculated with ±3 standard deviation, 95% confidence (5% significance level). As a result, 168 pregnant women were involved in the study (84 preeclamptic women and 84 healthy women).

Inclusion criteria were being at the age of 18-45, being at or after the 28$^{th}$ gestational week, being a T.R. citizen, being diagnosed with preeclampsia during pregnancy or being a healthy pregnant, taking part in the study voluntarily, and not being diagnosed any chronic disease.

### Data Collection Tools

#### Validity and Reliability Information of the Study

The data were collected in 3 stages:

**The descriptive information form:** Developed by the researcher using the literature, the form has 40 questions regarding the socio-demographic information, obstetric history, and health status of pregnant women. The data collection tools were administered by the researcher through face-to-face interviews with volunteer pregnant women. It took about 20-30 minutes to fill out the form.

**The healthy lifestyle behavior scale-II (HLBS-II):** It was developed (1987) and revised (1996) by Walker et al.[22] The Turkish adaptation study was performed by Bahar et al. in 2008. The scale measures an individual's health-promoting behaviors associated with a healthy lifestyle. The scale consists of 52 items and 6 sub-dimensions;[23] spiritual development, health responsibility, physical activity, nutrition, interpersonal relationships, and stress management. All the items of the scale are positive and in the form of a 4-point Likert scale (never (1), sometimes (2), often (3), regularly (4). The lowest score for the whole scale is 52, and the highest score is 208. The overall score of the scale gives the healthy lifestyle behaviors score. The Alpha reliability coefficient of the scale was reported as 0.94.[23] In this study, the Alpha reliability coefficient was found to be 0.899.

**The Beck depression inventory:** The Beck Depression Inventory constitutes the third part of the data collection phase. It was used to measure the level of depression in women in our study. It was first developed by Aaron Temkin Beck in 1961 and was revised in 1971.[24] The scale was adapted into Turkish by Hisli (1989). The aim of the scale is not to diagnose, but to determine the severity of depression symptoms numerically. There are 21 items on the scale in the form of a four-point Likert scale. The total score ranges from 0 to 63. Items are scored between 0-3, and the highest score to be obtained is 63. In the validity and reliability article of the scale for Turkish, the cut-off score was reported to be 17. A high score indicates that the severity of depression symptoms increases.[25,26] In the reliability study, the Cronbach Alpha coefficient was found to be 0.80, and the reliability of split-half was found to be r=.74.[25] In our study, the Cronbach' s alpha coefficient was found to be 0.863.

### Ethical Approval

To conduct the research, institutional permission was obtained from Istanbul Istanbul Kanuni Sultan Süleyman Training and Research Hospital, and ethics committee approval was received from Health Sciences University Hamidiye Non-invasive Ethics Committee (No: 46418926, Date: 28.06.2019-19/88). Our research was conducted in accordance with the provisions of the 1995 Declaration of Helsinki. The participants were informed about the purpose of the study, that their data would be kept confidential and that they could withdraw the study whenever they wanted, and their oral and written consents were obtained. As the study was conducted only in one hospital, the results cannot be generalized to the whole population, and they are based on the personal reports of pregnant women.

### Statistical Analysis and Evaluation of Data

The normality testing of continuous variables was performed with the Shapiro Wilk test. Parametric tests were utilized for the variables conforming to the normal distribution, and non-parametric methods for those that did not. The student's t-test and the Mann Whitney U test were used for the comparison of the mean scores of preeclamptic and healthy pregnant women, and the median comparison methods, respectively. Chi-square test was performed in the comparison of categorical data, and Fisher Exact test was used if the expected value less than 5 was above 20%. To examine the linear relationship between continuous variables, Pearson correlation coefficients were calculated. The data analysis was performed with SPSS 21 program. The statistical significance level was considered 0,05.

This study was created from an article produced from the Master's thesis of the University of Health Sciences, Department of Midwifery (May, 2021).

## RESULTS

The mean age of the women with preeclampsia was 30.71±6.13 (min=19, max=44), and the average week of gestation was 33.38±3.45 (min=28, max=41). **Table 1** presents the data regarding the age and gestational week the pregnant women.

Preeclamptic pregnant women had a higher age average and lower gestational week (p<0.05, **Table 1**).

We compared the pre-pregnancy and current weight averages between the groups and we found that the average weight in the preeclampsia group was statistically significantly higher (p<0.005). No statistically significant difference was seen between pre-pregnancy and current weights between preeclamptic and healthy pregnant women (p=.386, **Table 2**).

**Table 1. Comparison of the Data Regarding Age and Gestational Weeks of the Groups (N=168)**

| | Pregnant women with preeclampsia (N=84) | | Healthy pregnant women (N=84) | | t | p |
|---|---|---|---|---|---|---|
| | Mean±SD | Min-Max | Mean±SD | Min-Max | | |
| Age | 30.71±6.13 | 19-44 | 27.6±5.59 | 19-45 | 3.444 | 0.001 |
| Week of gestation | 33.38±3.45 | 28-41 | 38.75±1.8 | 34-41 | -12.652 | <0.001 |

p: Student's t-test

**Table 2. Results Regarding Pre-Pregnancy Weight, Current Weight and BMI Characteristics of the Groups**

| | Pregnant women with preeclampsia | | Healthy pregnant women | | t | $p_{group}$ |
|---|---|---|---|---|---|---|
| | Mean±SD | Min-Max | Mean±SD | Min-Max | | |
| Pre-pregnancy weight | 70.91±14.90 | 45-110 | 63.34±12.70 | 40-95 | 3.543 | 0.001 |
| Current Weight | 83.72±14.54 | 54.3-130 | 77.00±12.33 | 46-108.75 | 3.235 | <0.001 |
| Difference (%95 GA) | -12.82±6.43 | -14.22--11.42 | -13.66±6.10 | -14.98--12,34 | 0.870 | 0.386 |
| pr | t=-18.262 p<0.001 | | t=-20.537 p<0,001 | | | |
| Pre-pregnancy BMI | 27.85±5.79 | 17.03-42.06 | 24.30±5.04 | 14.34-38.05 | 4.240 | <0.001 |
| Current BMI | 32.84±5.35 | 22.6-48.83 | 29.52±4.83 | 16.49-42.16 | 4.216 | <0.001 |
| Difference (%95 GA) | -4.99±2.44 | -5.52--4.46 | -5.22±2.34 | -5.73--4.71 | 0.635 | 0.526 |
| pr | t=-18.739 p<0.001 | | t=-20.438 p<0.001 | | | |

$p_{group}$: Student's t test, pr: Paired t test

**Table 2**, pre-pregnancy and current BMI averages of pregnant women with preeclampsia were higher than healthy pregnant women (p<0.05). The pregnant women were evaluated separately, and the difference between pre-pregnancy and current BMI values was found to be statistically significant (p<0.05). The difference between pre-pregnancy and current BMI values between preeclampsia and healthy pregnant women was not statistically significant (p=.526).

A statistically significant difference was found between the pre-pregnancy and current weights of pregnant women (p<0.05). Pre-pregnancy weight, current weight, pre-pregnancy BMI, and current BMI values were found to be higher in preeclamptic pregnant women than healthy pregnant women.

Healthy Lifestyle Behaviors sub-scales of health responsibility, spiritual development, stress management and scale total scores were found to be higher in pregnant women with preeclampsia (p<0.05, **Table 3**).

There was no statistically significant difference between preeclamptic and healthy pregnant women according to the mean Beck depression scores (p>0,05, **Table 4**).

A negative, weak, linear relationship was found between Beck scores and health responsibility scores in pregnant women with preeclampsia (r=.267; p=.014). As Beck scores increased, health responsibility scores decreased.

**Table 5**, a negative, weak, linear relationship was also found between Beck scores and healthy lifestyle behaviors scale total scores in pregnant women with preeclampsia (r=.243; p=.026). As Beck scores increased, healthy lifestyle behaviors scale total scores decreased.

**Table 3. The Healthy Lifestyle Behaviors Scale II Scores of the Participants**

| HLBS-II Sub-Scales | Pregnant women with preeclampsia | | Healthy pregnant women | | t | p |
|---|---|---|---|---|---|---|
| | Mean±SD | Min-Max | Mean±SD | Min-Max | | |
| Nutrition | 24.17±3.71 | 17-32 | 23.76±4.1 | 16-36 | 0.672 | 0.503 |
| Physical activity | 14.63±4.01 | 8-26 | 14.42±4.31 | 8-28 | 0.334 | 0.739 |
| Interpersonal relations | 27.43±4.73 | 17-36 | 26.68±4.02 | 18-36 | 1.107 | 0.270 |
| Spiritual development | 29.15±4.16 | 19-36 | 27.71±4.19 | 19-36 | 2.235 | 0.027 |
| Health responsibility | 23.46±4.47 | 10-33 | 21.14±4.75 | 13-32 | 3.262 | 0.001 |
| Stress management | 21.31±3.86 | 12-30 | 20.11±4.02 | 13-32 | 1.977 | 0.050 |
| HLBS-II Total Score | 140.15±17.97 | 100-180 | 133.82±19.4 | 98-187 | 2.195 | 0.030 |

**Table 4. Comparison of the Data of Preeclampsia and Healthy Pregnant Women According to the BECK Depression Scale**

| | Pregnant women with preeclampsia | | Healthy pregnant women | | t | p |
|---|---|---|---|---|---|---|
| | Mean±SD | Min-Max | Mean±SD | Min-Max | | |
| BECK | 13.29±8.65 | 1-42 | 14.85±9.89 | 0-55 | -1.088 | 0.278 |

**Table 5. Comparison of the Total Scores of the Groups' According to the Healthy Lifestyle Behaviors Scale II and BECK Depression Scale**

| BECK | | Health responsibility | Physical activity | Nutrition | Spiritual development | Interpersonal relations | Stress management | Total |
|---|---|---|---|---|---|---|---|---|
| Preeclamptic pregnant | r | -0.267 | -0.024 | -0.161 | -0.186 | -0.191 | -0.208 | -0.243 |
| | p | 0.014 | 0.826 | 0.145 | 0.090 | 0.081 | 0.058 | 0.026 |
| Healthy pregnant | r | 0.020 | -0.019 | -0.022 | -0.156 | -0.191 | -0.169 | -0.112 |
| | p | 0.857 | 0.865 | 0.844 | 0.157 | 0.082 | 0.125 | 0.311 |

p: Pearson Correlation

## DISCUSSION

Advanced age is reported to be a risk factor for preeclampsia in the literature. According to Pandian et al., the risk of placental abruption increases with the risk of diabetes mellitus and preeclampsia in advanced age pregnancies.[27] The mean age of pregnant women in the preeclampsia group was also high in our study (**Table 1**).

Physiological changes during pregnancy, insufficient or excessive intake of nutrients are believed to cause epigenetic modifications in the fetus by showing short and long-term effects.[28] Rapid weight changes can be seen during pregnancy. A high Body Mass Index (BMI) can have negative outcomes for the mother and the baby. Pre-pregnancy obesity leads to the development of systemic diseases such as pregnancy-related hypertension, preeclampsia, gestational diabetes, and pregnancy complications such as neonatal death and cesarean section.[29] In the study of Sak et al., it was highlighted that the mean BMI of the preeclampsia group was higher than that of the control group, and the difference was significant.[30] Yurtsever determined that the BMI before and during pregnancy in pregnant women with preeclampsia, and in Dursun's study, the mean BMI of pregnant women with preeclampsia was significantly higher.[31,32] Consistent with the literature, in our study, we found that pre-pregnancy and current BMI averages of pregnant women with preeclampsia were higher than healthy pregnant women, and the difference between pre-pregnancy and current BMI values was statistically significant when evaluated separately in preeclampsia and healthy pregnant women ($p<0.05$, **Table 2**).

The ratio of preterm birth in pregnant women diagnosed with preeclampsia is reported to be higher.[31,33,34] Likewise, in our study (**Table 1**), the preeclampsia group had also higher preterm birth ratios in their previous pregnancies.

The mean score of HLBS of pregnant women with preeclampsia was 140.15±17.97, and the mean score of healthy pregnant women was 133.82±19.4. In our study, in both preeclampsia and healthy pregnant women, the lowest and the highest scores were obtained in the physical activity and the spiritual development sub-scales in HLBS respectively (**Table 3**). In a similar study conducted by Onat and Aba with pregnant women, it was reported that the lowest score in HLBS belonged to the physical activity sub-scale and the highest score belonged to spiritual development sub-scales.[35] No significant difference was found between total scale scores in a study by Aksoy et al. in which healthy life behaviors of high-risk pregnant women and healthy pregnant women were evaluated. However, there was a significant difference between the groups in the sub-dimensions of stress management, physical activity, and health responsibility. Health behavior scores are higher in risky pregnant women.[13] Auerbach et al. reported that health controls during pregnancy directly affect the health of the mother and baby.[36] Health responsibility and spiritual development are of vital importance in the acquisition of health behaviors. In our study, health responsibility, spiritual development, and stress management scores were higher in pregnant women with preeclampsia. Our study results are consistent with the literature, and the highest health behavior is spiritual development, and the lowest health behavior is physical activity, especially in risky groups. This shows us that in high-risk pregnancies, health searches and pregnancy follow-ups are performed more frequently, and pregnant women are effective in managing the process by avoiding stress.

The psychopathological symptoms experienced during pregnancy cause negative outcomes on the fetus. It has also been reported that preeclampsia and eclampsia, hypertensive diseases of pregnancy, are associated with depression.[21] In the study by Pişirgen with risky pregnancies, it was noted that the mean anxiety and depression in cases with risky pregnancies were significantly higher than in non-risky cases.[37] Contrary to the literature, in our study, no significant difference was found between depression scores in preeclampsia and healthy pregnant women, which may be due to the successful stress management of the pregnant women in the study (**Table 4**). A relevant study emphasizes that depression causes negative health behaviors in pregnant women and contributes to the occurrence of obstetric risks.[38]

According to our study results, the increase in depression status in pregnant women with preeclampsia decreased the responsibility for health, suggesting that the increase in the severity of depression symptoms in women harms their health behaviors during pregnancy. There was also a negative relationship between the Beck scores and healthy lifestyle behaviors scale total scores in pregnant women with preeclampsia (**Table 5**). As healthy lifestyle behaviors decreased, depression levels increased in pregnant women.

### Study Limitation

In this study, in terms of research generalizability, only this constitutes the limitations of the study because it was conducted in the gynecology ward of a university hospital.

## CONCLUSION

As a result, pregnancy is a unique experience for every woman. Therefore, the negative health behaviors of the woman during this period may endanger the development of the baby. Particularly, in preeclampsia, a high-risk disease for pregnancy, maternal stress is high. Primary health care services have significant functions in questioning the risky pregnancy history and early interventions to detect negative health behaviors (such as obesity, smoking, exercise status) before pregnancy.

To eliminate the complaints in pregnant women with preeclampsia, the lifestyle of the pregnant woman should be reviewed, and healthy lifestyle behaviors should be developed. Evaluation of depression before and during pregnancy and early intervention is important for maternal-fetal health. Therefore, women in the risk group should be supported to gain positive health behaviors in their daily lives. During prenatal, antenatal, and postnatal follow-ups, it is essential to approach pregnant women as a whole, both physically and mentally.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: This study was evaluated by Turkey Istanbul Kanuni Sultan Süleyman Training and Research Hospital, and ethics committee approval was received from Health Sciences University Hamidiye Non-invasive Ethics Committee (Decision No: 46418926, Date: 28.06.2019-19/88).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article / Orijinal Araştırma

# Middle Ear Barotrauma in Hyperbaric Chamber Inside Attendants

## Hiperbarik İç Yardımcılarında Orta Kulak Barotravması

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## Abstract

**Aim**: Hyperbaric oxygen therapy (HBOT) facilities and their use in various medical fields are increasing. Hyperbaric chamber inside attendants (HCIAs) are exposed to several occupational hazards, of which middle ear barotrauma (MEB) is the most common. This study aimed to prospectively investigate MEB incidence and severity in hyperbaric chamber inside attendants.

**Material and Method**: The HCIAs underwent an otoscopic examination by an otolaryngologist before and after the HBOT session, and their demographic characteristics, medical history, and otological symptoms were recorded. The appearance of the tympanic membrane in those who develop MEB is graded according to the Teed classification system. The data collected in the study were analyzed using statistical software.

**Results**: The research involved 56 HCIAs who underwent otoscopic examinations before and after HBOT sessions. The study revealed that 21.5% of the participants experienced MEB, with no significant correlations between MEB and demographic variables. According to the data, 25% of HCIAs who experienced MEB reported no pain.

**Conclusion**: No evidence in the literature suggests that MEB causes permanent damage to HCIAs. However, MEB in HCIAs may be more prevalent than previously thought. This study indicates that many MEB cases may be missed if HCIAs are not thoroughly screened and assessed. While MEB may not have a clinical impact, it is important to understand the risk of occupational MEB that HCIAs may be exposed to.

**Keywords**: Hyperbaric oxygen therapy, middle ear barotrauma, hyperbaric chamber ĭ nside attendants

## Öz

**Amaç**: Hiperbarik oksijen tedavisi (HBOT) olanakları ve çeşitli tıbbi alanlardaki kullanımı artmaktadır. Hiperbarik iç yardımcıları (HCIA'lar) çeşitli mesleki tehlikelere maruz kalmaktadır ve bunların arasında en yaygın olanı orta kulak barotravmasıdır (MEB). Bu çalışma, hiperbarik iç yardımcılarında MEB insidansını ve şiddetini prospektif olarak araştırmayı amaçlamaktadır.

**Gereç ve Yöntem**: HCIA'lar, HBOT seansından önce ve sonra bir kulak burun boğaz uzmanı tarafından otoskopik muayeneye tabi tutuldu ve demografik özellikleri, tıbbi geçmişleri ve otolojik semptomları kaydedildi. MEB geliştirenlerde timpanik membranın görünümü Teed sınıflandırma sistemine göre derecelendirildi. Çalışmada toplanan veriler istatistiksel yazılım kullanılarak analiz edildi.

**Bulgular**: Araştırmaya HBOT seanslarından önce ve sonra otoskopik muayeneye tabi tutulan 56 HCIA dahil edildi. Çalışma, katılımcıların %21,5'inin MEB yaşadığını ve MEB ile demografik değişkenler arasında anlamlı bir korelasyon olmadığını ortaya koydu. Verilere göre, MEB yaşayan HCIA'ların %25'i ağrı hissetmediğini bildirmiştir.

**Sonuç**: Literatürde MEB'in HCIA'larda kalıcı hasara yol açtığına dair bir kanıt bulunmamaktadır. Ancak, HCIA'larda MEB daha önce düşünülenden daha yaygın olabilir. Bu çalışma, HCIA'lar kapsamlı bir şekilde taranıp değerlendirilmediğinde birçok MEB vakasının gözden kaçabileceğini göstermektedir. MEB'in klinik bir etkisi olmasa da, HCIA'ların maruz kalabileceği mesleki MEB riskinin anlaşılması önemlidir.

**Anahtar Kelimeler**: Hiperbarik oksijen tedavisi, orta kulak barotravması, hiperbarik iç yardımcıları

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## INTRODUCTION

Barotrauma refers to injuries caused by pressure, such as direct pressurization of the body or the inability of a gas-filled body cavity to equalize pressure when there is no communication with the environment.[1] Middle ear barotrauma (MEB) occurs when a pressure difference between the middle ear and the external environment cannot be equalized. Symptoms include ear pain, tinnitus, and temporary conductive hearing loss. Clinical manifestations of MEB include accumulation of fluid or blood in the middle ear, hemotympanum, or rupture of the tympanic membrane (TM). Depending on the severity of the injury, symptoms may take up to four weeks to resolve.[2]

Hyperbaric Oxygen Therapy (HBOT) is recommended for the treatment of various conditions, including gas embolism, decompression illness (DCI), carbon monoxide poisoning, necrotizing fasciitis, acute traumatic ischaemic injury, and wound healing.[3] HBOT is a procedure in which the individual breathes intermittently near 100% oxygen in a hyperbaric chamber at a pressure higher than sea level.[4] HBOT can be provided in single or multi-place chambers.

During HBOT in a multi-place chamber with a capacity for many patients, patients are accompanied by Hyperbaric Chamber Inside Attendants (HCIAs) who provide technical support, medical care, and emergency intervention. These HCIAs can be nurses, doctors, or paramedics and are responsible for preparing both the patient and equipment before the session and monitoring the patient during the session.[5] HCIAs risk developing barotrauma due to pressure changes and compressed air in the chamber. This can cause harm to various systems and organs in the body. MEB is the most common occupational injury in HCIAs.[6] This study aimed to conduct a prospective investigation into the frequency and severity of MEB among HCIAs. The aim was to demonstrate that the risk may be greater than estimated.

## MATERIAL AND METHOD

At the start of the study, ethical approval was obtained from the Noninvasive Clinical Research Ethics Committee of 'BLINDED FOR REVIEW' on 30.11.2021 with registration number 21. All HCIAs were medically screened according to the UHMS Guidelines for Multiplace Inside Attendants Medical Fitness to Work 2018.[7] HCIAs between 18 and 65 years old who were willing to participate were included in the study. Pregnant women, individuals with a history of ear surgery, active upper respiratory infections or ear infections, those who were unable to align the ear at the initial examination, and individuals who experienced confinement anxiety were excluded from the study. Healthcare workers working as HCIAs in the HBOT unit of our hospital between December 2021 and April 2022 participated in the study. All participants were fully informed about the study and gave verbal and written consent. Demographic data, including race, age, sex, weight, height, and medical history, were recorded. A history of atopy and smoking habits of HCIAs was also recorded.

The HBOT unit has a multi-place chamber known as the Hypertech® Quadro Care, which has a capacity of 11+2 patients. The study was carried out during sessions when HCIAs had to monitor patients.

Each participant's tympanic membrane was photographed and recorded after undergoing otoscopic examination by the same otolaryngologist using a Heine® otoscope. The otolaryngologist checked the participants for any septum nasal deviations before the HBOT session. HCIAs were trained before treatment on the importance of MEB and pressure equalization; they were instructed to perform repetitive Valsalva maneuvers during compression and to raise the alarm in case of ear pain or discomfort. The same physician and technician monitored HCIAs outside the pressure chamber for side effects during compression and treatment. HCIAs were instructed to swallow or sip water if the Valsalva maneuver failed to equalize the ear. HBOT sessions were conducted for 90 minutes at a pressure of 2.5 ATA (250 kPa) with 5-minute air breaks every 20 minutes. Our compression rate was 0.75 meters per minute. All HCIAs breathed 100% oxygen from the last 15 minutes of the isobaric phase until leaving the pressurized chamber. During the sessions, other patients were being treated in the same room. At the end of the hyperbaric treatment, participants were asked if they experienced any otological symptoms such as pain, pressure, dizziness, hearing loss, or tinnitus. Immediately following the hyperbaric HBOT session all participants underwent a second otoscopic examination by the same otolaryngologist, and the otoscopic images were photographed again for comparison with the first photograph. The appearance of the TM was graded according to the Teed classification system.[8] The TEED scale is used for the classification of ear barotrauma. Grade 1 is a slight injection of the TM; Grade 2 is a partial hemorrhage of the TM; Grade 3 is a total hemorrhage of the TM; Grade 4 is a blue and bulging hemotympanum; and Grade 5 is a perforated TM.[9]

The study was carried out with the permission of Pamukkale University Noninvasive Clinical Research Ethics Committee (Date: 30.11.2021, Decision No: 21). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

### Statistical analysis

The data collected in the study were analyzed using a statistical program. The normality test was performed using the Kolmogorov-Smirnov test. The chi-square test was used to analyze the data related to sex, age, body mass index (BMI), smoking status, comorbidities, and septal deviation in MEB after the HBOT session. Pearson's correlation test and Spearman's rho test were used to determine the correlation between the occurrence of MEB and all the other factors (Sex, age, BMI, being a smoker, comorbidity, septal deviation). To determine statistical significance, $p < 0.05$ was considered significant.

## RESULTS

We started the study with fifty-eight HCIAs. One HCIA was excluded because of being pregnant, and one HCIA was excluded because of claustrophobia. Fifty-six HCIAs were assessed in the study. Thirty-eight (67.9%) participants were female and eighteen (32.1%) were male. The mean age of the participants was 23.63±3.00 (19-41) years. **Table 1** contains the data related to the demographics and examination findings only four participants had a positive medical history: one with migraine, one with hypothyroidism, one with gout, and one with polycystic ovary syndrome. One was receiving migraine treatment. Septal deviations were detected during pre-compression otolaryngological examinations in eight participants (14.3%).

**Table 1. Demographic data and examination results**

| Demographic data and examination results | Mean ±SD | Min-max |
|---|---|---|
| Age (years) | 23.63±3.00 | 19 - 41 |
| Height (cm) | 167.57±7.51 | 150 - 188 |
| Weight (kg) | 63.43±12.45 | 42 - 112 |
| BMI (kg/m2 ) | 22.61±3.58 | 16.10 – 31.70 |
| | n | % |
| Gender | | |
| Male | 18 | 32.1 |
| Female | 38 | 67.9 |
| Septum deviation | | |
| Yes | 8 | 14.3 |
| No | 48 | 85.7 |
| Smoking habit | | |
| Smoker | 33 | 58.9 |
| Non-smoker | 23 | 41.1 |
| Barotrauma | | |
| Yes | 12 | 21.5 |
| No | 44 | 83.5 |
| Affected ear | | |
| Right | 9 | 64.3 |
| Left | 5 | 35.7 |
| Bilateral | 2 | 14.3 |
| Barotrauma grade | | |
| Grade 1 | 6 | 42.9 |
| Grade 2 | 4 | 28.6 |
| Grade 3 | 2 | 14.3 |
| Grade 4 | 2 | 14.3 |

BMI: Body Mass Index

A total of 12 participants (21.5%) exhibited evidence of MEB at the post-session examination, with two cases presenting bilaterally. Six (42.9%) of the fourteen ears with MEB were graded by the otolaryngologist as grade 1, four (28.6%) as grade 2, two (14.3%) as grade 3, and two (14.3%) as grade 4 (**Figure 1**). During the study, eight participants with MEB experienced pain. Five participants reported ear fullness, two experienced dizziness, and three had temporary hearing loss. None of these complaints were permanent. On the following day, no further complaints were received.

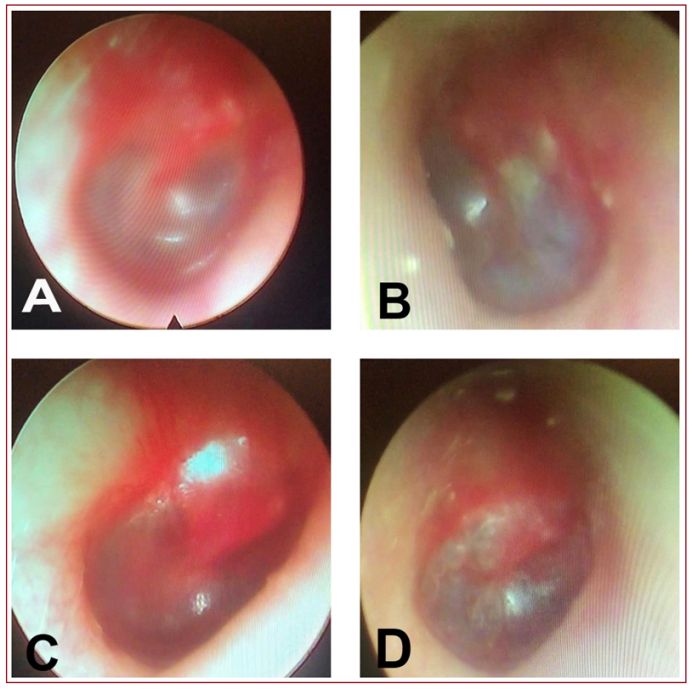


**Figure 1:** Middle ear barotraumas graded by an otolaryngologist. A: Grade 1, B: Grade 2, C: Grade 3, B: Grade 4.

In the statistical analyses, no association was found between height, weight, BMI, gender, or smoking and the occurrence of MEB ($p > 0.05$). Septal deviation did not statistically increase the risk of MEB (p: 0.514). The rate of MEB was 27.4% in men and 18.4% in women. There was no correlation between grade and height, weight, BMI, gender, smoking, or septal deviation ($p > 0.05$).

## DISCUSSION

Implementing proper safety protocols, providing training, and raising awareness about barotrauma can significantly reduce the risks of MEB for individuals working in environments with pressure changes, such as HBOT. Individuals must know the importance of frequent and early ear equalization to prevent MEB. In case of symptoms and visual changes in the TM with an otoscope, it is essential to seek appropriate medical evaluation and management promptly. This will help address potential MEB and prevent complications. Surprisingly, 21.5% of our study participants had MEB.

There are no prospective studies in the literature to support the risk of MEB in HCIAs. Conducting studies on patients may provide valuable insights. In patients treated with HBOT, significant differences in the incidence and prevalence of MEB, ranging from 8 to 94%, have been reported.[10] The reason for the high prevalence in some publications is that the study population was selected from particular groups, such as patients with cerebral palsy or unconscious patients.[11,12] Studies generally defined female sex, older age, and intubation as risk factors.[10,13] Factors such as allergy, septal deviation, smoking, and a history of otitis media are also thought to increase the risk of MEB.[9] In our study,

no statistically significant correlation was found between these variables. The finding of 37.5% MEB in HCIAs with septal deviation appears to increase the risk, although not statistically significant.

In a retrospective study in France reviewing occupational accidents occurring during HCIA, the risk of developing MEB during a session was reported to be 173 per 100,000 compression.[6] Another study reported 1 MEB per 400 compressions in HCIAs.[14] The risk of MEB in HCIAs was found to be relatively low in these retrospective studies. A short delay in ear equalization during compression in HCIAs may result in missed MEB with painless or mild ear pain, which may be overlooked in retrospective studies. Some studies have included grade 2 Teed in grade 1 when grading modified Teed.[15] Taking this into account in our study, we can conclude that 71.5% of participants in our study experienced low-grade MEB that caused little or no pain. It is worth noting that 25% of HCIAs with MEB did not report any pain, which suggests that a considerable number of MEB cases may go unnoticed if not properly investigated and examined.

The fact that these missed MEB were also detected in HCIAs in our prospective study may explain the high unexpected average. In other words, this study revealed the risk of MEB in HCIAs that we would not have been able to detect without testing, which is indeed high. In patients' studies, a retrospective study found the risk of MEB to be 2,8%,[16] while a prospective study found it to be 66.7%.[15] Hyperbaric centers should consider the 21.4% MEB rate.

No permanent ear damage has been reported in divers exposed to pressure changes similar to those experienced by HCIAs.[17,18] While this suggests that pressure changes may not cause permanent damage in HCIAs, this study aims to highlight this issue with a high MEB rate and establish a starting point for further research.

### Limitations

The main limitation of the study is its design. A proper incidence analysis typically involves looking at the number of cases per total number of sessions. In this case, calculating an incidence based on only one session could be misleading. The sample size in the clinical study is relatively small, which makes it challenging to capture statistical significance. Additionally, the study did not consider the repeatability of MEB, only whether it occurred in a single session. As a result, the study's findings may not be generalizable since the data were only collected from one HBOT session at a single center.

## CONCLUSION

This study indicates that many MEB cases may go unnoticed without proper screening and assessment. Despite the occurrence of MEB, there is no evidence to suggest permanent damage to HCIAs. The study emphasizes the need for comprehensive inspection and monitoring to understand the occupational risk of MEB for HCIAs. The findings imply that the risk of MEBs in HCIAs may be greater than previously thought, highlighting the necessity for further research to comprehend and prevent this occupational injury.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was carried out with the permission of Pamukkale University Noninvasive Clinical Research Ethics Committee (Date: 30.11.2021, Decision No: 21).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article / Orijinal Araştırma


# Usage of Magnetic Resonance Imaging-Based Texture Analysis Features in Discrimination of Benign and Malignant Sinonasal Tumors

## Benign ve Malign Sinonazal Tümörlerin Ayırımında Manyetik Rezonans Görüntüleme Tabanlı Doku Analizi Özelliklerinin Kullanımı

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## Abstract

**Aim**: The objective of this study was to differentiate between benign and malignant sinonasal tumors using magnetic resonance imaging (MRI)-based texture analysis features.

**Material and Method**: Histopathologically proven benign or malignant sinonasal tumor patients were included in the study from MRI examinations performed between January 2013 and December 2020. Inclusion criteria included a tumor size of at least 1 cm and preoperative magnetic resonance imaging with axial T1W, axial fat-suppressed T2W, and axial T1W postcontrast sequences. After the images were transferred to a dedicated workstation, texture analysis calculations were performed. Differences between benign and malignant groups were compared.

**Results**: The mean age of 37 patients (8 female, 29 male) included in the study was 50.8 ± 21.9 years. In our study, we found no statistically significant difference between malignant and benign sinonasal tumors in nine tissue analysis parameters obtained by MRI.

**Conclusion**: MRI-based texture analysis needs identical MRI protocols for evaluating tumors. MRI-based texture analysis is not a useful diagnostic tool to discriminate between benign and malignant sinonasal tumors when specific pathologic types are not selected and scanning protocols are not identical.

**Keywords**: Magnetic resonance imaging, sinonasal, tumor, texture analysis

## Öz

**Amaç**: Bu çalışmanın amacı, manyetik rezonans görüntüleme (MRG) tabanlı doku analizi özelliklerini kullanarak benign ve malign sinonazal tümörleri ayırt etmektir.

**Gereç ve Yöntem**: Ocak 2013 ile Aralık 2020 tarihleri arasında çekilmiş MRG incelemelerinden histopatolojik olarak kanıtlanmış benign ya da malign sinonazal tümor hastaları çalışmaya dahil edildi. Dahil edilme kriterleri 1 cm'den büyük tumor boyutu ve MR görüntülerinde T1 aksiyal, T2 aksiyal ve kontrastlı T1 aksiyal sekansların bulunmasıdır. Görüntüler iş istasyonuna aktarıldıktan sonra doku analizi hesaplamaları yapıldı. Benign ve malign gruplar arasındaki farklılıklar karşılaştırıldı.

**Bulgular**: Çalışmaya dahil edilen 37 hastanın ortalama yaşı 50,8±21,9 (8 kadın, 29 erkek). Çalışmamızda MRI ile elde edilen dokuz doku analiz parametresi malign ve benign sinonazal tümörler arasında istatistiksel olarak farklılık bulmadık.

**Sonuç**: MRG tabanlı doku analizi ile tümörlerin değerlendirilmesinde çekim protokollerinin aynı olması gerekmektedir. Spesifik patolojik tipler seçilmediğinde ve çekim protokolleri aynı olmadığında sinonazal tümörlerde benign ve malign ayrımında MRG tabanlı doku analizi yararlı değildir.

**Anahtar Kelimeler**: Manyetik rezonans görüntüleme, sinonazal, tümör, doku analizi

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## INTRODUCTION

Sinonasal tumors constitute 3% of head and neck cancers and 1% of all malignancies. Patients in most cases are asymptomatic. Clinical signs are generally non-specific and include nasal discharge, nasal obstruction, lacrimation, and epistaxis. The primary etiological factor reported is occupational exposure. A number of agents have been identified as increasing the risk of sinonasal carcinoma, including wood dust, which is particularly associated with adenocarcinoma, leather dust, welding fume, nickel, arsenic, and chromium.[1,2]

Paranasal sinuses and nasal cavity are commonly evaluated with computed tomography (CT) imaging in clinical practice. It is accepted as the gold standard technique, particularly for inflammatory lesions.[3] Beside this, the sinonasal region contains various histopathological types of benign and malignant tumors. Bony destruction caused by a tumor is accepted as a malignancy criterion in CT imaging. Determination of an exact diagnosis and prediction of the clinical outcome need histopathological evaluation of the surgical specimen in sinonasal tumors. Presurgical and non-invasive differentiation between benign and malignant sinonasal tumors using radiological imaging modalities is crucial and effects surgical treatment approach and clinical prognosis. Radiologists commonly strive to discriminate benign tumors from malignant ones in head and neck. Magnetic resonance imaging (MRI) is a diagnostic modality with high soft tissue resolution. It is commonly used in the diagnosis and characterization of sinonasal tumors, particularly when malignancy is suspected. MRI provides anatomic details, and also gives additional metabolic and biologic information in tumors.[4-8]

In the field of medicine, texture analysis is a mathematical approach used for non-invasive evaluation of the spatial variability of regions of interest (ROI) in medical images.[9,10] It is commonly used in non-invasive characterization and grading of tumors. In the past decade, there has been a growing interest in the use of texture analysis for the diagnosis, prediction of treatment outcomes, and association with tumor genomic properties in head and neck tumors.[6,11-13]

The objective of the present study was to ascertain whether texture analysis features derived from MRI scans can distinguish between benign and malignant sinonasal tumors.

## MATERIAL AND METHOD

### Patients

This retrospective study was approved by the local ethics committee (file number: 2020/231). A radiology database search was conducted in our hospital. All MRI examinations performed from January 2013 to December 2020 at our institution were scanned. Patients who have a pathologically proven benign and/or malignant sinonasal tumor having a size of 1 cm or larger in MRI examinations were included. 45 patients with sinonasal neoplasm who underwent pre-surgical head and neck MRI were identified. Three patients were excluded from the study due to the presence of motion artifacts in their images. Tumors smaller than 1 cm were not included (n=2). Three patients were excluded because MRI images did not include postcontrast series .

### MRI Examinations

All MRI examinations were performed with a 1.5 Tesla MRI platform (Siemens, Magnetom, Aera and, Toshiba, Vantage, Titan) in supine position by using an 8-channel head coil. MRI protocol included non-contrast T1W axial (TR, 505 ms; TE, 8.8 ms; acquisition matrix, 256×168; field of view, 19x21 cm; slice thickness, 5.5 mm), and coronal (TR, 464 ms; TE, 8.7 ms; acquisition matrix, 320×224; field of view, 22x22 cm; slice thickness, 4.5 mm), T2W sagittal (TR, 5000 ms; TE, 81ms; acquisition matrix, 320×224; field of view, 22×22 cm; slice thickness, 4 mm), fat suppressed T2W axial (TR, 5150 ms; TE, 80 ms; acquisition matrix, 320×210; field of view, 19×21 cm; slice thickness, 5.5 mm), coronal (TR, 3100 ms; TE, 51 ms; acquisition matrix, 320×224; field of view, 22×22 cm; slice thickness, 4.5 mm), postcontrast T1W axial and coronal images.

### Image Analysis and Post-processing

The relationship and distribution of pixel intensities in an image are analyzed by texture analysis, which yields a quantitative assessment of tumor heterogeneity. For texture analysis and segmentation, all images were loaded into the software program (OLEA Sphere 3.0, OLEA Medical, France). Interpretation and postprocessing steps of images were performed by a seven-year-experienced neuroradiologist without knowing final histopathological results. T1W axial, fat suppressed FS-T2W axial, and post-contrast T1W axial images were used to calculate the texture analysis features. An ROI of 30-50 mm² was manually drawn on the solid part of the tumor in the mentioned sequences. Cystic and necrotic parts were avoided. **Figure 1** shows the placement of the ROI to the tumor. Six first-order intensity based features (entropy, mean, median, skewness, kurtosis, variance) and three gray level co-occurrence matrix based features (contrast, correlation, joint energy) among texture analysis parameters were calculated for each ROI.

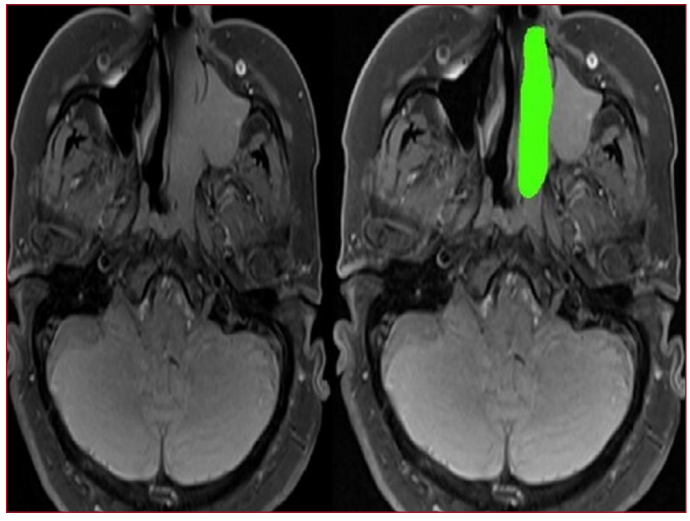

**Figure 1.** Tumor in the left nasal cavity on T1A sequence and placement of the region of interest on the solid part of the tumor.

### Statistical Analysis

The statistical analysis was performed using SPSS Version 21.0. Kolmogorov-Smirnov test was used to assess whether the variable distributed normally or abnormally. The variables were given as median (min-max) since the data did not show normal distribution. Mann-Whitney U test was used in comparison of the groups.

## RESULTS

Thirty seven patients with histopathological proven sinonasal tumor enrolled in the study. The mean age of the patients was 50 years (range, 12–90 years) at the time of diagnosis. 29 (78%) patients were male and 8 (28%) were female (**Table 1**). Malignant sinonasal tumor group included seven patients and all were male. Demographic characteristics of patients are presented in **Table 1** and texture analysis parameters of benign and malignant sinonasal neoplasms are presented in **Tables 2**, **3**, and **4**.

**Table 1: Demographic characteristics of patients**

| | Benign (n=30) | Malignant (n=7) |
|---|---|---|
| Age - median(min-max) | 51 (14-90 years) | 55 (12-72) years |
| Gender (M/F) | 22/8 | 7/0 |

**Table 2: Texture analysis features of benign and malignant sinonasal tumors on T1W sequence.**

| | Benign | Malignant | P value |
|---|---|---|---|
| Entropy | 4.8 (3.9-5.8) | 4.3 (4-5.5) | 0.458 |
| Mean | 298.4 (134.6-1640.9) | 317.3 (253.1-1439) | 0.582 |
| Median | 299 (137-1639.8) | 319 (264-1461.6) | 0.435 |
| Skewness | -0.2 (-3.9-2.6) | -0.4 (-2.5-1.2) | 0.391 |
| Kurtosis | 5.1 (1.7-22.8) | 5.6 (1.9-13.1) | 0.506 |
| Variance | 1658.9 (109.9-345973.6) | 2108.4 (774.3-46888.6) | 0.556 |
| Contrast | 14.9 (1.7-21790) | 8 (3.5-43.9) | 0.413 |
| Correlation | 0.9 (-0.1-0.9) | 0.9 (0.7-0.9) | 0.805 |
| Joint energy | 0 (0-0.1) | 0 (0-0) | 0.312 |

Variables are expressed as median (min-max). T1W: T1 weighted

**Table 3: Texture analysis features of benign and malignant sinonasal tumors on FS-T2W sequence.**

| | Benign | Malignant | P value |
|---|---|---|---|
| Entropy | 5.2 (4.2-5.7) | 5.2 (3.5-5.6) | 0.938 |
| Mean | 618.4 (258.1-1497.6) | 444.6 (62-1243.9) | 0.287 |
| Median | 613.5 (244.5-1470.8) | 448 (29-1258.7) | 0.221 |
| Skewness | -0.1 (-1.7-1.7) | 0.35 (-0.9-3.6) | 0.153 |
| Kurtosis | 3.1 (1.4-12.6) | 3.2 (2.6-19.2) | 0.433 |
| Variance | 37204.7 (4052.3-279488.3) | 28314.3 (7591-212481) | 0.667 |
| Contrast | 27 (7.2-1208.7) | 26.4 (4.7-35.1) | 0.410 |
| Correlation | 0.8 (-0.4-0.9) | 0.8 (0-0.9) | 0.725 |
| Joint energy | 0 (0-0.3) | 0 (0-0) | 0.815 |

Variables are expressed as median (min-max). FS-T2W: fatsuppressed T2 weighted

**Table 4: Texture analysis features of benign and malignant sinonasal tumors on CE-T1W sequence.**

| | Benign | Malignant | P value |
|---|---|---|---|
| Entropy | 5.1 (3.8-5.7) | 5 (4.7-5.5) | 0.719 |
| Mean | 684.3 (297-2885) | 565.3 (376.1-2127.7) | 0.776 |
| Median | 677 (307-2882.2) | 579 (338-2107.1) | 0.865 |
| Skewness | -0.3 (-0.1-1.7) | 0 (-1.4-1.5) | 0.835 |
| Kurtosis | 3.7 (1.6-16.5) | 4.1 (2.4-6.2) | 0.435 |
| Variance | 16421.4 (2062.5-166204.5) | 14444.8 (3045.3-438620.3) | 0.805 |
| Contrast | 13.5 (2.5-75.7) | 11.2 (6.3-125.3) | 0.894 |
| Correlation | 0.9 (0.4-0.9) | 0.9 (0.6-0.9) | 0.531 |
| Joint Energy | 0 (0-0) | 0 (0-0) | 0.293 |

Variables are expressed as median (min-max). CE-T1W: contrast enhanced T1 weighted.

There were 30 patients diagnosed with benign pathology in our study. The histopathological types of the tumors were nasal polyp (n=13), inverted papilloma (n=11), paraganglioma (n=1), angiofibroma (n=2), vascular leiomyoma (n=2), plasmocytoma (n=1). In addition, there were 7 patients diagnosed with malignant pathology in our study. The histopathological types of the tumors were Ewing sarcoma (n=1), non-keratinized carcinoma (n=1), olfactory neuroblastoma (n=1), verrucous carcinoma (n=1), lymphoma (n=1).

In our study, texture analysis of six first-order intensity-based features (entropy, mean, median, skewness, kurtosis, variance) and three gray-level co-occurrence matrix-based features (contrast, correlation, joint energy) was studied between benign and malignant sinonasal tumor groups. We found no statistically significant difference in T1W, FS-T2W and CE-T1W sequences. (p≥0.05) (**Tablea 2-4**).

## DISCUSSION

The present study employed texture analysis with first-order intensity-based and gray-level co-occurrence matrix-based features on T1W, FS-T2W, and postcontrast T1W MRI. The results indicated that there was no significant difference between benign and malignant sinonasal tumors.

Texture analysis is a mathematical method and includes multiple various parameters. Dedicated software was developed for texture analysis in the last decade. Various imaging modalities can be used for texture analysis, such as MRI, CT, perfusion weighted imaging, susceptibility weighted imaging, positron emission tomography, and ultrasonography. However, MRI is the most preferred imaging technique for performing texture analysis of head and neck tumors in previous literature. When previous studies regarding MRI-based texture analysis in the literature are investigated, it is not possible to make one-to-one comparisons because of the differences between the parameters and sequences included in the study, and even the shooting parameters in the same sequences. There are few previous reports that investigated the role of MRI-based texture analysis in sinonasal tumors in last decade. In a recent multicenter study conducted by Fruehwald-Pallamar et al.[11]

the role of MRI-based texture analysis in 100 head and neck tumor is investigated. The authors of that study used FS-T2W images and concluded that MRI-based texture analysis has the potential for differentiation of benign and malignant tumors in the head and neck region, but they indicated that the same MRI scanner with an identical MRI protocol is needed to achieve good results. Different MRI equipment and imaging protocols cause unreliable results. Our results supported this conclusion, though benign and malignant groups in the present study included various tumor types and MRI examination protocols were not identical. Another study investigated texture analysis in parotid tumors and reported that MRI-based texture analysis is able to discriminate between benign and malignant parotid gland tumors.[14] In a recent article conducted by Fujima et al.[5] SCC and lymphoma located in head and neck region were compared in terms of texture analysis features, and it was concluded that FS-T2WI-based texture analysis may provide useful data for imaging prediction of histopathological type and grade in head and neck malignancy. Ramkumar et. al.[13] investigated the role of MRI-based texture analysis to differentiate inverted papillomas from sinonasal SCCs. They used T1W axial, T2W axial, and postcontrast T1W axial sequences. The results of their study concluded that MRI-based texture analysis has the potential for discrimination of inverted papillomas and SCCs. Previous reports in the literature commonly included homogeneous tumor groups. We think the small cohort sample, heterogeneity in benign and malignant groups, and different MRI scanners with different imaging protocols are responsible for the unsuccessful performance of MRI-based texture analysis in the present study.

This study has some limitations. Primarily, the sample sizes of both benign and malignant groups were small. Particularly, the malignant group consist of only 7 lesions. Second, two groups were heterogeneous in terms of histopathological tumor types. As the authors of the present study, we think this is the major factor that caused the insignificant difference between benign and malignant sinonasal tumors. The analysis of a large number of patients and more homogeneous tumor groups may reveal significant differences in these tumors through texture analysis. Third, the examinations were performed on two different MRI equipment, and the imaging protocols were not identical. This may influence texture analysis parameters. Beside these, the fact that all patients included in the study had a pathological diagnosis is the superior aspect of the present study.

## CONCLUSION

MRI-based texture analysis is not a reliable and practical diagnostic tool for discriminating between benign and malignant sinonasal tumors when different MRI scanners and non-identical protocols are used. Future studies with homogenous and larger study populations are needed to assess the diagnostic performance of MRI-based texture analysis in sinonasal tumors.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was carried out with the permission of Selçuk University Local Ethics Committee (Date: 03.06.2020, Decision No: 2020/231).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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# Taste alteration, Food Habits and Nutritional Status of Childhood Cancer Survivors

## Kanserden Hayatta Kalan Çocukların Tat Alma Değişikliği, Beslenme Alışkanlığı ve Durumu

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## Abstract

**Aim**: This study was carried out to examine the taste alteration, food habits, and nutritional status of childhood cancer survivors.

**Material and Method**: The research is descriptive and cross-sectional. The study sample was formed by children between the ages of 8 and 18 who ended cancer treatment between March 2021 and 2022, followed by the pediatric hematology and oncology outpatient clinic of a University Medical Faculty Oncology Hospital. Child Introduction Form, Taste Alteration Scale for Children with Cancer Receiving Chemotherapy (TAS-CRC), Mediterranean Diet Quality Index (MDQI), and Subjective Total Taste Acuity Scale (STTA) were used to collect data.

**Results**: It was determined that 80.4% of children had a Body Mass Index (BMI) score between -2 and +2 (normal), 9.8% were above ≥+2 (obese) and 7.6% were under ≤-2 (malnutrition). Analysis showed that 18.5% of the children had a very low nutrition quality (≤3), while nutrition quality was moderate in 48.9% (4-7) and good in 32.6% (≥8). It was found that there was no statistically significant difference between the weight Z score of the children, the current height Z score and the BMI Z score, and the average score TAS-CRC.

**Conclusion**: Nearly half of the children experienced taste alteration during cancer treatment, and less than 10% of them currently experience taste alteration. In addition, no association was determined between taste alteration and nutrition quality, in other words, taste alteration had no effect on quality of nutrition.

**Keywords**: Childhood cancer survivors, food habits, nutritional status, nursing, taste alteration

## Öz

**Amaç**: Bu araştırma kanserden hayatta kalan çocukların tat alma değişikliği, beslenme alışkanlığı ve durumunu incelemek amacıyla yapılmıştır.

**Gereç ve Yöntem**: Tanımlayıcı ve kesitsel tipte bir araştırmadır. Araştırmanın evrenini bir üniversitesinin tıp fakültesi onkoloji hastanesi pediatri hematoloji ve onkoloji polikliniğinde Mart 2021-2022 tarihleri arasında izlenen, 8-18 yaş arasındaki kanser tedavisi biten çocuklar oluşturmuştur. Verilerin toplanmasında Çocuk Tanıtım Formu, Kemoterapi Alan Çocuklar İçin Tat Alma Değişikliği Ölçeği (KAÇ-TADÖ), Akdeniz Diyet Kalitesi Ölçeği (ADKİ) ve Subjektif Total Tat Keskinliği Ölçeği (STTKÖ) kullanılmıştır.

**Bulgular**: Çocukların Beden Kitle İndeksi (BKİ) Z skoru %80.4'ünde -2 ile +2 arasında (normal), %9.8'inde ≥+2'nin üstünde (obez) ve %7.6'sında ≤-2'nin altında (yetersiz beslenme) olduğu belirlenmiştir. Çocukların %18.5'inin çok düşük (≤3), %48.9'unun orta (4-7) ve %32.6'sının iyi beslenme kalitesine (≥8) sahip olduğu saptanmıştır. Çocukların KAÇ-TADÖ puan ortalaması ile kilo, boy ve BKİ Z skoru arasında istatiksel olarak anlamlı fark olmadığı saptanmıştır (p>0.05).

**Sonuç**: Çocukların neredeyse yarısı kanser tedavisi sırasında ve bunların %10'undan azı ise şu anda tat alma duyusunda değişiklik yaşıdığı belirlenmiştir. Ayrıca, tat alma duyusunda değişiklik ile beslenme kalitesi arasında bir ilişki olmadığı, yani tat alma duyusundaki değişikliğin beslenme kalitesi üzerinde bir etkisi olmadığı saptanmıştır.

**Anahtar Kelimeler**: Beslenme alışkanlığı, beslenme durumu, hemşirelik, kanserden hayatta kalan çocuk, tat alma değişikliği

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## INTRODUCTION

Cancer is a disease characterized by abnormal, uncontrollable cell growth and proliferation.[1] It is a significant cause of death among children worldwide. According to the World Health Organization (WHO), some 300.000 children aged 0-19 are diagnosed with cancer every year.[2] Leukemia is the most common form of cancer in the pediatric age group.[1]

Visible improvement has been achieved in survival rates from childhood cancers in recent years.[3] More than 80% of children in high-income countries are treated with new and advanced therapies.[2,4]

Not only is the treatment of cancer a lengthy and difficult process, it also leads to psychological and physiological problems.[5] Symptoms such as pain, lack of appetite, mucositis, nausea, vomiting, taste alteration, and xerostomia-related insufficient nutritional intake may be seen in association with cancer treatment.[6] Taste alteration is one of the most frequent and underestimated symptoms among cancer patients.[3] Studies have reported that taste perception alterations are the most important cause of altered food preferences and nutritional problems in children with cancer.[7] Taste alteration can also play an important role in the development of disease-related weight loss and causes several problems including a distaste for various foods, decreased food intake, and undernourished in severe cases.[3] Insufficient nutrition leads to impairment of quality of life and a greater risk of infection and increased mortality.[5] Identifying risk factors leading to altered taste perception in children with cancer and routine evaluation of taste alteration are therefore highly important.[5] Very little is known about the nutritional habits of children who survive childhood cancers.[4] However, the effects of food preferences and nutritional habits acquired during the treatment of cancer persist in children even after treatment.[5] Some studies have observed insufficient calcium and folate intake in young people who survive childhood cancers.[5,8] In addition, children's parents have reported changes in their children's nutritional habits compared to before the diagnosis of cancer, with insufficient fruit and vegetable consumption.[8] Some children who survive pediatric cancer are also at risk of becoming overweight or obese due to nutritional changes occurring during or after treatment,[9] while others are at risk of lack of appetite and being underweight.[5] Children who survive pediatric cancers are at risk of various chronic long-term health problems in adulthood, such as obesity associated with poor nutritional habits, cardiovascular diseases, metabolic syndrome, and osteoporosis.[4-6,8]

Children who have completed their treatment require long-term care to reduce the potential toxic effects associated with cancer treatment.[2] It is important for children's nutritional status to be evaluated in terms of their achieving normal growth and development.[10] Although several studies have investigated nutritional habits in cancer-surviving children[1,4,5,11-15] there has been insufficient research into taste alteration. No previous study has evaluated taste alteration and nutritional status and habits together. It was also intended to reveal the long-term effects of chemotherapy on taste perception and nutritional status and habits in cancer-surviving children, and thus to represent a source of information for subsequent studies on the subject. We therefore think that the research will be important.[15]

## MATERIAL AND METHOD

### Aim

To examine taste alteration and nutritional habits and status in cancer-surviving children.

### Type of Research

The research was performed as a descriptive and cross-sectional study.

### Study Setting and Sampling

The study was performed in a University Oncology Hospital pediatric hematology and oncology clinic, between March 2021 and March 2022. Two hundred children aged 8-18 years followed-up in the Gaziantep University Faculty of Medicine Oncology Hospital pediatric hematology and oncology outpatient clinic between March 2021 and March 2022. Sample size determined as 82 children using power analysis; 92 children who agreed to participate in the study were included in the sample.

The mean age of the children was 12.78±3.14 years, 50% were girls, and 38% attended middle school. Weight Z scores were between -2 and +2 in 88% of children, height Z scores between -2 and +2 in 70.7%, and BMI Z scores between -2 and +2 in 80.4% (**Table 1**).

**Table 1: Distribution of the children's sociodemographic characteristics**

| Sociodemographic Characteristics | X±SD | |
|---|---|---|
| Mean age | 12.78±3.14 | |
| | n | % |
| Sex | | |
| Female | 46 | 50.0 |
| Male | 46 | 50.0 |
| Education | | |
| Primary school | 32 | 34.8 |
| Middle school | 35 | 38.0 |
| High school | 25 | 27.2 |
| Weight Z score | | |
| Between -2 and +2 (normal) | 81 | 88.0 |
| ≤-2 (undernourished) | 3 | 3.3 |
| ≥+2 (obese) | 6 | 6.5 |
| No reply | 2 | 2.2 |
| Height Z score | | |
| Between -2 and +2 | 65 | 70.7 |
| ≤-2 | 23 | 25.0 |
| ≥+2 | 2 | 2.2 |
| No reply | 2 | 2.2 |
| BMI Z score | | |
| Between -2 and +2 (normal) | 74 | 80.4 |
| ≤-2 (undernourished) | 7 | 7.6 |
| ≥+2 (obese) | 9 | 9.8 |
| No reply | 2 | 2.2 |

### Research Population and Sample

Inclusion Criteria

- Voluntary participation on the part of the mother and child,
- The child being aged 8-18,
- The child having recovered from cancer, and
- At least one year having elapsed since the end of cancer treatment.

### Dependent and Independent Variables of the Study

The dependent variables of the study are taste alteration, eating habits and status. The independent variables are the children's sex, age, education status, weight, height, BMI, cancer type, cancer diagnosis date, age at cancer diagnosis, treatments received during cancer treatment, treatment duration, treatment end date, experiencing taste alteration during cancer treatment, experiencing taste alteration now, foods they like and dislike after cancer treatment.

### Data Collection Tools

### Child Description Form

This form was developed by the authors based on a scan of the literature.[1-5,11,14,17] It consisted of two sections containing six questions concerning the child's sociodemographic characteristics and nine concerning the disease.

### Taste Alteration Scale for Children with Cancer Receiving Chemotherapy (TAS-CrC)

This scale allows the child to express his sense of taste in a subjective manner. It was developed by Bilsin and Bal Yılmaz[18] for the evaluation of taste alteration in children with cancer aged 8-18 years receiving chemotherapy. It consists of nine items. Five items (1, 4, 5, 6 and 7) express dysgeusia, while the other items refer to cacogeusia (2), phantogeusia (3), parosmia (8), and cacosmia (9). Each item is scored between 0 and 4 on a Likert-type scale (0: None, 1: Mild, 2: Moderate, 3: Severe, 4: Very severe). The total scale score is calculated by adding the scores for each individual item. Possible scores range between 0 and 36. Higher scores indicate a greater severity of taste alteration. The scale's Cronbach alpha reliability coefficient was calculated as 0.88. [18] In the present research the Cronbach alpha reliability coefficient was determined as 0.957.

### Mediterranean Diet Quality Index (MDQI)

The MDQI was developed by Serra Majem et al.[19] The validity and reliability of the Turkish version were established by Akar Şahingöz, Özgen and Yalçın.[20] The index consists of 16 questions, 12 (1, 2, 3, 4, 5, 7, 8, 9, 10, 11, 13, and 15) denoting positive connotations to the Mediterranean diet, and (6, 12, 14, and 16) involving negative connotations. The responses were designed as yes/no options. Yes responses are scored +1 in positive items and -1 in negative items. Possible scores range between 0 and 12. Scores ≥8 indicate good adherence to the optimal Mediterranean diet, scores of 4-7 indicate a need to improve adherence to the Mediterranean diet, and scores ≤3 indicate a very low quality diet19. The Cronbach alpha reliability coefficient of the Turkish-language version was calculated as 0.72.[20]

### Scale of Subjective Total Taste Acuity (STTA)

The STTA is a scoring system used to evaluate taste acuity. [21] The Late Effects Normal Tissue Task Force (LENT) adapted from the Subjective, Objective, Management, Analytic (SOMA) scoring system was established in 1995 by a specialist working group (the European Organization for Cancer Research and Treatment and Radiation Therapy Oncology Group) to grade radiotherapy-related side effects.[22] It consists of five items evaluating taste acuity (from 0 to 4) (Grade 0: Taste acuity before treatment, Grade 1: Mild loss of taste acuity, but not troublesome in daily life, Grade 2: Moderate loss of taste acuity, sometimes causing inconvenience in daily life, Grade 3: Severe loss of taste acuity generally troublesome in daily life, and Grade 4: Complete or almost complete loss of taste acuity. These items indicate a decrease in taste acuity from 0 to 4. Each item on the scale is evaluated in yes/no form.[21]

### Validation of the STTA

The Content Validity Ratio (CVR) for the items was 0.80-1.00, and the Content Validity Index (CVI) was calculated as 0.96. Since CVI≥CVR, the content validity of the scale was regarded as statistically significant.

### Data Collection

The Child Description Form, TAS-CRC, STTA, and MDQI were applied online to the children aged 8-18 included in the study. The research was explained to the parents and children by telephone. A Google survey form link was sent to the parents and children consenting to take part in the research. The parents of children aged 8-12 and children aged 12-18 themselves were asked to complete the questionnaire. The pre-questionnaire was applied to 10 children and their parents as a pilot study, after which any necessary amendments were made to the pre-questionnaire, and the final version thus assumed its final form.

### Data Analysis

Data analysis was performed on Statistical Packages for the Social Sciences (SPSS) version 20.0 software. The Kolmogorov Smirnov test showed that the data were not normally distributed and non-parametric tests were therefore employed. CVI, mean, number and percentage distributions, Cronbach Alpha coefficients, Spearman Brown Rank Order Correlation analysis, and the Mann Whitney U, Kruskal Wallis, and chi-square tests were used in the analysis.

## RESULTS

The children's mean age at the time of diagnosis of cancer was 6.01±3.57, mean duration of treatment was 33.75±21.13 months, and the mean time elapsed since the end of treatment was 49.34±34.09 months. Seventy-five percent

of the children were diagnosed with ALL, 100% received chemotherapy during cancer treatment, and 54.3% reported taste alteration during cancer treatment and 7.6% at the time of the study (**Table 2**).

**Table 2: Distributions of information concerning children's disease**

| Information About the Disease | X±SD | |
|---|---|---|
| Age at diagnosis of cancer | 6.01±3.57 | |
| Duration of treatment (months) | 33.75±21.13 | |
| Time since end of treatment (months) | 49.34±34.09 | |
| **Type of cancer** | **n** | **%** |
| ALL | 69 | 75 |
| Lymphoma | 18 | 19.6 |
| Brain tumor | 3 | 3.3 |
| Acute myeloid leukemia | 2 | 2.2 |
| Therapies Employed * | | |
| Chemotherapy | 92 | 100.0 |
| Radiotherapy | 33 | 35.9 |
| Bone marrow transplantation | 15 | 16.3 |
| Surgery | 8 | 8.7 |
| Experience of taste alteration during cancer treatment | | |
| Yes | 50 | 54.3 |
| No | 42 | 45.7 |
| Current taste alteration | | |
| Yes | 7 | 7.6 |
| No | 85 | 92.4 |

*More than one option was marked.

In terms of foods that children enjoyed eating or found unpleasant after cancer treatment, 100% enjoyed fizzy drinks, 38% red meat, 18.5% fruit, 14.1% white meat, 14.1% snacks, 6.5% pasta, 5.4% vegetables, 5.4% yoghurt, 4.3% soup, 4.3% rice, and 3.3% eggs. In contrast, 14.1% of children found vegetables unpleasant, 6.5% milk and milk products, 6.5% red meat, 6.5% white meat, 5.4% eggs, 3.3% olives, 2.2% snacks, and 1.1% fizzy drinks.

Analysis showed that 18.5% of the children had a very low nutrition quality (≤3), while nutrition quality was moderate in 48.9% (4-7) and good in 32.6% (≥8). The mean total TAS-CRC score was 5.79±7.77 (**Table 3**).

**Table 3: MDQI category distributions and mean TAS-CRC score**

| Scale Categories | n | % |
|---|---|---|
| Very low nutrition quality (≤3) | 17 | 18.5 |
| Moderate nutrition quality (4-7) | 45 | 48.9 |
| Good nutrition quality (≥8) | 30 | 32.6 |
| **Mean TAS-CRC Score** | **Min-Max** | **X±SD** |
| | 0-31 | 5.79±7.77 |

Grade 0 loss of taste acuity was determined in 35.9% of the children, Grade 1 in 37.0%, Grade 2 in 30.4%, Grade 3 in 18.5%, and Grade 4 in 8.7%.

No statistically significant association was observed between MDQI categories and the mean TAS-CRC score (p>0.05). No association was found between children's taste alteration and nutrition quality, and taste alteration had no effect on quality of nutrition (**Table 4**).

**Table 4: A comparison of MDQI categories and the mean TAS-CR score**

| MDQI Categories | TAS-CRC X±SD | Statistical Analysis |
|---|---|---|
| Very low nutrition quality (≤3) | 5.00±9.24 | |
| Moderate nutrition quality (4-7) | 5.31±7.45 | KW=1.985 p=0.371 |
| Good nutrition quality (≥8) | 6.96±7.49 | |

*p<0.05

No significant association was observed between the mean TAS-CRC score and the STTA grades 0, 1, 2, or 3 (p<0.05), although a significant association was found with Grade 4 (p>0.05). Taste alteration was greater in children with mild, moderate, and severe taste acuity loss (**Table 5**).

## DISCUSSION

In general terms, some pediatric cancer patients are insufficiently nourished, while others are overnourished.[23] Obese or overweight pediatric patients have lower survival and higher recurrence rates and are more resistant to treatment.[24] In the present study, 80.4% of the children were normally nourished, 9.8% were obese, and 7.6% were undernourished. Comparing our results with those of similar studies of cancer-surviving children, Teixeira et al.[17] reported that 72% of children were of normal weight, 25.5% were overweight, and 2.5% were underweight.[17] Naomi Belle et al.[4] study, 4.9% of children were underweight on the basis of BMI, 61.1% were of normal weight, 22.1% were overweight, and 9.4% were obese.[4] Fleming et al.[13] described 61% of their children as normal weight, 21% as overweight, and 5% as obese.[13] Half or more of the children in those studies were of normal weight. In contrast to those studies, Murphy-Alford et al.[6] described 8% of the children in their study as underweight, 23% as overweight, and 2% as obese.[6] Murphy et al.[6] reported that 53% of children were obese according to their fat percentages and 53% were inadequately nourished on the basis of BMI values.[6] Hansen et al.[24] reported that 48% of children surviving ALL were of normal weight, 12% were overweight, and 40% were obese, while 58.3% of children surviving brain tumors were of normal

**Table 5: A comparison of STTA items and the mean TAS-CRC score**

| | STTA Items | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Grade 0 | | Grade 1 | | Grade 2 | | Grade 3 | | Grade 4 | |
| Mean TAS-CRC Score | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No |
| | X±SD | X±SD | X±SD | X±SD | X±SD | X±SD | X±SD | X±SD | X±SD | X±SD |
| | 3.54±6.55 | 9.81±8.25 | 9.91±7.81 | 3.37±6.71 | 12.10±3.03 | 3.03±6.26 | 14.35±7.44 | 3.85±6.46 | 7.87±4.15 | 5.59±8.02 |
| Statistical Analysis | U=465.000 p=0.000* | | U=494.000 p=0.000* | | U=269.000 p=0.000* | | U=159.000 p=0.000* | | U=228.000 p=0.119 | |

*p<0.05

weight, 12.5% were overweight, and 29.2% were obese.[24] Fang Zhang et al.[12] described 59.1% of the children in their study as being of normal weight and 40.9% as overweight or obese.[12] The rates of overweight or obesity were much higher in these studies. We attribute this variation to the type and stage of cancer, the child's age at diagnosis, weight, nutritional habits, appetite, gender, the type and dose of drugs used (especially corticosteroids), infections occurring during treatment, and the child's immune system.

Despite its being an important determinant of survival among children recovering from cancer, very little is known about children's nutritional habits and nutrient intake4. Almost one-fifth of the children in the present research had a very low quality of nutrition, with half having a moderate quality, and a third being well-nourished. Fleming et al.13 found that these exhibited higher rates of food selectivity than peers of the same age. Those authors also reported that 27% of cancer-surviving children had a normal diet quality, 15% a poor diet quality, and 58% a poor quality of nourishment.[13] Another study of cancer-surviving children, by Fang Zhang et al.[12] reported low fruit and vegetable consumption among children, that the true amount consumed was less than half the recommended intake, and that they consumed low levels of fiber and grains and high levels of saturated fat.[12] In Teixeira et al.'s[17] study, carbohydrate constituted 54% of children's diet, protein 20.8%, and lipid consumption 24.6%m while fiber consumption below recommended levels, and children's diet quality was reported to be low.[17] Cohen et al.[5] reported decreased fruit and vegetable consumption among children, with increased snack food consumption and portion sizes.[5] In another study, Cohen et al.[11] reported that 54% of children consumed more food than necessary to meet their recommended energy requirements, and that their folate, calcium, and iron requirements were not met.[11] Another study by Cohen et al.[14] found that 80% of children consumed insufficient fruits and vegetables and that almost none consumed sufficient fiber. It may be concluded that cancer-surviving children generally consume insufficient fiber, fruit, and vegetables and have a low quality of nutrition.[14]

The sense of taste makes it possible to assess the contents of food and assists with food intake.[25] Taste alteration associated with chemotherapy is a condition frequently encountered in oncological patients.[18] However, permanent taste perception disorder is frequently seen in cancer survivors and has an adverse impact on quality of life.[26]

Approximately half of the children in the present study experienced taste alteration during cancer treatment, and 7.6% at the time of the research. Studies of taste alteration in children with cancer have reported that this is experienced by 36-95% of patients.[7] In terms of studies of taste alteration in cancer-surviving children, Cohen et al.[15] reported taste alteration in 27.5% of children, with sweet taste perception disorder in 9.8%, bitter taste disorder in 15.7%, salty taste disorder in 7.8%, and salty or sour taste perception disorder in 11.8%. An examination of the results of this research and other studies that have discussed the subject show that children experience greater taste alteration during cancer treatment than in the post-treatment period. Our findings are also consistent with the previous literature. However, the experience of taste alteration after the end of treatment was lower compared to other studies. We attribute this to differences in the types of cancer and chemotherapy in other studies, and in the methods employed to evaluate taste alteration.

Mild and moderate loss of taste alteration was most frequently observed in the children in this research. Taste alteration was also greater in children with mild, moderate and severe loss of taste acuity. Taste and smell receptor cells are regularly renewed in a few weeks or longer, but cancer treatment causes long-term taste and smell receptor cell damage.[15] We encountered no previous studies investigating taste alteration and taste acuity together. Based on the findings of the present research, we concluded that taste alteration and taste acuity are directly proportional to one another.

No association was determined between taste alteration and quality of nutrition in this research, and taste alteration had no effect on that quality. Similarly, no significant variation or relationship was observed between food groups and taste scores in Cohen et al.'s[15] study of cancer-surviving children, and no association was also found between taste function or preferred foods and quality of life.[15] In contrast to that research, Bomben et al.[27] reported that taste alteration adversely affected nutrition and daily life in cancer-surviving children, and that the presence of unpleasant tastes during eating made food consumption problematic.[27] Van Den Brink et al.'s [7] study of children with cancer reported that eating disorders increased in line with taste function impairment.[7]

**Relevance to Clinical Practice**

Taste perception disorders have an adverse impact on children. Scales permitting the evaluation of taste alterations and preventive nursing interventions are therefore needed. The aim of nursing care in patients receiving chemotherapy is to prevent or reduce treatment-related symptoms and problems. Nurses play an important role in patients' adaptation to taste alterations. They must support patients in coping with the undesired effects of treatment by means of education, evaluate taste alteration and the severity thereof, and assist with the application of measures directed toward taste alteration.[28] This will prevent potential treatment related symptoms in patients receiving chemotherapy.[18]

Nurses also play an important role in establishing continuity of nutrition in children with cancer.[29] It is important for nurses to weigh and measure children with cancer and to evaluate their daily nutrition. Children's nutritional problems need to be identified, and appropriate measures should be taken to deal with them. Daily evaluation of nutrition helps to identify nutritional problems in the early period, to initiate prompt treatment, to prevent problems that may develop in association with undernourished,[10] to reduce lengths of hospital stay and costs, and to increase the child's treatment adherence and quality of life.[23]

## CONCLUSION

To summarize, nearly half of the children in this research experienced taste alteration during cancer treatment, and less than ten percent of them currently experience taste alteration. In addition, no association was determined between taste alteration and nutrition quality, in other words, taste alteration had no effect on quality of nutrition. Greater taste alteration was observed in children with mild, moderate, and severe loss of taste acuity.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was carried out with the permission of Gaziantep University Clinical Researches Ethics Committee (Date: 24.03.2021, Decision No: 2021/95).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

**Note**: This study is Master's thesis. This study presented as oral presentation in I. International and IV. National Health Services Congress: Oral Presentation, 10-11 June 2022, Isparta, Turkey

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Original Article / Orijinal Araştırma

# Prognostic Value of Monocyte-to-High-Density Lipoprotein Cholesterol Ratio in COVID-19 Patients

## COVID-19 Hastalarında Monosit-Yüksek Yoğunluklu Lipoprotein Kolesterol Oranının Prognostik Değeri

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## Abstract

**Aim**: A significant portion of individuals infected with COVID-19 experience severe illness and require intensive care. Especially in these cases, the disease may ultimately be fatal. Monocyte-to-high-density lipoprotein cholesterol ratio (MHR) has been reported to be a novel marker for major adverse outcomes in many diseases. In this study, we aimed to reveal the relationship of MHR with the prognostic markers of COVID-19 and its role in predicting the severity of disease and in-hospital mortality in COVID-19.

**Material and Method**: This single-center, retrospective, and cross-sectional study included 195 hospitalized patients diagnosed with COVID-19. The patients who were discharged from the hospital constituted the survivor group, while those who died constituted the non-survivor group. Clinical, laboratory and radiologic data of patients were retrospectively reviewed from medical records.

**Results**: The age of the patients ranged from 19 to 92 years and the mean age was 57.0±16.3 years. Ninety-eight (50.3%) of the patients were female. Forty-one of the patients died during hospitalization due to COVID-19 and related complications. MHR was significantly higher in the non-survivor group than in the survivor group. MHR was significantly correlated with age, ferritin, uric acid, urea, and creatinine levels. No difference was found between the MHR values of patients according to their disease severity at the time of admission (p=0.600). Univariate logistic regression analysis demonstrated no significant association between MHR and in-hospital mortality (p=0.132).

**Conclusion**: MHR is increased in COVID-19 survivors compared to non-survivors and correlates with age, ferritin, uric acid, urea, and creatinine levels. However, MHR cannot be used as a prognostic marker to predict the severity of the disease and in-hospital mortality in COVID-19 patients.

**Keywords**: COVID-19 virus disease, in-hospital mortality, monocyte, HDL cholesterol, prognostic factor

## Öz

**Amaç**: COVID-19'a yakalanan bireylerin önemli bir kısmı ağır hastalık geçirmekte ve yoğun bakıma ihtiyaç duymaktadır. Özellikle bu vakalarda hastalık nihayetinde ölümcül olabilir. Monosit-yüksek yoğunluklu lipoprotein kolesterol oranının (MHR) birçok hastalıkta önemli olumsuz sonuçlar için yeni bir belirteç olduğu bildirilmiştir. Bu çalışmada, MHR'nin COVID-19'un prognostik belirteçleriyle ilişkisini ve COVID-19'da hastalığın şiddetini ve hastane içi mortaliteyi tahmin etmedeki rolünü ortaya koymayı amaçladık.

**Gereç ve Yöntem**: Tek merkezli, retrospektif ve kesitsel çalışmaya COVID-19 tanısı almış ve hastaneye yatırılmış 195 hasta dahil edildi. Hastaneden taburcu edilen hastalar sağ kalan grubu oluştururken, hayatını kaybedenler ise sağ kalamayan grup olarak kategorize edildi. Hastaların klinik, laboratuvar ve radyolojik verileri tıbbi kayıtlardan retrospektif olarak incelendi.

**Bulgular**: Hastaların yaşları 19 ile 92 arasında değişiyordu ve ortalama yaş 57,0±16,3 yıldı. Hastaların 98'i (%50,3) kadındı. Hastaların 41'i COVID-19 ve ilgili komplikasyonlar nedeniyle hastanede yatarken öldü. MHR, hayatta kalmayan grupta hayatta kalan gruba göre anlamlı şekilde daha yüksekti. MHR, yaş, ferritin, ürik asit, üre ve kreatinin seviyeleriyle anlamlı şekilde ilişkiliydi. Hastaların başvuru sırasındaki hastalık şiddetlerine göre MHR değerleri arasında fark bulunmadı (p=0.600). Tek değişkenli lojistik regresyon analizi, MHR ile hastane içi mortalite arasında anlamlı bir ilişki olmadığını gösterdi (p=0,132).

**Sonuç**: MHR, COVID-19'dan sağ kurtulanlarda hayatta kalmayanlara göre artmıştır ve yaş, ferritin, ürik asit, üre ve kreatinin seviyeleriyle ilişkilidir. Ancak MHR, COVID-19 hastalarında hastalığın şiddetini ve hastane içi mortaliteyi tahmin etmek için prognostik bir belirteç olarak kullanılamaz.

**Anahtar Kelimeler**: COVID-19 virüs hastalığı, hastane içi mortalite, monosit, HDL kolesterol, prognostik faktör

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## INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel coronavirus that emerged in China, in December 2019, has caused a coronavirus disease 2019 (COVID-19) pandemic and led to significant loss of life all over the world.[1] Apart from causing pneumonia, SARS-CoV-2 can also damage various organs and systems, such as the heart, liver, and kidneys.[2] COVID-19 has been associated with ischemic complications such as myocardial infarction and stroke, especially in older individuals.[3] SARS-CoV-2 binds to cells expressing appropriate viral receptors, particularly angiotensin-converting enzyme 2 (ACE-2).[2] ACE-2 is also expressed in the heart, providing a link between SARS-CoV-2 and the cardiovascular system. SARS-Co-V-2 can down-regulate myocardial and pulmonary ACE-2 pathways, thereby mediating myocardial inflammation, lung edema, and acute respiratory failure.[4] Pro-inflammatory cytokines are up-regulated in the lungs and other organs of patients, and the systemic inflammatory response syndrome provides a possible mechanism for multi-organ failure (usually involving the heart) in severe cases. Complications may also develop from COVID-19 due to the formation of endothelial dysfunction.[5] One of the mechanisms for the development of endothelial dysfunction is oxidative stress, which develops during infection with the SARS-CoV-2.[6] The increase in levels of reactive oxygen species during a COVID-19 infection is well-established.[7] In COVID-19 patients, inflammation and oxidative stress markers guide the prognosis and treatment strategies of the disease.[8]

The clinical course of COVID-19 may range from asymptomatic cases to severe disease. Studies report the mortality rate of COVID-19 to be below 5%. However, 15-18% of patients are diagnosed with severe or critical disease and need treatment in the intensive care unit. The mortality rate is 49% in patients diagnosed with critical disease.[9] Anticipating poor outcomes early in COVID-19 patients could help decrease the demand for intensive care treatment and reduce mortality rates. Therefore, early identification of critically ill patients is important.

Monocytes are involved in the synthesis and release of proinflammatory and prooxidant cytokines and contribute to the development of atherosclerosis. These cells play a particular role in vascular endothelial damage, which is the most important stage in the pathogenesis of atherosclerosis.[10] High-density lipoprotein (HDL) cholesterol has been shown to protect the endothelium from the harmful effects of low-density lipoprotein (LDL) cholesterol and inhibit the oxidation of LDL cholesterol.[11] In this way, HDL cholesterol acts as an anti-inflammatory and antioxidant substance. The effects of HDL particles on monocytes include mediating the cholesterol influx from macrophages and protecting endothelial cells from oxidation and inflammation.[12]

Research indicates that the monocyte-to-HDL cholesterol ratio (MHR) could serve as a novel indicator of systemic inflammation and oxidative stress. Moreover, MHR is closely linked to the occurrence and prognosis of specific cardiovascular conditions.[13,14] MHR can serve as a predictive marker for atherosclerosis development and an estimate of cardiovascular events.[15-17] The role of MHR in determining systemic inflammation and oxidative stress, which are important mechanisms of systemic effects of COVID-19, has raised the possibility of its use as a prognostic marker in COVID-19. The few studies investigating the predictive value of MHR in COVID-19 have conflicting results.[18,19] In this study, we aimed to investigate the predictive value of MHR on in-hospital mortality and its relationship with prognostic markers in COVID-19.

## MATERIAL AND METHOD

A total of 195 patients, hospitalized with the diagnosis of COVID-19 between March 2020 and July 2020, were included in our single-center, retrospective, and cross-sectional study. Patients who died during hospitalization due to COVID-19 and related complications constituted the non-survivor group, and those who recovered and were discharged constituted the survivor group. COVID-19 diagnosis was confirmed through the polymerase chain reaction test (Rotor-Gene Q, Qiagen, Hilden, Germany). Patients using medications that may affect complete blood count and lipid metabolism including antiviral agents, those with hematological or liver disease, and patients with malignancy were excluded from the study. Demographic characteristics and laboratory test results of the patients were obtained from medical records. Laboratory results including complete blood count, renal and liver function, lipid profiles, and inflammation markers were recorded within 2 days of admission and before initiation of any treatment for COVID-19 including antiviral therapy. Monocyte counts and HDL cholesterol levels were calculated from blood samples taken simultaneously. MHR was calculated by division of monocyte count (cells/μL) to HDL cholesterol level (mg/dL). The severity of COVID-19 disease was classified according to symptoms of patients at hospital admission, vital signs, laboratory test results, findings in chest computed tomography (CT), levels of respiratory distress, and need for respiratory support. Upper respiratory tract infection (URTI) was defined as an upper respiratory tract disease in which no radiographic evidence of COVID-19 pneumonia was detected in the review of radiology reports. Mild-to-moderate COVID-19 was defined as fever, cough, and other symptoms with pneumonia on chest CT. Severe COVID-19 was defined as pneumonia on chest CT with at least one of the following conditions met 1) Respiratory distress with respiratory rate ≥30/minute. 2)

Oxygen saturation on room air at rest ≤93%. 3) The ratio of the partial pressure of oxygen in arterial blood to the fraction of inspired oxygen ≤300 mmHg. Acute respiratory distress syndrome (ARDS) was defined as pneumonia on chest CT with at least one of the following conditions met. 1) Respiratory failure occurs and mechanical ventilation is required. 2) Shock occurs. 3) Other organ dysfunction is present, requiring intensive care unit monitoring and treatment.

This retrospective study involving human participants was carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study was carried out with the permission of Kütahya Health Sciences University, Clinical Research Ethics Committee (Date: 17 September 2020, Decision No: 2020/14-18).

### Statistical Analysis

We conducted statistical analyses using SPSS for Windows version 22.0 (SPSS, Chicago, IL, USA). We assessed the normal distribution of continuous variables using the Kolmogorov-Smirnov and Shapiro-Wilk tests. To compare continuous variables between the two groups, we used the student's t-test for normally distributed data and the Mann-Whitney U test for non-parametric data. We compare categorical parameters using the Chi-square test and Fisher's Exact test. Spearman's rank correlation was used to measure the level of association between two variables. Univariate logistic regression analysis was used to assess the predictive value of clinical and laboratory parameters for in-hospital mortality. To assess the discrimination ability of MHR to survive, the receiver-operating characteristic (ROC) curve was calculated, and the optimal cutoff value was determined by maximizing the Youden index. Time to a composite endpoint was investigated using survival analysis by a Kaplan–Meier plot and compared using the log-rank test. P <0.05 was considered statistically significant for all tests.

## RESULTS

The age of the patients ranged from 19 to 92 years and the mean age was 57.0 ± 16.3 years. Ninety-eight of the patients (50.3%) were women. Forty-one of the patients (21%) died during hospitalization due to COVID-19 and related complications. The clinical presentations of COVID-19 at admission according to the clinical outcome of the patients are shown in **Figure 1**. The most common clinical presentations of COVID-19 at admission were severe COVID-19 (n=31, 75.6%) and ARDS (n=7, 17.1%) in the non-survivor group and mild-to-moderate COVID-19 (n=88, 57.1%) and URTI (n=30, 19.5%) in the survivor group. There were no admissions with URTI in the non-survivor group.

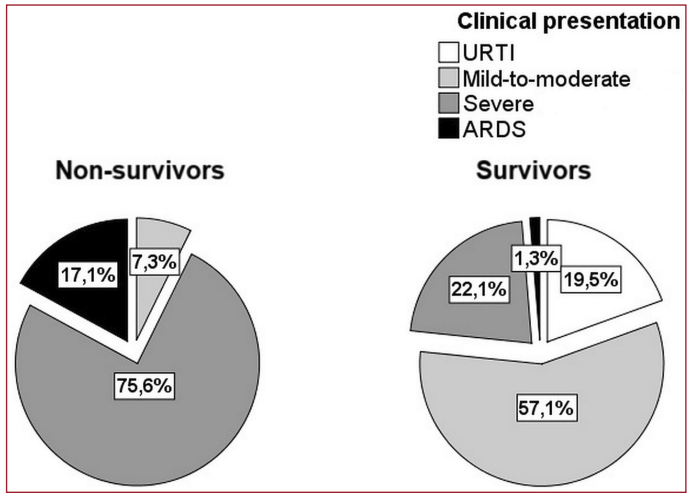


**Figure 1.** Clinical presentations of COVID-19 patients at admission (URTI, Upper respiratory tract infection; ARDS, Acute respiratory distress syndrome).

Comparison of clinical characteristics and laboratory parameters according to the outcome of patients are presented in **Table 1**. The age of the non-survivor group was significantly higher (p<0.001) but there was no significant difference in terms of gender distribution (p=0.205). The prevalence of cardiovascular disease and chronic kidney disease was significantly higher in the non-survivor group. The monocyte count was similar between the groups (p=0.333). HDL cholesterol level was significantly lower and MHR was significantly higher in the non-survivor group (p=0.031 and p=0.046, respectively).

HDL cholesterol level was significantly lower, and monocyte count and MHR ratio were significantly higher in men than in women (p=0.028, p=0.005, p=0.001, respectively) (**Table 2**). There was a weak negative correlation between HDL cholesterol level and age (correlation coefficient -0.23, p=0.001). Although monocyte count was not correlated with age, a weak but significant correlation was observed between MHR and age (correlation coefficient 0.13, p=0.075, correlation coefficient 0.19, p=0.008). HDL cholesterol levels were significantly lower in smokers than in nonsmokers [31 (26-37) mg/dL vs 33 (29-41) mg/dL, p=0.034].

**Table 2. Comparison of monocyte counts, HDL cholesterol levels, and MHR values according to gender.**

| Parameters | Women (n=98) | Men (n=97) | p value |
|---|---|---|---|
| Monocyte count, cells/μL | 340 (240-510) | 440 (320-575) | 0.005 |
| HDL-C, mg/dL | 33 (28-42) | 31 (27-37) | 0.028 |
| MHR, ratio | 10.00 (6.56-15.40) | 12.94 (9.62-19.51) | 0.001 |

Data are presented as median with interquartile ranges (25th-75th percentiles). Abbreviations: HDL-C, high-density lipoprotein cholesterol; MHR, monocyte-to-high-density lipoprotein cholesterol ratio.

No difference was found between the MHR values of COVID-19 patients according to their disease severity at the time of admission (**Figure 2**). There was a weak positive correlation between MHR and age, ferritin, uric acid, urea, and creatinine (**Table 3**).

**Table 1. Comparison of clinical characteristics and laboratory parameters of the patients.**

| Parameters | Non-survivor (n=41) | Survivor (n=154) | p value |
|---|---|---|---|
| Clinical Parameters | | | |
| Women, n (%) | 17 (41.5%) | 81 (53%) | 0.205 |
| Age, years | 73 (66-82) | 54 (43-63) | <0.001 |
| Hospital stay, days | 9 (6-17) | 10 (6-14) | 0.826 |
| Smoking, n (%) | 12 (29%) | 69 (45%) | 0.116 |
| Hypertension, n (%) | 19 (46%) | 49 (32%) | 0.083 |
| Diabetes mellitus, n (%) | 18 (44%) | 64 (42%) | 0.787 |
| COPD, n (%) | 9 (22%) | 26 (17%) | 0.452 |
| Cardiovascular disease, n (%) | 13 (32%) | 9 (6%) | <0.001 |
| Chronic kidney disease, n (%) | 13 (20%) | 3 (2%) | <0.001 |
| Laboratory Parameters | | | |
| C-reactive protein, mg/L | 90.2 (47.9-228.5) | 12.9 (4.7-31.1) | <0.001 |
| Procalcitonin, ng/ml | 0.32 (0.19-1.10) | 0.12 (0.07-0.24) | <0.001 |
| Ferritin, ug/L | 354 (166-976) | 96 (44-192) | <0.001 |
| D-dimer, ng/mL | 1718 (691-3284) | 518 (300-768) | <0.001 |
| Lactate, mmol/L | 2.2 (1. 5-3.4) | 1.7 (1.3-2.4) | 0.033 |
| Lactate dehydrogenase, U/L | 411 (253-502) | 247 (195-336) | <0.001 |
| Fibrinogen, mg/dL | 512 (377-639) | 435 (352-529) | 0.022 |
| Troponin-I, ng/L | 26.3 (10.5-56.4) | 3.2 (2.0-6.4) | <0.001 |
| Total cholesterol, mg/dL | 129 (107-168) | 146 (125-173) | 0.168 |
| HDL-C, mg/dL | 29 (24-37) | 33 (28-39) | 0.031 |
| LDL-C, mg/dL | 74 (49-104) | 88 (65-108) | 0.061 |
| Triglycerides, mg/dL | 141 (114-185) | 121 (90-165) | 0.024 |
| Uric acid, mg/dL | 6.9 ± 2.7 | 4.8 ± 1.7 | <0.001 |
| Urea, mg/dL | 64 (45-96) | 30 (23-39) | <0.001 |
| Creatinine, mg/dL | 1.35 (1.00-2.01) | 0.91 (0.80-1.05) | <0.001 |
| Aspartate transaminase, U/L | 32.0 (22.5-52.5) | 25.5 (19.0-36.3) | 0.010 |
| Alanine transaminase, U/L | 17.0 (11.0-27.5) | 20.5 (14.8-31.0) | 0.086 |
| Leukocyte count, ×1000/µL | 7.52 (5.29-11.92) | 5.02 (3.95-6.63) | <0.001 |
| Neutrophil count, ×1000/µL | 5.88 (3.75-9.62) | 2.94 (2.23-4.30) | <0.001 |
| Lymphocyte count, ×1000/µL | 0.93 (0.57-1.21) | 1.43 (1.10-1.85) | <0.001 |
| Neutrophil-to-lymphocyte ratio | 7.12 (4.03-13.48) | 2.12 (1.48-3.17) | <0.001 |
| Platelet count, x1000/µL | 155 (133-230) | 198 (159-239) | 0.075 |
| Platelet-to-lymphocyte ratio | 155 (121-329) | 136 (106-181) | 0.040 |
| Monocyte count, cells/µL | 460 (250-610) | 380 (270-550) | 0.333 |
| Lymphocyte-to-monocyte-ratio | 2.50 (1.24-3.55) | 3.79 (2.80-5.29) | <0.001 |
| MHR, ratio | 13.16 (9.29-21.40) | 11.67 (8.24-16.76) | 0.046 |
| Hemoglobin, g/dL | 12.6 ± 2.7 | 13.1 ± 1.8 | 0.268 |
| Mean corpuscular volume, fL | 90 (87-95) | 88 (85-91) | 0.001 |
| Red blood cell count, x106/µL | 4.380 ± 0.842 | 4.536 ± 0.563 | 0.267 |
| Mean platelet volume, fL | 10.5 (9.4-11.6) | 9.7 (8.9-10.5) | 0.002 |
| RDW, % | 14.5 (13.6-15.7) | 13.4 (12.7-14.0) | <0.001 |

Normally distributed data are presented as mean ± standard deviation and non-normally distributed data are presented as median with interquartile ranges (25th-75th percentiles). Abbreviations: COPD, chronic obstructive pulmonary disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol, MHR, monocyte-to-high-density lipoprotein cholesterol ratio; RDW, red blood cell distribution width.

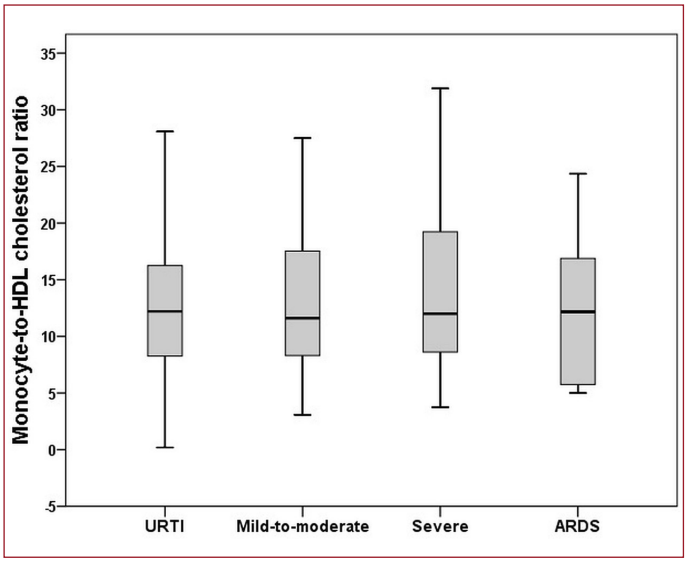


**Figure 2.** Comparison of monocyte-to-high-density lipoprotein cholesterol ratio according to the clinical presentation of COVID-19 patients at admission to the hospital (URTI, Upper respiratory tract infection; ARDS, Acute respiratory distress syndrome).

**Table 3. The correlation of monocyte-to-high-density lipoprotein cholesterol ratio with clinical and laboratory parameters.**

| Parameters | Spearman's Rank Correlation Coefficient | p-value |
|---|---|---|
| Age | 0.18 | 0.010 |
| Ferritin | 0.16 | 0.033 |
| Uric acid | 0.22 | 0.003 |
| Urea | 0.19 | 0.009 |
| Creatinine | 0.18 | 0.011 |

In the univariate regression analysis, the MHR was found not to predict survival (OR 1.013, 95% CI 0.996-1.030, p=0.132). According to the regression analysis model, age, cardiovascular disease, chronic kidney disease, C-reactive protein, D-dimer, lactate dehydrogenase, troponin-I, uric acid, urea, leukocyte count, neutrophil count, lymphocyte count, neutrophil-to-lymphocyte ratio, lymphocyte-to-monocyte-ratio, mean corpuscular volume and red blood cell distribution width were the most significant factors in predicting survival (p<0.001). Univariate logistic regression analyses for the determinants of in-hospital mortality are shown in **Table 4**.

ROC analysis revealed that MHR showed a weak prediction of mortality (AUC, 0.602; 95% CI 0.500-0.703, p=0.046). At a threshold of 16.83 determined by maximizing the Youden index, MHR predicts mortality with 46% sensitivity and 76% specificity (**Figure 3**). The Kaplan-Meier survival curves and log-rank tests showed that patients with higher MHR (>16.83) had the same survival rate as patients with lower MHR (<16.83) (divided according to the best threshold) (p=0.054) (**Figure 4**).

**Table 4. Univariate logistic regression analyses for the determinants of mortality.**

| Parameters | Odds Ratio | 95% CI | p value |
|---|---|---|---|
| Clinical Parameters | | | |
| Female gender | 0.638 | 0.318-1.282 | 0.207 |
| Age | 1.107 | 1.069-1.146 | <0.001 |
| Hospital stay | 1.048 | 1.007-1.091 | 0.021 |
| Smoking | 0.508 | 0.216-1.193 | 0.120 |
| Hypertension | 1.851 | 0.918-3.731 | 0.085 |
| Diabetes mellitus | 1.101 | 0.549-2.205 | 0.787 |
| Chronic obstructive pulmonary disease | 1.385 | 0.591-3.244 | 0.454 |
| Cardiovascular disease | 7.480 | 2.918-19.174 | <0.001 |
| Chronic kidney disease | 23.369 | 6.252-87.355 | <0.001 |
| Laboratory Parameters | | | |
| C-reactive protein | 1.017 | 1.011-1.023 | <0.001 |
| Procalcitonin | 20.179 | 2.735-148.885 | 0.003 |
| Ferritin | 1.003 | 1.002-1.004 | <0.001 |
| D-dimer | 1.001 | 1.001-1.002 | <0.001 |
| Lactate | 1.602 | 1.108-2.315 | 0.012 |
| Lactate dehydrogenase | 1.007 | 1.004-1.010 | <0.001 |
| Fibrinogen | 1.003 | 1.001-1.006 | 0.006 |
| Troponin-I | 1.040 | 1.019-1.062 | <0.001 |
| Total cholesterol | 0.998 | 0.990-1.006 | 0.630 |
| High-density lipoprotein cholesterol | 0.959 | 0.920-0.999 | 0.043 |
| Low-density lipoprotein cholesterol | 0.994 | 0.984-1.004 | 0.239 |
| Triglycerides | 1.003 | 0.999-1.007 | 0.116 |
| Uric acid | 1.591 | 1.311-1.929 | <0.001 |
| Urea | 1.038 | 1.024-1.053 | <0.001 |
| Creatinine | 1.674 | 1.238-2.264 | 0.001 |
| Aspartate transaminase | 1.018 | 1.003-1.033 | 0.016 |
| Alanine transaminase | 0.992 | 0.971-1.014 | 0.471 |
| Leukocyte count | 1.000 | 1.000-1.000 | <0.001 |
| Neutrophil count | 1.000 | 1.000-1.001 | <0.001 |
| Lymphocyte count | 0.998 | 0.998-0.999 | <0.001 |
| Neutrophil-to-lymphocyte ratio | 1.390 | 1.231-1.570 | <0.001 |
| Platelet count | 0.996 | 0.990-1.001 | 0.135 |
| Platelet-to-lymphocyte ratio | 1.005 | 1.001-1.008 | 0.007 |
| Monocyte count | 1.000 | 1.000-1.001 | 0.160 |
| Lymphocyte-to-monocyte-ratio | 0.567 | 0.439-0.733 | <0.001 |
| MHR | 1.013 | 0.996-1.030 | 0.132 |
| Hemoglobin | 0.887 | 0.750-1.049 | 0.161 |
| Mean corpuscular volume | 1.141 | 1.060-1.228 | <0.001 |
| Red blood cell count | 0.670 | 0.382-1.174 | 0.161 |
| Mean platelet volume | 1.620 | 1.203-2.181 | 0.001 |
| Red blood cell distribution width | 1.591 | 1.277-1.982 | <0.001 |

Abbreviations: CI, confidence interval; MHR, monocyte-to-high-density lipoprotein cholesterol ratio.

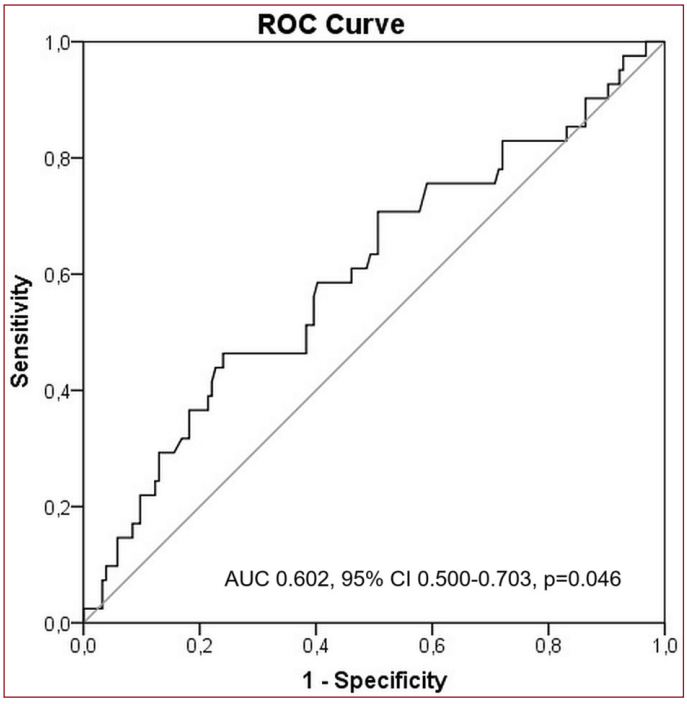


**Figure 3.** Receiver-operating characteristic (ROC) curve analysis of monocyte-to-high-density lipoprotein cholesterol ratio for predicting mortality. Receiver-operating characteristic (ROC) curve for the predictive ability of monocyte-to-high-density lipoprotein cholesterol ratio for in-hospital death of patients with COVID-19.

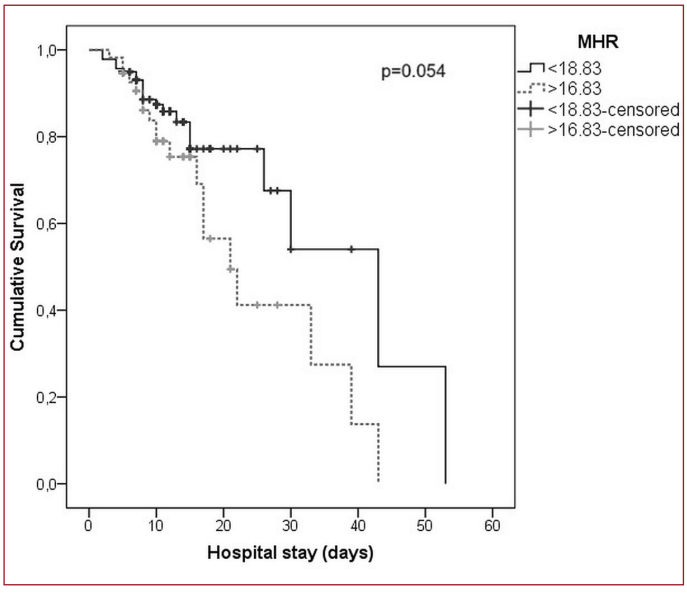


**Figure 4.** Kaplan-Meier survival curves according to MHR optimal cutoff value. A log-rank test was used to evaluate the difference between groups (MHR, monocyte-to-high-density lipoprotein cholesterol ratio).

## DISCUSSION

The present study has revealed the relationship between MHR and prognostic markers, as well as the value of MHR in predicting in-hospital mortality in patients hospitalized with a diagnosis of COVID-19. While MHR shows a weak correlation with some of the prognostic biomarkers in COVID-19, it appears to be not useful in predicting in-hospital mortality in COVID-19 patients. The results of previous studies on the prognostic value of MHR in COVID-19 are contradictory. Gunay-Polatkan et al. showed that MHR does not predict in-hospital mortality in COVID-19.[18] In another study, Argun et al. showed that MHR predicts the severity of COVID-19 disease and patient outcomes.[19] However, as we found in our study, MHR was found to be high in the non-survival group in these studies.[18,19]

In SARS-COV-2 infection, an immune response develops through the immune system and various cytokines, mainly interferons, are released to control the infection.[20] In some cases, uncontrolled immune response and excessive release of cytokines trigger a cytokine storm, leading to the development of multiple organ damage, especially in the respiratory system, and consequently, death.[20] Therefore, evaluation of certain clinical features and laboratory findings has come to the fore so that clinicians may be able to predict the clinical severity and prognosis of COVID-19. Several lab parameters have been evaluated to determine the severity of COVID-19 in studies conducted to date.[21]

MHR has been investigated in several conditions such as cardiovascular disease, polycystic ovary syndrome, chronic obstructive pulmonary disease, psoriasis, pulmonary thromboembolism, and aggressive periodontitis.[22-25] MHR represents a new marker indicating inflammation and oxidative stress, and it is closely linked to the occurrence and prognosis of specific cardiovascular conditions.[14,26,27] Efe et al. demonstrated that the MHR independently predicted mortality in patients with acute pulmonary embolism.[26] Oylumlu et al. demonstrated that increased MHR was a significant and independent predictor of in-hospital and long-term mortality in patients with acute coronary syndrome.[27]

Monocytes are immune system cells that play a role in the inflammatory response, phagocytosis, antigen presentation, and various immune functions.[28] In COVID-19, SARS-CoV-2 infects the pulmonary epithelium and capillary endothelial cells, stimulates the inflammatory response, and triggers a monocyte and neutrophil influx.[20] Tumor necrosis factor-alpha and interleukin 1 and 6, released from monocytes and other macrophages, enhance the inflammatory response. There are conflicting results concerning monocyte count in COVID-19. While some studies have reported an increased monocyte count, others showed no significant changes and a few reported a decrease in the number of monocytes.[29] In our study, although the monocyte count increased in the non-survivor group compared to the survivor group, it did not reach statistical significance. In studies conducted on patients with COVID-19, monocyte count was not found to be valuable in distinguishing patients who test positive and those who test negative for COVID-19.[30] Furthermore, it has been shown that monocyte count does not provide valuable data for predicting the prognosis of COVID-19 at the time of admission or hospitalization.[29] This controversy shows that

alteration in monocytes is still open to debate and this issue remains to be extensively discovered.

It is widely recognized that viral infections lead to alterations in plasma lipid levels.[31] Infections typically lead to decreased levels of total cholesterol, LDL cholesterol, and HDL cholesterol, along with either elevated or normal triglyceride levels. Generally, the changes in blood lipid levels correlate with the severity of the underlying infection.[32] That is to say, the more severe the infection, the more severe the changes in lipid and lipoprotein levels.[31-33] Numerous studies have been conducted to investigate cholesterol levels in COVID-19 patients. A decrease has been observed in total cholesterol, triglyceride, LDL cholesterol, and HDL cholesterol levels in patients with COVID-19 compared to healthy individuals.[34,35] HDL cholesterol concentration was found to be negatively correlated with C-reactive protein and positively correlated with lymphocytes.[35] Decreased serum apolipoprotein A-1 and HDL cholesterol levels are predictors for severe disease and in-hospital mortality in COVID-19 patients.[33-35] In our study, total cholesterol and HDL-cholesterol levels were lower and triglyceride levels were higher in patients with a fatal outcome compared to survivors, and a relationship between HDL-cholesterol and in-hospital mortality has been demonstrated. The decrease in the immunomodulatory, antithrombotic, and antioxidant effects of HDL cholesterol due to low HDL cholesterol levels may contribute to the poor prognosis observed in COVID-19.

Age, current smoking, body mass index, alcohol intake, triglyceride, and LDL cholesterol level have significant impacts on HDL cholesterol level.[36] Women have higher levels of HDL cholesterol than men.[37] In our study, we found that HDL cholesterol levels were lower, and monocyte counts and MHR levels were higher in men than in women. In COVID-19, factors associated with in-hospital mortality are increasing age, male sex, and major comorbidities.[38] Older age, smoking, and overweight or obesity are associated with lower HDL-C levels.[36] We found a weak negative correlation between HDL cholesterol and age in our study. This negative correlation between HDL cholesterol and age is reflected as a positive correlation between MHR and age. Age was also found to be one of the predictors of mortality in our study but a similar result was not found in gender. HDL cholesterol levels were significantly lower in smokers than in nonsmokers. However, smoking was not one of the predictors of mortality in our study. There are contradictory reports about the effect of smoking on COVID-19 infections. A large meta-analysis of over 17,278,392 COVID-19-infected adults showed a lower incidence of infection in smokers.[39] However, several studies showed adverse effects of smoking on COVID-19 outcomes.[40] We speculate that the complex effect of smoking on COVID-19 disease may account for our result.

Older age, presence of chronic kidney disease, and increased ferritin levels are poor prognostic markers in COVID-19 patients.[41] In a retrospective study by Zheng et al., uric acid levels were found to be high in COVID-19 non-survivors, and serum uric acid level was positively correlated with inflammatory markers.[42] The researchers proposed that uric acid released from damaged cells might act as a danger signal, intensifying the hyperinflammatory response in severe COVID-19 cases, and that lowering uric acid levels through therapy could be beneficial for these patients.[42] In our study, patients with a fatal outcome were older than survivors, and similar to previous study results, the rate of chronic kidney disease was higher, and higher ferritin and uric acid levels were observed in non-survivors compared to survivors. We found weak but significant and positive correlations between MHR and age, ferritin, uric acid, urea, and creatinine.

Our study has several limitations. The main limitation is the small study population, which may have limited our ability to detect the predictive value of MHR for disease severity and in-hospital mortality in COVID-19. Furthermore, due to the small study population, we were unable to divide the patients into subgroups and further investigate potential confounding factors influencing our results such as age, cardiovascular disease, and chronic kidney disease. Another limitation is the study's retrospective design. As a result, we were unable to obtain parameters that could affect study results, such as the heights and weights of patients.

## CONCLUSION

Although MHR is higher in in-patient COVID-19 cases with a fatal outcome compared to survivors, it does not predict the severity of disease or in-hospital mortality. However, MHR shows a positive correlation with age, ferritin, uric acid, urea, and creatinine levels, which have been previously reported to be prognostic indicators in COVID-19 patients.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was carried out with the permission of Kütahya Health Sciences University, Clinical Research Ethics Committee (Date: 17 September 2020, Decision No: 2020/14-18).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article / Orijinal Araştırma

# Work-Family Conflict Among Resident Physicians: A Comparative Analysis of Surgical and Internal Medicine Specialties

## Asistan Hekimler Arasında İş-Aile Çatışması: Cerrahi ve Dahili Tıp Uzmanlıklarının Karşılaştırmalı Bir Analizi

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## Abstract

**Aims**: To investigate whether there is a difference in work-family conflict between surgical and internal medicine residents and to determine the factors associated with work-family conflict

**Material and Method**: A cross-sectional, questionnaire-based survey study was conducted with 443 resident physicians working at a university hospital. A form about demographic data and a Turkish version of the Work-Family Conflict Inventory (WFCI) were used to gather data during in-person interviews.

**Results**: Three-hundred-forty-eight residents responded (76.8%). Weekly working time was significantly more in surgical medical sciences (SMS) residents than in internal medicine sciences (IMS) residents (62.3±13.8 vs 53.2±13.6 hours respectively, p<0.001). The mean WFCI scores of the SMS and IMS residents were 19.5±4.3 and 17.9±5.1, respectively (p=0.002). Working hours and the number of shifts were associated with increased WFCI scores. Residents with incomes less than expenses had higher WFCI scores. Satisfaction, including institution, salary, and area of specialization, was negatively associated with the WFCI scores. Working as an SMS resident was found to be related to higher conflict scores than being an IMS resident. Income status, weekly working hours, and institution satisfaction were significant independent predictors of WFCI scores. Being an SMS or IMS resident did not come out to be a significant predictor of work-family conflict.

**Conclusion**: WFCI scores are very high in resident physicians. The findings highlight the urgent need to address this issue through a multi-faceted approach that includes reducing working hours, improving income levels, enhancing institutional satisfaction, and providing support and resources to help residents balance work and family responsibilities.

**Keywords**: Work-family conflict, resident physicians, surgical medical sciences, internal medicine sciences

## Öz

**Amaç**: Cerrahi ve dahiliye asistanı doktorlar arasında iş-aile çatışması açısından farklılık olup olmadığını araştırmak ve iş-aile çatışmasıyla ilişkili faktörleri belirlemek.

**Gereç ve Yöntem**: Bir üniversite hastanesinde görev yapan 443 asistan hekim ile kesitsel, ankete dayalı bir çalışma yapıldı. Yüz yüze görüşmelerde veri toplamak amacıyla demografik verileri içeren bir form ve İş-Aile Çatışmaları Envanteri'nin (İAÇE) Türkçe versiyonu kullanıldı.

**Bulgular**: Üç yüz kırk sekiz asistan doktor yanıt verdi (%76,8). Haftalık çalışma süresi cerrahi tıp bilimleri (CTB) asistanlarında dahili tıp bilimleri (DTB) asistanlarına göre anlamlı olarak daha fazlaydı (sırasıyla 62,3±13,8 ve 53,2±13,6 saat, p<0,001). CTB ve DTB asistanlarının ortalama İAÇE skorları sırasıyla 19,5±4,3 ve 17,9±5,1 idi (p=0,002). Çalışma saatleri ve vardiya sayısı artmış İAÇE skorları ile ilişkili bulundu. Gelirleri giderlerinden az olan asistanların İAÇE puanları daha yüksekti. Kurum, maaş ve uzmanlık alanı da dahil olmak üzere memnuniyet, İAÇE skorlarıyla ters yönde ilişkiliydi. CTB asistanı olarak çalışmanın, DTB asistanı olmaktan daha yüksek çatışma skorları ile ilişkili olduğu bulundu. Gelir durumu, haftalık çalışma saatleri ve kurum memnuniyeti İAÇE skoru için anlamlı bağımsız belirleyicilerdi. CTB veya DTB asistanı olmanın, iş-aile çatışması için anlamlı bir belirleyici olmadığı bulundu.

**Sonuç**: Asistan hekimlerde İAÇE skorları oldukça yüksek olarak bulundu. Bulgular, çalışma saatlerinin azaltılması, gelir düzeylerinin iyileştirilmesi, kurumsal memnuniyetin arttırılması ve asistan hekimlerin iş ve aile sorumlulukları arasında denge kurmasına yardımcı olacak destek ve kaynakların sağlanmasını içeren çok yönlü bir yaklaşımla bu konunun acilen ele alınması ihtiyacını vurgulamaktadır.

**Anahtar Kelimeler**: İş-aile çatışması, asistan doktor, cerrahi tıp bilimleri, dahili tıp bilimleri,

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## INTRODUCTION

The most challenging and stressful period in medical education is the residency period. In this period, which coincides with the period of starting a family and having children, the stress of work, long working hours and the need to meet high expectations may prevent resident doctors from fulfilling their responsibilities to their families.[1] This incompatibility between work and family decreases both work success and makes it difficult to establish a healthy family relationship in this group, which is in the most important period of medical education, thus causing psychosocial wear and tear and burnout.

According to the Scarcity hypothesis, a person's energy is limited and when there are multiple obligations, he/she has to sacrifice other obligations in order to fulfill some obligations.[2,3] This ultimately leads to stress and a conflict between roles. Work-Family Conflict (WFC) is defined as an interrole conflict where work and family demands are incompatible.[4] This conflict occurs when the obligations and expectations of work negatively affect family life. The opposite, that is, it is also possible for family responsibilities to interfere with one's work, and this is also called family-work conflict.[4] But work-family conflict is more common. This is because family obligations are more flexible, whereas work obligations are more stringent.[5,6]

In Türkiye, no research on work-family conflict has been conducted on physicians who are in their residency period in medical education. However, in recent years, the tendency to go abroad has started to increase especially among young doctors.[7] The desire to continue their professional life abroad after graduating from medical school or during or immediately after residency is attributed to many factors. These include the socioeconomic situation of the country, increased workload, inadequate income, exposure to violence while doing their job, and psychosocial stress, including work-family conflict.[7]

In recent years, significant differences in stress, pressure and workload have been reported between medical specialties. There are studies showing that work stress is significantly higher in physicians working in surgical specialties.[8,9] However, there has not been sufficient research on residents so far. The aim of this study is to investigate whether there is a difference in work-family conflict between surgical and internal medicine residents and to determine the factors associated with work-family conflict.

## MATERIAL AND METHOD

This is a cross-sectional, questionnaire-based survey study. Data were obtained from resident physicians working at Mersin University Hospital between December 1, 2023, and January 31, 2024. The sole requirements for inclusion were consenting to participate and being employed as a resident physician at Mersin University Hospital. All of the 443 residents who were actively working in a surgical or internal medicine specialty were invited to take part. A form about demographic data and a Turkish version of the Work-Family Conflict Inventory (WFCI) were used to gather data during in-person interviews with two investigators (EO and HY). The institution's ethical committee approved the study with the number 2024/870.

Netemeyer et al. created the original WFCI.[10] The survey is divided into two subscales: family-work conflict (FWCI) and work-family conflict (WFCI). Each subscale has five items and is scored on a 5-point Likert scale that ranges from "strongly disagree" to "strongly agree." In this study, just the work-family conflict domain was used. Five is the lowest score on the WFC scale, and 25 is the highest. The values of the WFC scales are determined by adding the answers to the five items. Higher scores represent more conflict. Efeoglu et al. developed and verified the Turkish version, which has a Cronbach alpha value of 0.88 for WFCI.[11] In the current investigation, the Cronbach alpha value for the WFCI was calculated as 0.910.

### Statistical Analysis

Statistical analysis was carried out with SPSS V21. The data's normalcy was examined using histograms and the Kolmogorov-Smirnov test. Percentages, means, and standard deviations were used to express descriptive data. For comparisons, chi-square and t-tests were applied as needed. Bivariate correlation analysis was performed using Pearson correlation coefficients to identify the variables associated with the WFCI scores. The significant variables were subjected to linear regression analysis with the enter method to find the independent predictors. A p-value of less than 0.05 was deemed significant.

## RESULTS

Three hundred forty-eight physicians working as surgical and internal medical sciences residents responded (n:348/453; response rate: 76.8%). **Table 1** depicts the comparison of the sociodemographic characteristics of the responding residents. The residents working in surgical medical sciences (SMS) were significantly older than those of internal medicine sciences (IMS) (30.7±4.1 vs. 29.1±2.5 years old, respectively, $p<0.001$). There was a significant male gender dominance in SMS and female gender dominance in IMS (**Table 1**). More SMS residents were married than IMS residents; however, this was not statistically significant. 44.3% of the SMS residents had at least one child, significantly higher than the 30% of IMS residents. Weekly working time was significantly more in SMS than IMS residents (62.3±13.8 vs 53.2±13.6 hours respectively, <0.001). Although insignificant, SMS residents had more night shifts during weekdays in a month (3.9±1.3

vs 3.6±1.7 days; p= 0.061). The number of shifts on the weekends did not differ between the groups. The income was reported to be less than the expenses in 43.9% and 44.5% of the SMS and IMS residents, and satisfaction with the salary was very low in both groups, 2.9% and 1.9%, respectively (**Table 1**). Institution satisfaction and satisfaction in the area of specialization were also similar (**Table 1**). None of these parameters showed a significant difference. The mean WFCI score of the SMS residents was 19.5±4.3, significantly higher than the 17.9±5.1 of the IMS residents (p=0.002) (**Table 1**).

**Table 1. Comparison of demographic characteristics of the resident physicians of Internal Medicine Sciences (IMS) and Surgical Medical sciences (SMS)**

| | IMS (N:209) | SMS (139) | p |
|---|---|---|---|
| Age | 29.1±2.5 | 30.7±4.1 | <0.001 |
| Gender | | | |
| Male | 87 (41.6) | 97 (69.8) | <0.001 |
| Female | 122 (58.4) | 42 (30.2) | |
| Marital status | | | 0.067 |
| Single | 108 (51.7) | 87 (62.6) | |
| Married | 100 (47.8) | 50 (36) | |
| Divorced | 1 (0.5) | 2 (1.4) | |
| Having children | | | 0.025 |
| No | 76 (70) | 50 (55.7) | |
| Yes | 33 (30) | 39 (44.3) | |
| Owing a house | | | 0.150 |
| Own a house | 63 (30.1) | 34 (24.5) | |
| Rent a house | 146 (69.9) | 105 (75.5) | |
| Spouse's employment status | | | 0.497 |
| Working | 91 (79.8) | 72 (51.8) | |
| Not working | 23 (20.2) | 17 (12.2) | |
| Weekly working hours | 53.2±13.6 | 62.3±13.8 | <0.001 |
| Number of night shifts during weekdays in a month | 3.6±1.7 | 3.9±1.3 | 0.061 |
| Number of shifts on the weekends in a month | 2.0±0.9 | 1.9±0.7 | 0.207 |
| Income status | | | 0.988 |
| Income less than expenses | 93(44.5) | 61 (43.9) | |
| Income just covers expenses | 78 (37.3) | 53 (38.1) | |
| Income more than expenses | 38 (18.2) | 25 (18) | |
| Institution satisfaction | | | 0.120 |
| Not satisfied | 64 (30.6) | 46 (33.1) | |
| Neither satisfied nor dissatisfied | 76 (36.4) | 61 (43.9) | |
| Satisfied | 69 (33) | 32 (23) | |
| Satisfaction of the area of specialization | | | 0.170 |
| Not satisfied | 45 (21.5) | 41 (29.5) | |
| Neither satisfied nor dissatisfied | 74 (35.4) | 39 (28.1) | |
| Satisfied | 90 (43.1) | 59 (42.4) | |
| Satisfaction with the salary | | | 0.171 |
| Not satisfied | 181 (86.6) | 127 (91.4) | |
| Neither satisfied nor dissatisfied | 24 (11.5) | 8 (5.8) | |
| Satisfied | 4 (1.9) | 4 (2.9) | |
| Work-family conflict scores | 17.9±5.1 | 19.5±4.3 | 0.002 |

IMS: Internal medicine sciences, SMS: Surgical medical sciences

Correlation analysis was used to analyze factors associated with WFCI scores. **Table 2** shows the parameters found to be significantly correlated. Being married was associated with higher WFCI scores. Working hours and the number of shifts, either during the week or at the weekends, were associated with increased work-family conflict scores. Residents with incomes less than expenses had higher WFCI scores. Satisfaction, including institution, salary, and area of specialization, was negatively associated with the WFCI scores, indicating that more conflict is experienced when there is less satisfaction. Working as an SMS resident was found to be related to higher conflict scores than being an IMS resident.

**Table 2. Factors significantly correlated with the work-family conflict scores**

| Variables | Correlation coefficient | p |
|---|---|---|
| Marital Status (married:1, single:2, divorced:3) | -0.128 | 0.014 |
| Weekly working hours | 0.408 | <0.001 |
| Number of shifts except for weekends per month | 0.231 | <0.001 |
| Number of shifts in the weekends in a month | 0.203 | <0.001 |
| Income status (I<E:1, I~E: 2, I>E:3) | -0.266 | <0.001 |
| Institution satisfaction (NS:1, NS/DS: 2, S:3) | -0.252 | <0.001 |
| Satisfaction of the area of specialization (NS:1, NS/DS: 2, S:3) | -0.320 | <0.001 |
| Salary satisfaction (NS:1, NS/DS: 2, S:3) | -0.134 | 0.01 |
| Residency of internal/surgical medical sciences (IMS:1, SMS:2) | 0.160 | 0.003 |

I<E: Income less than expenses, I~E: Income just covers expenses, I>E: Income more than expenses, NS: not satisfied, NS/DS: neither satisfied nor dissatisfied, S: satisfied

Regression analysis was performed to determine the independent predictors of WFCI scores (**Table 3**). Income status, weekly working hours, and institution satisfaction were found to be significant independent predictors of WFCI scores. Being an SMS or IMS resident did not come out to be a significant predictor of work-family conflict (beta: 0.033, t: 0.605, p: 0.546, 95% CI: -0.708 and 1.337).

**Table 3. Regression analysis for the factors associated with the work-family conflict scores**

| | Beta | t | p | 95% CI |
|---|---|---|---|---|
| Income status | -0.149 | -2.697 | 0.007 | -1.604 – -0.25 |
| Weekly working hours | 0.258 | 4.061 | <0.001 | 0.044 – 0.127 |
| Institution satisfaction | -0.163 | -2.61 | 0.01 | -1.738 – -0.244 |

CI: Confidence Interval

## DISCUSSION

The present study aimed to investigate the presence of work-family conflict (WFC) among resident physicians and identify the factors associated with it. The study revealed that WFC is a prevalent issue among resident physicians, particularly those in surgical medical sciences (SMS). The findings also highlighted that weekly working hours, income status, and institutional satisfaction are independent predictors of WFC. The mean WFCI score in this study was considerably higher than those reported in studies involving other healthcare professionals and non-healthcare workers, emphasizing the severity of WFC among resident physicians.

The higher WFCI scores observed in SMS residents compared to internal medicine sciences (IMS) residents might be attributed to the demanding nature of surgical specialties, characterized by higher occupational distress and quantitative working demands.[12,13] The greater number of job tasks performed by surgeons compared to other specialties could contribute to increased WFC.[14] The significant association between being married and higher WFCI scores aligns with previous research indicating that married individuals, especially those with children, often face challenges in balancing work and family responsibilities.[9] The positive correlation between working hours and the number of shifts with WFCI scores underscores the detrimental impact of long working hours and frequent shifts on family life. The negative association between income status and WFCI scores suggests that financial strain can exacerbate WFC, as individuals struggling to meet their financial needs may experience heightened stress and conflict between work and family demands.

The negative association between institutional satisfaction and WFCI scores highlights the importance of a supportive and satisfying work environment in mitigating WFC.[15] When residents are dissatisfied with their institution, they may experience decreased motivation and increased stress, which can spill over into their family lives. Factors contributing to institutional dissatisfaction, such as lack of support from supervisors, inadequate resources, or a hostile work environment, can create a sense of frustration and disillusionment, making it challenging for residents to maintain a healthy work-life balance. Similarly, the negative association between satisfaction with the area of specialization and WFCI scores emphasizes the significance of aligning residents' career choices with their interests and values. When residents are dissatisfied with their chosen specialty, they may experience frustration and decreased well-being, potentially leading to WFC. This dissatisfaction may stem from a mismatch between their expectations and the reality of the specialty, a lack of interest in the field, or a perceived lack of autonomy and control over their work.

The study's findings have several important implications for addressing WFC among resident physicians. Firstly, interventions aimed at reducing working hours and improving working conditions could be effective in mitigating WFC. This could involve implementing stricter regulations on resident work hours, promoting a culture of work-life balance, and providing adequate support and resources to help residents manage their workload effectively.[16] Secondly, addressing the financial concerns of resident physicians is crucial. Increasing their income levels, providing financial counseling and support, and offering loan repayment assistance programs could alleviate financial stress and reduce WFC. Thirdly, enhancing institutional satisfaction is essential. Creating a supportive and positive work environment, fostering a culture of respect and appreciation, and providing opportunities for professional development and growth could improve residents' overall satisfaction and reduce WFC. Additionally, providing support and resources to help residents balance work and family responsibilities, such as flexible scheduling, childcare assistance, and parental leave policies, could be instrumental in reducing WFC.[17,18] Moreover, promoting career counseling and mentorship programs could help residents make informed choices about their specialties, potentially leading to increased satisfaction and reduced WFC.[19,20]

The study's limitations include its cross-sectional design, which precludes causal inferences. Longitudinal studies are needed to examine the temporal relationship between the identified factors and WFC. Additionally, the study relied on self-reported data, which may be subject to recall bias and social desirability bias. Future research could incorporate objective measures of WFC and utilize diverse samples to enhance the generalizability of the findings. Furthermore, future studies could explore the potential impact of other factors, such as personality traits, coping mechanisms, and social support networks, on the development and management of WFC among resident physicians.

## CONCLUSION

This study provides valuable insights into the prevalence and predictors of WFC among resident physicians. The findings highlight the urgent need to address this issue through a multi-faceted approach that includes reducing working hours, improving income levels, enhancing institutional satisfaction, and providing support and resources to help residents balance work and family responsibilities.[21-23] By implementing such interventions, we can foster a healthier and more sustainable work environment for resident physicians, ultimately benefiting both their personal well-being and the quality of patient care they provide. Healthcare institutions, policymakers, and educators must collaborate to create a supportive and empowering environment for resident physicians, enabling them to thrive both personally and professionally.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was obtained from Mersin University Clinical Research Ethics Committee (Date: 18.09.2024, Decision no: 2024/870).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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# Developing a Culturally-Responsive Training Program: Workplace Violence Against Physicians in Türkiye

## Kültüre Duyarlı Bir Eğitim Programı Geliştirme Süreci: Türkiye'de Hekimlere Yönelik İşyerinde Şiddet

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## Abstract

**Aim**: This paper outlines the development of a culturally responsive training program designed to equip Turkish physicians with the skills and knowledge necessary to effectively address workplace violence. In line with this objective, the paper provides a detailed report on how the training program was developed, based on the findings from four studies, and how it was implemented as a pilot program in a medical school in Türkiye.

**Material and Method**: This study employs a mixed-methods approach, drawing from four quantitative and qualitative studies: (1) semi-structured interviews with four Turkish physician-managers, (2) an online national survey of 136 healthcare workers, (3) a historical analysis of workplace violence incidents against physicians using Turkish online newspaper archives, and (4) insights gathered from a workshop with practitioners and professionals from the medical field.

**Results**: The findings from the four studies show that the training program, consisting of 17 interactive units, was specifically designed to integrate cultural sensitivity with empirical evidence to address the needs of Turkish physicians. Additionally, the program incorporates real-life scenarios, practical suggestions, and legislative guidelines, providing Turkish physicians with hands-on experience in managing and mitigating workplace violence. It addresses the specific challenges, and cultural dynamics present in Turkish hospital settings, ensuring that the content is both relevant and practical.

**Conclusion**: By considering the unique cultural context of Turkish healthcare environments, the training program enhances the ability of Turkish physicians to perform their duties safely and effectively. This culturally tailored approach is essential for ensuring the safety and well-being of healthcare professionals in Türkiye, making the training program both impactful and vital for mitigating workplace violence in this context.

**Keywords**: Workplace violence, physicians, Türkiye, training program, culturally responsive, healthcare.

## Öz

**Amaç**: Bu makale, Türk hekimlerinin işyeri şiddeti ile etkili bir şekilde başa çıkmaları için gerekli beceri ve bilgiyle donatmayı amaçlayan kültüre duyarlı bir eğitim programının geliştirilme sürecini sunmaktadır. Bu amaca uygun olarak, makale, araştırmanın temelinde yer alan dört çalışmanın bulgularına dayanarak bu eğitim programının nasıl geliştirildiğini ve Türkiye'deki bir tıp fakültesinde pilot program olarak nasıl uygulandığını ayrıntılı bir şekilde ortaya koymaktadır.

**Gereç ve Yöntem**: Bu çalışma, dört farklı nicel ve nitel çalışmaya dayalı karma yöntemli bir araştırmadır: (1) dört Türk hekim/yönetici ile yarı yapılandırılmış görüşmeler, (2) 136 sağlık çalışanının katıldığı çevrimiçi ulusal anket, (3) Türk çevrimiçi gazete arşivlerinden hekimlere karşı işlenen işyeri şiddeti olaylarının tarihsel çözümlemesi ve (4) tıp alanında çalışanlarla yapılan çalıştaydan elde edilen görüşlerin çözümlenmesi.

**Bulgular**: Bu dört çalışmadan elde edilen bulgular, 17 etkileşimli üniteden oluşan eğitim programının, Türk hekimlerinin ihtiyaçlarını karşılamak üzere kültüre duyarlı ve ampirik kanıtlara dayandırılmış şekilde özel olarak tasarlandığını göstermektedir. Ayrıca, eğitim programı gerçek hayat senaryoları, pratik öneriler ve yasal yönergeler içermekte olup Türk hekimlerine işyeri şiddeti ile baş etme ve şiddetin etkisini azaltma konusunda uygulamalı deneyim sunmaktadır. Eğitim program, Türkiye'deki sağlık kuruluşlarındaki zorlukları ve kültürel dinamikleri ele alarak program içeriğinin hem hekimler için uygulamalı hem de alanda örnek olmasını sağlamaktadır.

**Sonuç**: Türkiye'deki sağlık kuruluşlarının kültürel özellikleri dikkat ederek hazırlanan bu eğitim programı, Türk hekimlerinin görevlerini güvenli ve etkili bir şekilde yerine getirmeleri için bir platform yaratmaktadır. Kültürel açıdan uyarlanmış bu yaklaşım, Türkiye'deki sağlık çalışanlarının güvenliğini ve refahını sağlamada hayati önem taşıyarak, eğitim programını işyeri şiddetini azaltma bağlamında hem etkili hem de vazgeçilmez kılmaktadır.

**Anahtar Kelimeler**: İşyerinde şiddet, doktorlar, hekimler, eğitim programı, kültüre duyarlı, sağlık hizmeti.

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## INTRODUCTION

On July 21, 2017, around 1 am, a mother brought her 3-year-old son to the emergency department at the state hospital in Sapanca, Sakarya. The physician on duty was examining the child's throat using a wooden depressor when the child began to cry out in distress. Reacting to her child's cries, the mother violently attacked the physician. She grabbed the physician by the hair and dragged her across the examination room, causing significant disruption and distress within the emergency department. Due to the traumatic incident, the physician resigned from her position the following day, citing the violence she experienced as the reason for her departure.[1]

On May 2, 2023, two brothers assaulted a surgeon working at a teaching hospital in Nilüfer, Bursa. The brothers blamed the surgeon for their mother's death, which had occurred in the intensive care unit of the same hospital. The brothers, who had previously issued death threats against the surgeon, followed him as he was on his way home. They attacked him with a firearm, aiming to hold him accountable for their mother's demise. The surgeon sustained injuries and was treated in the same hospital where he worked. The two brothers were subsequently arrested and charged with planned assault.[2]

On January 5, 2023, a patient arrived approximately an hour late for his scheduled appointment at the internal medicine department in a state hospital in Elazığ. While the attending physician was examining another patient, the patient entered the examination room with his wife and initiated a heated argument about his appointment time. He demanded that the physician display his appointment time on the computer screen. When his demands were not immediately met, he became physically aggressive, striking the physician in the face and assaulting him multiple times.[3]

The news reports above are just common examples of widespread problem in Turkish healthcare system. Numerous sources have indicated that healthcare workers in Türkiye face a concerning extent of workplace violence. Important evidence of this is the official reports from the Turkish Ministry of Health, indicating a significant rise in reported cases of Beyaz Kod (a hospital emergency code used to alert security about violent incidents). According to the findings in the report, there were 101,984 instances of Beyaz Kod documented in 2021, a substantial increase from 46,274 cases in 2019.[4] The other formal evidence is the annual report by the Turkish Ministry of Health. The report in 2021 highlights the severity of the issue, recording 27,560 cases of workplace violence, including threats and assaults.[4]

Comprehensive surveys further illuminate the pervasive nature of workplace violence in the Turkish healthcare system. For example, a study conducted by Pınar et al., which included 12,944 healthcare workers in Türkiye, revealed that 44.7% of respondents experienced violence at work in 2012.[5] The study also found that 52.3% of these healthcare workers encountered at least one form of violence throughout their careers. Similarly, Ayrancı et al. reported that nearly half of healthcare workers in western Türkiye experienced verbal or physical violence at least once in their careers.[6] Biçkici found that 55% of healthcare providers working in a state hospital in Ankara were subjected to verbal or physical violence at work in 2002.[7] In another study, Er et al. revealed that 61.1% of healthcare workers in Zonguldak experienced workplace violence at least once during their professional lives.[8] Demiroğlu et al. further suggested that at least three-quarters of healthcare workers in Turkey would encounter some form of violence at least once in their careers.[9]

Serious cases of workplace violence against physicians in Türkiye have led to both formal and informal initiatives aimed at thorough examination and urgent intervention. A significant event that triggered these efforts was the murder of a cardiac surgeon in Gaziantep.[10] On April 17, 2012, a patient's relative visited the cardiac surgeon, aged 30, in his examination room in a state hospital in Gaziantep. The patient's relative, aged 17, holding the surgeon accountable for his grandfather's death (aged 85 and diagnosed with cancer), who had been lost in the operation ten days earlier, stabbed the surgeon in his chest while he was having his lunch break. Later in the investigation, the murder was claimed to be a revenge for his grandfather's death, and he was sentenced to 24 years imprisonment.[11] On May 29, 2015, another alarming incident occurred when a surgeon was shot three times by a patient in a hospital corridor in Samsun.[12] On March 29, 2017, a retired policeman, upset over his wife's discharge, shot a physician in the abdomen in his office at a state clinic in Aksaray.[13] On July 6, 2022, a cardiologist was fatally shot by a patient's relative in a state hospital in Konya.[14] In 1988, a surgeon was killed by a patient's relative in Istanbul. In 2005, another surgeon was shot ten times at work in Istanbul. In 2008, a pulmonologist was murdered by his patient in Giresun. In 2015, an OB-GYN specialist was stabbed by a patient in Samsun. The violence continued in 2017 with the shooting of the chief manager of a medical school in Elazığ, and in 2018, a psychiatrist was shot by a patient in Istanbul.[15]

These serious cases of violence and studies collectively highlight the critical issue of workplace violence in the Turkish healthcare sector, emphasizing the urgent need for comprehensive measures to protect healthcare workers and ensure their safety and wellbeing. This ongoing threat not only affects the mental and physical health of medical professionals but also undermines the overall efficiency and quality of healthcare services in the country.[16] Addressing this alarming issue requires a multi-faceted approach, including stricter enforcement of laws, increased security measures in healthcare facilities, and enhanced support systems for victims of workplace violence. Finding its main interest in addressing this alarming threat, the project,

which this paper reports here in detail, aimed to develop a training program to provide healthcare workers in Türkiye with the tools and skills to recognize, prevent, and respond to workplace violence, thereby improving the overall healthcare environment. Also, because the training program was designed particularly for Turkish healthcare workers, the curriculum design was structured to emphasize the cultural responsiveness and practical applications specifically tailored to Turkish healthcare settings.

This paper reports the development of this training program, with a focus on demonstrating how cultural elements of workplace violence were embedded into the training program. First, the foundation of the training program will be outlined. The foundation here particularly refers to the needs assessment stage. It focused on exploring in-detail how workplace violence took place in the hospitals, understanding how the culture played a role in Turkish healthcare settings, and determining what skills and tools Turkish healthcare workers need to recognize, prevent, and respond to workplace violence. Three key needs assessment studies were carried out to build this foundation: (1) Semi-structured interviews with Turkish physicians, (2) the online national survey with 136 healthcare workers in Türkiye, and (3) the historical analysis of workplace violence against the physicians in Turkish online newspaper archives.

The paper then explains how these findings were translated into a set of learning objectives. This stage is essentially based on the detailed discussions from the workshop, centering on the significant role the culture played in shaping workplace violence against Turkish healthcare workers. It also covers how healthcare workers can effectively respond to violence by considering the cultural characteristics unique to the Turkish healthcare system. The final sections of the paper describe the implementation of the training program and provide notes on the evaluation process. The implementation phase details the methods and strategies used to deliver the training, while the evaluation process focuses on the plan to assess the program's effectiveness and impact on reducing workplace violence and improving the safety and wellbeing of healthcare workers in Türkiye.

### Ethical considerations

It is also important to note that the researcher obtained ethical approval from the local research ethics committee, ensuring adherence to established ethical guidelines throughout the study. Research ethics approval for this study was granted by the Research Ethics Committee at Çanakkale Onsekiz Mart University on 25.08.2022 (No 15/25). Prior to the commencement of interviews, survey and workshop, the participants provided informed consent, affirming their voluntary participation, and understanding of the study's objectives and procedures. Additionally, they were explicitly informed about the audio recording of interviews, fostering transparency and ensuring their awareness of the data collection process.

## MATERIAL AND METHOD

Developing a culturally-responsive training program to address workplace violence against physicians in Türkiye requires a comprehensive theoretical framework. This framework integrates key elements of curriculum design, the basic characteristics of workplace violence in healthcare settings, and the distinctive cultural and professional dynamics of Turkish healthcare settings. The initial step in developing the training program thus involves identifying the specific types and causes of workplace violence faced by physicians in Türkiye. To achieve this, the project gathered comprehensive data through three methods. The project first engaged four healthcare professionals, working also managers, in semi-structured interviews to gain in-depth and thorough insights into their personal experiences and perceptions of workplace violence. These interviews provided a deeper understanding of the contexts and triggers of violent incidents. It was followed by an online national survey. The project conducted an online nationwide survey of physicians to collect quantitative and qualitative data on the prevalence and types of workplace violence they experience. It helped to understand the scope and common characteristics of the issue. Finally, the project collected historical documents and records on the development of workplace violence within the Turkish healthcare system. This analysis offered a contextual background, highlighting trends and systemic issues that contribute to the current state of workplace violence. As a result, this study employed a mixed-methods approach, drawing from four quantitative and qualitative studies.

### Semi-structured interviews

The first study involved in-depth interviews with four manager/physicians working in Turkish healthcare settings. The semi-structured interviews were conducted to explore participants' experiences, perceptions, and insights regarding workplace violence against physicians. The researcher used criterion (purposive) sampling and personal connections to recruit four participants who met the following criteria: (1) working as a hospital physician, (2) having managerial experience in a healthcare institution, and (3) possessing at least 25 years of work experience. The study took place in a town with three hospitals—a state, teaching, and private hospital—limiting the pool of eligible participants. Of the six physicians contacted, two declined to participate due to their demanding administrative responsibilities.[17]

All four physician-managers, residing in a small town in northwest Türkiye, were senior, married male medical experts with over 30 years of experience. Their careers included work across Türkiye and internationally. Participant A, an ENT specialist, practiced at a private hospital after serving in the navy. Participant B, a surgical oncologist, was the dean of a medical school. Participant C, an OB-GYN specialist, led the OB-GYN department in a teaching hospital. Participant D, the chief physician of a teaching hospital, specialized in anesthesiology and had managed the hospital for four years.[17]

The research involved two rounds of in-person interviews conducted between November and December 2022, with follow-ups in November 2023. All interviews, except Participant D's, were audio-recorded. After the initial interviews, participants reviewed findings and provided feedback for follow-up discussions. Interviews occurred in various locations and durations, sometimes interrupted by emergencies. Participant A's first interview lasted 92 minutes at a restaurant, followed by a 30-minute clinic session. Participant B's 40-minute interview was in his office, followed by two days of follow-ups. Participant C's 20-minute interview was conducted in his office, but he declined further sessions. Participant D, who allowed note-taking instead of recording, had an initial 2-hour interview and a 4-hour follow-up, interrupted by calls in his office. Interviews were transcribed verbatim, and thematic analysis was applied to identify recurring patterns and themes related to workplace violence.[17]

The interview protocol focused on participants' career backgrounds, experiences with workplace violence, perspectives on its causes, and prevention suggestions. Follow-up interviews began with a summary of findings and incorporated participant feedback. Additional questions explored why physicians are targeted, the skills needed to manage violence, and the concept of "spoiled patients." The interviews were audio-recorded and transcribed verbatim to ensure accuracy during data analysis. The thematic analysis was employed to identify recurring patterns, themes, and categories within the interview transcripts. This involved a systematic process of coding and categorizing data to extract meaningful insights related to workplace violence, using Colaizzi's framework.[18] Key statements related to workplace violence were extracted from the interviews, forming the basis for creating meaningful interpretations of the participants' experiences. These were organized into thematic clusters, allowing for a structured analysis of the issue. The findings were synthesized into a detailed account of workplace violence, highlighting its complexities. To ensure accuracy, participants were given the opportunity to review and validate the preliminary findings. Their additional insights were incorporated, enriching the final narrative on the lived experiences of workplace violence.[19]

The participants identified two major forms of workplace violence against physicians: physical and verbal. Physical violence ranged from unexpected punches to threats involving objects like chairs, while verbal violence encompassed insults, threats, and humiliation.[20-22] The physicians often found themselves vulnerable during interactions with patients and their relatives, contributing to the risk of violence. Additionally, according to their reports, the misuse of communication channels like WhatsApp and instrumental aggression further exacerbated the issue. The findings also suggested that overcrowded hospitals emerged as a primary contributor to workplace violence, leading to heightened tensions among patients and their relatives.[23,24] Lack of communication training for physicians was also identified as a significant factor, as ineffective communication could escalate tensions. Furthermore, the phenomenon of "spoiled patients," accustomed to readily available healthcare services, contributed to patient entitlement and abuse.[25] The participants emphasized legal punishment as a deterrent against workplace violence, advocating for consistent application and minimal allowance for extenuating circumstances.[26] They also recommended the establishment of effective physician unions to address organizational gaps and advocate for physicians' rights. Additionally, they proposed the development of comprehensive training programs for physicians, focusing on communication and flexibility skills to navigate complex patient interactions effectively.

**The national survey**

Through an online survey distributed between October and December 2023, 136 healthcare workers from diverse roles and settings across Türkiye shared their experiences with workplace violence. The sample included professionals from various healthcare sectors, such as medical students, residents, attending physicians, nurses, and support staff, representing a broad spectrum of experiences within the Turkish healthcare system. The participants in this survey were recruited through a multi-faceted approach that leveraged both social media platforms and the support of organizations within the Turkish healthcare community. The recruitment process was designed to reach a diverse group of workers across various geographic regions and academic backgrounds. Social media played a crucial role in the recruitment strategy. Platforms such as Twitter/X, Facebook, and Instagram were used to share the survey advertisement widely. These platforms were chosen for their ability to quickly disseminate information to a large audience. The use of hashtags and mentions of relevant academic groups and influencers within the community helped increase the visibility of the survey, encouraging participation from both established researchers and early-career scholars.[27]

Also, the recruitment process prioritized reaching a diverse pool of participants by actively seeking representation across various demographics, including age, gender, and levels of professional experience within the healthcare sector. To achieve this, the researcher targeted different healthcare institutions, such as hospitals, clinics, and private practices, ensuring that professionals from various specializations and career stages were included. Additionally, efforts were made to balance gender representation by specifically encouraging participation from both male and female healthcare workers, while also accounting for varying years of experience, from early-career professionals to those with decades in the field. This approach helped create a comprehensive and well-rounded dataset, reflective of the broader healthcare workforce.[27]

The survey was designed to capture demographic information, experiences of workplace violence, management strategies employed, and recommendations for prevention. The structured questions allowed for quantitative analysis of prevalence and demographics, while the open-ended questions facilitated in-depth exploration of participants' experiences and perspectives. The thematic analysis techniques were employed to analyze qualitative responses obtained from open-ended survey questions. This approach involved systematically identifying, organizing, and interpreting patterns and themes within the data. Through iterative coding and categorization, themes related to the prevalence, forms, impacts, and management strategies of workplace violence emerged, providing rich insights into the participants' experiences. The descriptive statistics were used to analyze structured survey responses, providing an overview of sample characteristics, including demographics, prevalence rates, and distribution across different healthcare settings. The quantitative data analysis facilitated the identification of patterns and trends within the dataset, complementing the qualitative findings.[18,19]

The demographic analysis revealed a diverse composition of healthcare workers, ranging from medical students to attending physicians, representing various healthcare settings, including teaching hospitals, state hospitals, private hospitals, and general practitioner practices. Next, verbal abuse emerged as a predominant form of violence, encompassing insults, threats, and humiliation. The participants recounted instances of verbal aggression from patients, their relatives, and even coworkers.[28] Physical violence posed significant risks to healthcare workers' safety, with reports of assaults, including incidents resulting in injuries. The data underscored the pervasive nature of workplace violence across different healthcare settings and interactions, highlighting the need for systemic interventions.

Healthcare workers employed various strategies to manage workplace violence, including seeking peer support, engaging in communication and conflict resolution techniques, and resorting to institutional assistance such as hospital security or legal intervention. However, challenges in accessing support and addressing perpetrators were evident, emphasizing the importance of comprehensive training programs and enhanced institutional protocols.[29] The respondents offered recommendations for preventing workplace violence, ranging from enhancing security measures and utilizing surveillance technology to implementing support systems and advocacy efforts.[17] Suggestions also targeted governmental actions, including alleviating patient overcrowding and strengthening legal measures to hold perpetrators accountable. Training programs focusing on emotional management, crisis intervention, and professionalism were deemed essential for equipping healthcare workers with necessary skills and resources.

**Document analysis on the history of workplace violence**

The third study investigates workplace violence against physicians in Türkiye from 1998 to 2023, using online newspaper archives. Keywords such as "physicians," "violence," and "healthcare" were used to systematically analyze 16,440 pages, identifying 286 relevant cases. The research combines quantitative analysis with interpretive phenomenological analysis (IPA) to uncover the underlying reasons for workplace violence.[30] Several previous studies have examined workplace violence through Turkish newspapers and social media. For example, Beyazadam et al. investigated physical violence against physicians in Turkish print media from 2008 to 2018.[31] Şantaş and Erdoğan analyzed health violence news on an online portal in 2019, while Hoşgör and Türkmen explored incidents from 2005 to 2021 on the same platform.[32,33] Similarly, Küçükavcı reviewed 120 incidents of workplace violence across 12 popular online news portals.[34] These studies primarily focus on quantifying news articles based on specific variables, with limited attention to qualitative insights from the reports.

The study reveals a pervasive occurrence of workplace violence against physicians across various regions in Türkiye, with a higher frequency in densely populated areas. For instance, Istanbul reported 53 incidents, while Izmir and Ankara reported 23 and 14 cases, respectively. Other notable locations include Adana (13 cases), Şanlıurfa (12 cases), and Gaziantep (12 cases).[31,32] Violence incidents primarily occurred in emergency departments (98 cases) and primary care units (39 cases). Other departments frequently affected include obstetrics and gynecology, surgery, internal medicine, neurology, psychiatry, pulmonology, and orthopedics. Violence also extended beyond clinical settings to areas like hospital gardens, car parks, and lifts.[6,35]

The study found that most violence incidents occurred during regular working hours (152 cases), with a significant number also taking place during on-call duty periods (69 cases). Physicians were the primary targets (230 cases), followed by nurses (34 cases), paramedics, emergency medical technicians, hospital managers, medical technicians, clinic secretaries, and hospital security personnel. Male healthcare workers experienced more violence (207 cases) compared to female workers (100 cases). The majority of offenders were male (245 cases), with patients' accompanying relatives being the primary perpetrators (170 cases), followed by patients themselves (105 cases). Isolated cases involved violence perpetrated by police officers, prosecutors, and clinic secretaries. Most violence incidents were physical (268 cases), involving knives (30 cases) and guns (16 cases). Verbal violence included death threats, mobbing, and sexual assault. Some violence incidents were planned rather than spontaneous, typically arising from actions taken by patients' relatives after the patient had been treated or had passed away.[6,33,34]

The study categorizes the underlying reasons for workplace violence into two main groups: violence caused by patients, or their accompanying relatives and violence instigated by colleagues. These incidents were often triggered by illegal requests, spontaneous reactions, extended waiting times, drug-related factors, mental disorders, and political abuse. Common illegal requests included soliciting false medical certificates, seeking prescriptions for individuals not under the physician's care, and requesting examinations without proper registration. Instances of violence by colleagues often involved mobbing or sexual abuse within the workplace.

### The basic characteristics of workplace violence in Türkiye

The comprehensive examination of workplace violence against healthcare professionals in Türkiye, through the semi-structured interviews, online national survey, and document analysis, reveals a complex and pervasive issue that demands urgent attention. The semi-structured interviews with senior physicians highlighted that both physical and verbal violence are endemic in healthcare settings, driven by factors such as overcrowded hospitals, ineffective communication strategies, and the entitlement exhibited by some patients. These findings align with broader research that underscores the importance of communication training and legal deterrents in mitigating violence in healthcare settings.[36,37] The physicians interviewed advocated for the consistent application of legal punishments and the establishment of robust physician unions to safeguard their rights, echoing calls for systemic reforms in other contexts.[38]

The national survey further illuminated the widespread nature of workplace violence across various healthcare settings, with verbal abuse emerging as the most common form, followed by physical assaults. The participants reported significant challenges in accessing institutional support and effectively addressing perpetrators, a concern that is consistent with findings from other studies on healthcare violence.[39,40] The survey emphasized the need for comprehensive training programs focused on emotional management, crisis intervention, and professionalism, to equip healthcare workers with the necessary tools to manage and prevent violence. These recommendations are critical in addressing the systemic inadequacies that leave healthcare workers vulnerable to violence and highlight the importance of organizational and governmental interventions in creating safer work environments.[41]

The document analysis provided a broader historical context, revealing that workplace violence has been a persistent issue across Türkiye, particularly in densely populated urban areas. The analysis showed that violence is not limited to specific departments but spans across emergency rooms, primary care units, and specialized departments like psychiatry and obstetrics and gynecology. This widespread nature of violence is indicative of broader systemic issues that require a national-level approach, including tailored preventive measures for different clinical settings and enhanced security during peak working hours. Similar to international findings, this study underscores the necessity for comprehensive, culturally responsive strategies to address workplace violence, ensuring the safety and well-being of healthcare professionals in Türkiye.[42,43]

### Setting the program goals

Setting the goals for the training programs involves two consecutive stages. In the first stage, the findings from the needs assessment are organized into an interim report and shared with the advisory group between December 2023 and January 2024. This group comprises a diverse array of professionals from medical and educational backgrounds, including practicing physicians, medical professors from teaching hospitals, nurses, professors from education schools, experts in communication and liberal arts, and patients. Their informal feedback mainly includes suggestions on what topics to discuss in the subsequent stage, how to present the findings to a general audience, and specific requests to be addressed.

The second stage is the workshop held in February 2024. This workshop, attended by the advisory team and project members, spanned one day and had several objectives. The primary goal was to first define the philosophical framework, then set the training program's objectives, and select suitable delivery methods and assessment tools to measure learning outcomes. The workshop began with a presentation of the needs assessment findings. This was followed by a discussion on how to translate these findings into program goals.

The discussion emphasized the cultural factors that influence perceptions of violence, sensitivity to diverse patient populations and cultural norms, and strategies for promoting cultural competence among healthcare professionals. Depending on these cultural elements, the participants then listed the most frequently encountered forms of workplace violence in healthcare settings, culminating in the identification of 15 specific cases (see **Figure 1** for the screenshot of discussions and **Table 1** for the unit list). During this process, the delivery method for the training program was also determined. The consensus was to adopt an online format, given the time constraints faced by physicians, including those still in training, which made face-to-face instruction impractical. According to the consensus in the meeting, an online training program would allow these professionals to engage in learning at their own pace and convenience.

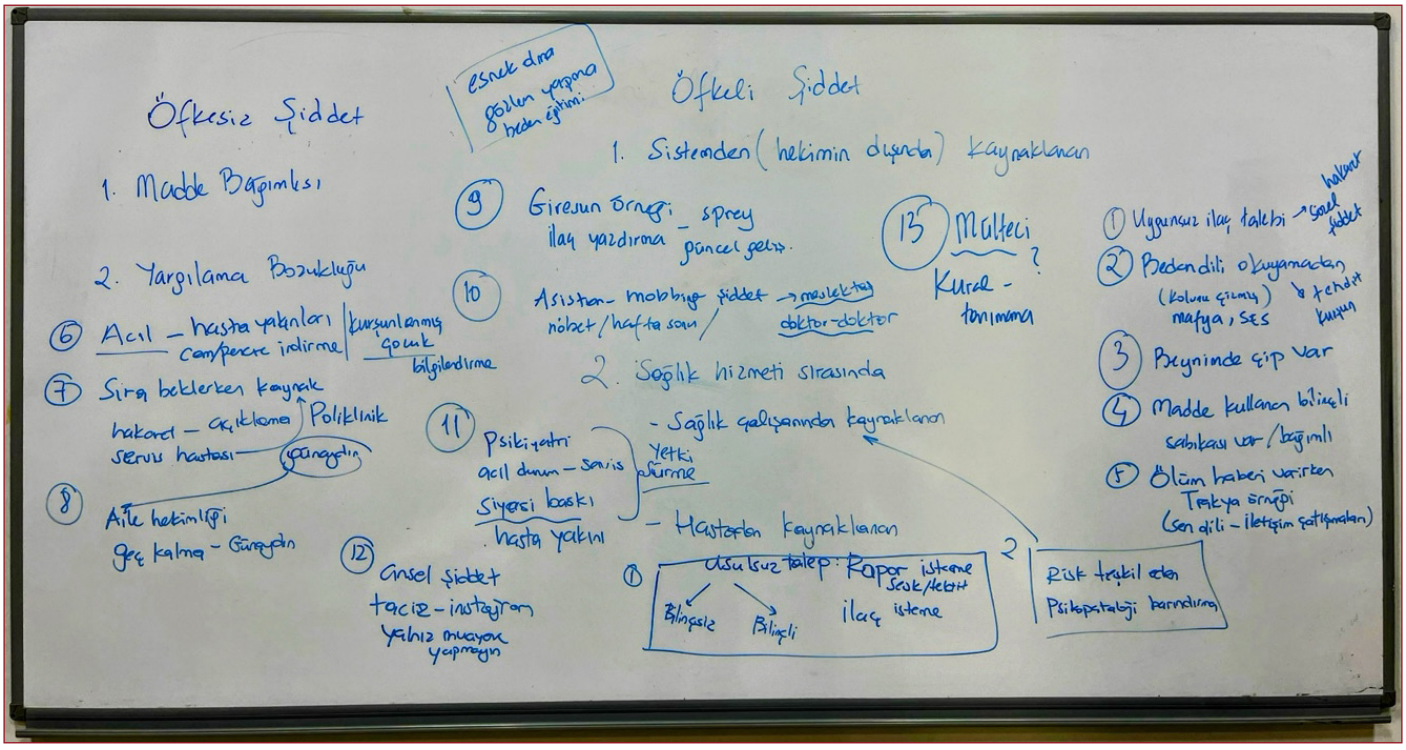


**Figure 1.** Identifying the 15 specific cases of workplace violence (in Turkish).

**Table 1. The unit list in the training program.**

| Unit# | Title | Real-life scenario |
|---|---|---|
| Unit 1 | Introduction | Introducing the concepts of violence and workplace violence. Includes statistics on workplace violence within the Turkish healthcare system. |
| Unit 2 | Illegal request for medication | A family doctor manages an illegal request for a prescription from an angry patient in her office. |
| Unit 3 | Patient's body language | An ENT consultant observes the behavior of a mafia member during a consultation in his office. |
| Unit 4 | Inappropriate complaint | A brain surgeon manages a male patient with schizophrenia who believes he has an imaginary problem in his brain. |
| Unit 5 | Impaired by drug | A cardiology consultant deals with a physical assault by a patient who is impaired by drugs in his office. |
| Unit 6 | Delivering bad news | An emergency resident delivers the news of a patient's death to her son, who then attacks the doctor. |
| Unit 7 | Breaking windows in the emergency | The family of a patient, who has been shot and brought to the emergency room for surgery, attacks the staff and breaks the windows. |
| Unit 8 | Waiting in the line | An internal medicine consultant manages angry patients who have been waiting for their appointments for a long time. |
| Unit 9 | Being late for work | A family doctor, who is late for work, manages angry patients who have been waiting for her for two hours. |
| Unit 10 | Illegal prescription | An angry patient physically assaults a doctor who refuses to prescribe medication for the patient's wife (who is not present in the office). |
| Unit 11 | Mobbing from coworkers | An OB-GYN resident experiences psychological harm from coworkers' bullying in the hospital and begins using anti-depressants. |
| Unit 12 | Political violence | A psychiatry consultant on duty is threatened by a political party member to see a patient illegally. |
| Unit 13 | Sexual violence | An internal medicine consultant's inappropriate photographs are taken by a patient's son during an examination, leading to blackmail. |
| Unit 14 | Miscommunication - Immigrants | A neurology consultant is attacked by a Syrian refugee due to a communication barrier. |
| Unit 15 | Illegal request by patients | A family doctor manages an illegal request for a sick note from a patient. |
| Unit 16 | Communication matters | A senior veteran patient becomes furious when an internal medicine consultant uses impolite language. |
| Unit 17 | Assessment | The assessment includes 20 multiple-choice questions to evaluate understanding. |

### Defining the philosophic framework

The training program developed to address workplace violence against physicians in Türkiye is grounded in a pragmatic philosophical framework. The key characteristic of the pragmatism in this training program emphasizes the importance of practical outcomes and the application of knowledge to solve real-world problems, particularly in dynamic and complex environments like healthcare.[44] This approach prioritizes strategies that are effective, adaptable, and responsive to the specific needs and challenges of healthcare environments in Türkiye.

At the core of this framework is the belief that healthcare practices and interventions should be designed to achieve the best possible outcomes in the specific context in which they are applied. This aligns with Dewey's notion that the value of any theory lies in its ability to inform and improve practice.[45] The training program is consequently focused on equipping healthcare professionals with practical tools and strategies that can be immediately implemented to mitigate and manage workplace violence. By providing clear, actionable guidance that is directly relevant to the day-to-day realities of healthcare providers, the program ensures that the knowledge gained can be applied effectively in practice.[46]

The pragmatic approach also recognizes the importance of cultural context in shaping both the challenges faced, and the solutions needed in healthcare settings. This is consistent with the view that effective action must be sensitive to the cultural and social environment in which it is applied.[47] The training program is therefore designed to be culturally responsive, acknowledging that effective communication and conflict resolution require an understanding of the cultural backgrounds of patients and their families.[48] By incorporating culturally specific scenarios and strategies, the program ensures that healthcare professionals are prepared to navigate the unique dynamics of Turkish healthcare environments, leading to more effective and contextually appropriate interventions.[49]

### Setting the objectives

By grounding the training program in pragmatism, the emphasis is placed on practical, evidence-based solutions that are adaptable to the specific needs of healthcare providers in Türkiye. The program aims to foster a healthcare environment where the tools and strategies taught are not only theoretically sound but also practically effective in reducing workplace violence and improving the overall safety and wellbeing of both healthcare workers and patients.[50] By engaging the advisory group's diverse expertise and thoroughly discussing cultural and practical aspects, the workshop effectively set comprehensive and culturally sensitive goals for the training program. At the end of the workshop, the participants agreed on the following two primary objectives:

Raising the awareness of workplace violence: This goal is accomplished by presenting sample cases that represent the most frequently encountered forms of violence in healthcare settings. Through these real-life examples, the participants can gain a deeper understanding of the various types of violence that healthcare professionals may face, their prevalence, and the contexts in which they occur. These examples also demonstrate how Turkish patients (and their accompanying relatives) perceive violence, how violence in Turkish hospitals is culturally shaped, and how healthcare workers can pay attention to those cultural aspects in workplace violence.

Developing the strategies to manage and mitigate violence: By examining these sample cases, the program will outline practical strategies and interventions that can be implemented to manage and mitigate workplace violence. This includes identifying early warning signs, implementing de-escalation techniques, establishing protocols for reporting and responding to incidents, and fostering a supportive environment that prioritizes the safety and well-being of healthcare workers.

By focusing on these objectives, the training program not only aims to enhance awareness but also equips healthcare professionals with the knowledge and tools necessary to effectively address and prevent workplace violence.

### Implementing the program

The implementation stage of the program development is accomplished in two steps. In the first step, the content for the 15 cases was developed and organized. In the second step, these cases were transferred to the online learning platform in the university (see **Figure 2** for the screenshot of the online training program).

One of the key outcomes from the workshop was the decision to enhance the training program by using real-life cases of workplace violence to raise awareness. In alignment with this decision, the workshop participants provided 15 cases, which were then sorted according to their frequency of occurrence in healthcare settings. Following this goal, the project members developed the content for these cases through a structured process. First, the specific objectives for each case were determined. The relevant findings from the needs assessment were incorporated to outline these objectives, ensuring that each case addressed pertinent issues identified during the assessment. Also, they included the cultural characteristics of violence. Next, an introduction to the form of violence was created to provide context and background information.

Subsequently, a scenario for each case was written in the form of a dialogue to make the situations relatable and engaging for the learners. These scenarios were designed to reflect realistic interactions and challenges that healthcare professionals might encounter. Each unit concluded with appropriate strategies to manage and mitigate the violence presented in the case, offering practical solutions and best practices for dealing with such incidents. This comprehensive approach ensures that the training program not only raises awareness about workplace violence but also equips healthcare professionals with the necessary tools and strategies to effectively address and prevent these situations (see **Figure 3** for the screenshot of a sample unit).

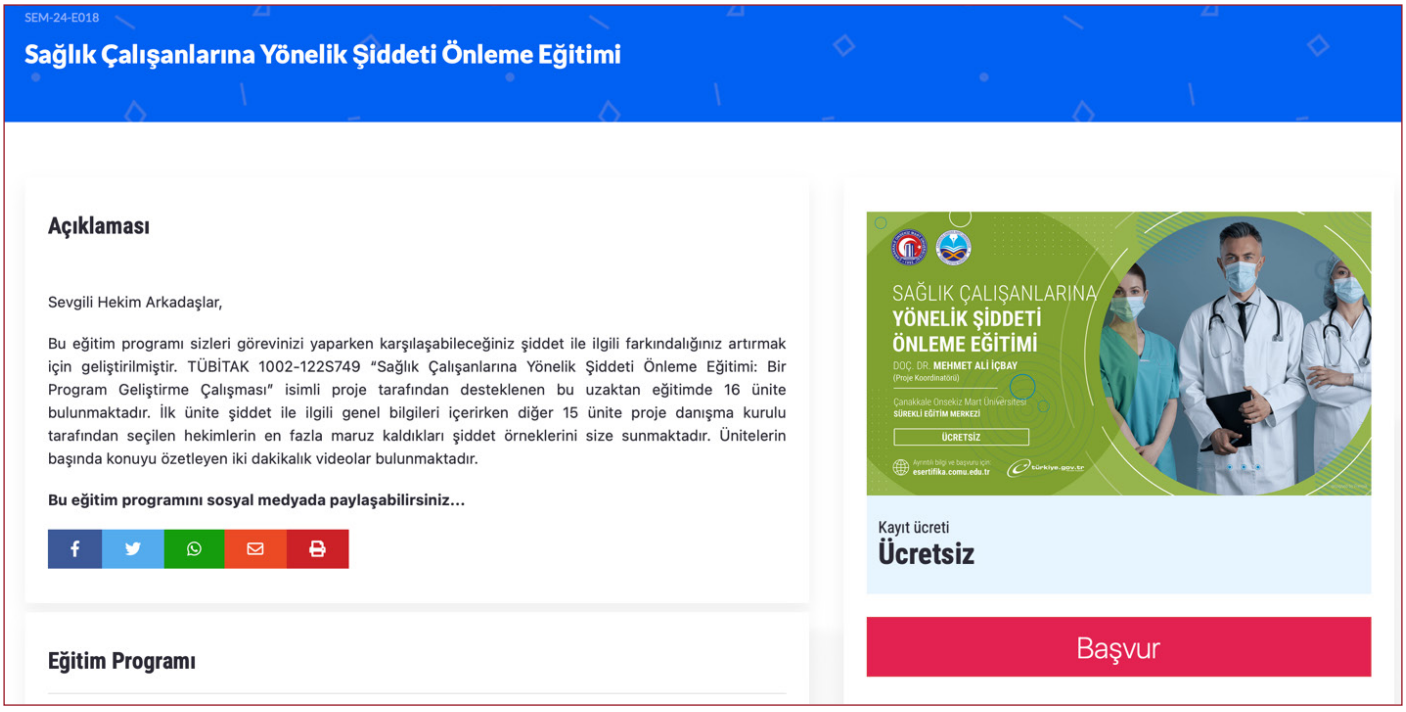


**Figure 2.** The screenshot from the online training program (in Turkish).

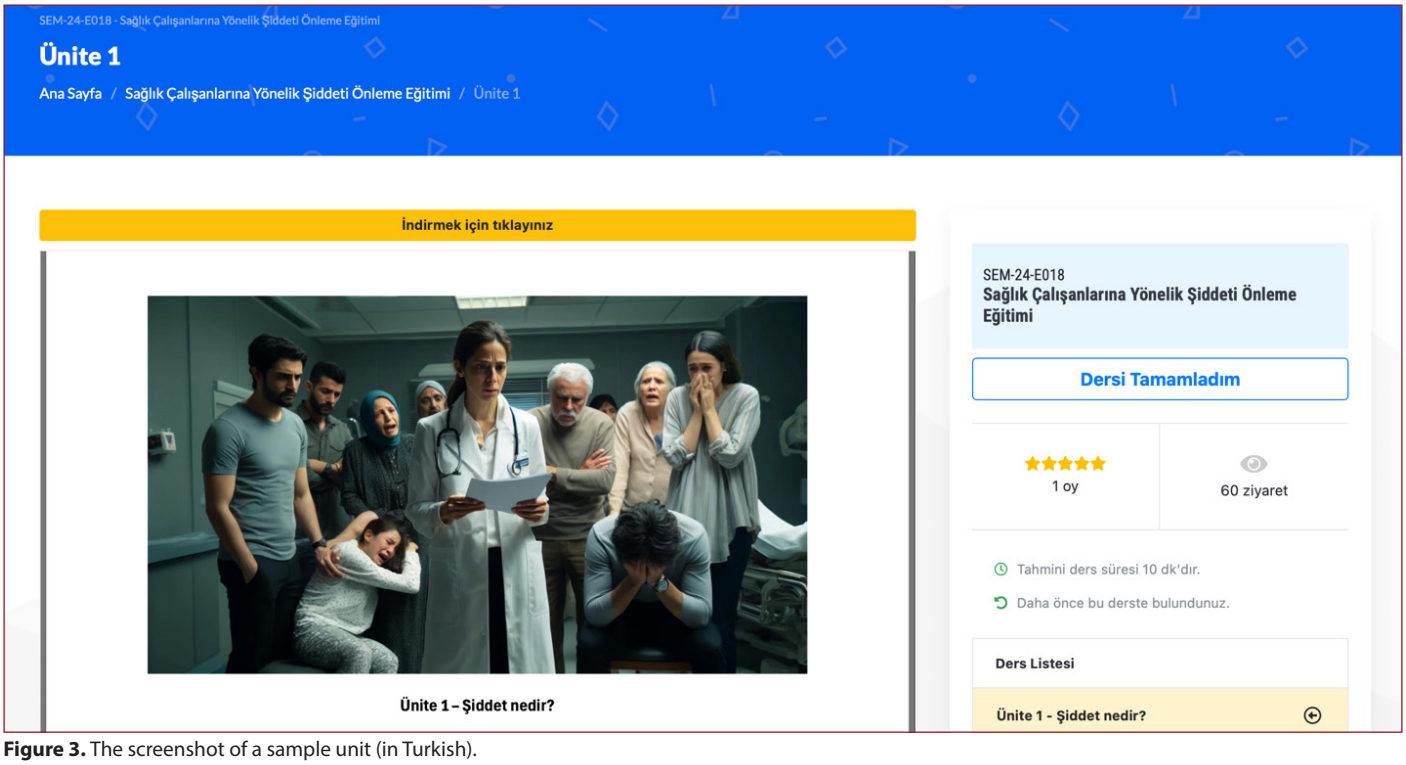


**Figure 3.** The screenshot of a sample unit (in Turkish).

As of the end of August 2024, 53 participants, the majority of whom were medical students from Çanakkale Onsekiz Mart University, have benefited from this program. Some participants were enrolled from institutions such as Istanbul University, Atatürk University, Anadolu University, Karamanoğlu Mehmetbey University, Malatya Turgut Özal University, Afyon Kocatepe University, European University of Lefke, Nuh Naci Yazgan University, Mehmet Akif Ersoy University, Hasan Kalyoncu University, Trabzon University, Istanbul Medipol University, İnönü University, Munzur University, Ankara Yıldırım Beyazıt University, Balıkesir University, Ağrı İbrahim Çeçen University, Istanbul Rumeli University, Gaziantep University, the Ministry of Health, Alaaddin Keykubat University, and Kafkas University.

## RESULTS

The training program for dealing with workplace violence against physicians in Türkiye is designed to be culturally responsive, recognizing and addressing the unique cultural dynamics and sensitivities within Turkish healthcare settings. Following the previous sections outlining how this training program was developed based on the four studies and how it was implemented as an online pilot program in a medical university, this section explains the specific ways in which the program has been tailored to meet these cultural needs, ensuring its relevance and effectiveness for Turkish physicians.

The cultural sensitivity as the key foundation of curriculum development for this training program evolves acknowledging and respecting the diverse cultural backgrounds and practices of individuals. In the context of Turkish healthcare, this means recognizing the unique social, historical, and cultural factors that influence both patient and physician behaviors. Based on this framework, the training program incorporates this understanding by integrating cultural characteristics into its content and delivery methods. It begins by acknowledging the distinct characteristics of Turkish society, including the hierarchical nature of social interactions, the significance of family ties, and the high value placed on respect and honor. For instance, the expectation of deference to authority figures can lead to conflicts if patients or their families feel disrespected or ignored by medical staff. This issue was highlighted by Participant B during an interview when he recounted an incident involving a physical assault by the patient's future husband:

"The patient's relative punched me while I was examining the patient. As a physician, I initially suspected an ectopic pregnancy. However, I was unaware that she was unmarried. The groom, her future husband, believed I was making false accusations and unexpectedly punched me from across the room. I never anticipated the physical assault and found myself on the floor."

**Participant B from the interview**

Participant B was physically attacked after suggesting the possibility of an ectopic pregnancy because sexual intercourse before marriage was a taboo for the patient and her community. The groom perceived the physician's initial diagnosis as a defamatory accusation, which led to the violent outburst. This incident underscores the importance of cultural sensitivity in medical practice, particularly in regions where certain topics, such as premarital sexual activity, are highly stigmatized. To address this issue, Units 3 and 16 in the training program focus on teaching healthcare workers how to accurately interpret patients' behavior and body language and communicate effectively using a set of principles. To exemplify this critical issue, Unit 3 presents a case study involving an ENT physician and a mafia member as his patient. It emphasizes the importance of approaching delicate patient interactions with sensitivity to culturally specific issues. It provides detailed strategies for navigating these complex situations, ensuring that the healthcare provider respects and understands the patient's cultural background while the healthcare worker secures himself. Similarly, Unit 16 covers the scenario of an internal medicine consultant who fails to appropriately address her patients, neglecting the implicit cultural characteristics that influence patient care. Similar to Unit 3, it highlights the consequences of cultural insensitivity and offers guidance on how to recognize and integrate cultural nuances into patient interactions to improve communication and treatment outcomes.

The other dimension to illustrate the role of culture in shaping workplace violence is the political violence heavily experienced by the healthcare workers in Türkiye. The document analysis provided two illustrative cases. The first one took place in a state hospital in Yıldızeli, Sivas.[51]

On August 3, 2017, at 9 pm, the district governor called the on-call physician to visit and examine him at his home. The attending physician declined the governor's request, emphasizing his duty in the hospital. Subsequently, the governor rushed to the hospital and threatened the physician, stating, "I am the owner of this hospital. Do you want me to fire you?"

The second case occurred in Kandıra, Kocaeli, in 2015.[52]

The on-call physician faced threats from the district leader of a political party in 2015. According to court records, the district leader berated the physician, saying, "Do your job properly!" In response, the physician warned him, stating, "Then leave the examination room, and we will do our job properly!" The district leader then threatened the on-call physician, saying, "I will kick you, woman! I am the district leader of AKP [the ruling political party]!" Due to the political harassment, the physician resigned from her position in the state hospital.

The cases presented above underline the critical role culture plays in shaping workplace violence against healthcare workers in Türkiye. In the first case, the respect for authority figures in Turkish culture is deeply ingrained, often leading to an imbalance of power in professional relationships. This cultural norm can enable individuals in positions of power to misuse their authority, as seen in this incident. The governor's expectation of unquestioning compliance from the physician reflects a cultural dynamic where authority is often wielded without accountability, contributing to a climate where workplace violence can thrive.

In the second case, political violence is a manifestation of broader societal issues where political affiliation and power dynamics impact professional interactions. The district leader's actions reflect a culture where political connections are leveraged to bypass professional protocols and exert undue influence, leading to a hostile work environment for healthcare workers. Unit 12 in the training program, for example, addresses these specific aspects by demonstrating the healthcare workers effective communication strategies that align with these cultural expectations. Based on these real-life cases, the unit describes how a psychiatry consultant deals with an illegal request from a member of a political party.

Language and communication are pivotal in preventing and managing workplace violence.[25,29] The training program emphasizes the importance of clear, compassionate communication in Turkish, incorporating common phrases and culturally appropriate ways to express empathy and understanding. It also provides training on recognizing and responding to non-verbal cues, which can be critical in de-escalating potentially violent situations. Unit 14, for example, focuses on equipping healthcare workers with basic language skills and effective communication strategies to bridge the language gap. It includes a real-life case where a Syrian immigrant, unable to communicate effectively with a physician, becomes frustrated and attacks the doctor. The physician's inability to understand and respond to the patient's needs due to the language barrier exacerbates the patient's distress, leading to a physical altercation.

Understanding the legal and administrative context is crucial for managing workplace violence.[26,53] The training program includes comprehensive information on Turkish laws and hospital policies related to workplace violence, providing detailed instructions on navigating these regulations. This ensures that physicians are well-informed about their rights and responsibilities. This legal awareness is particularly important in the Turkish context, where there can be significant variations in the enforcement of laws and policies across different regions and institutions. A good illustration of these variations is highlighted by Participants C and D in their interviews. Participant C emphasized the importance of physicians not being burdened with following legal cases in court, suggesting that physicians spend a great amount of time in lengthy legal processes related to violence.

"Then comes the protracted process of filing a complaint [against the patient]. It involves a lot of bureaucratic hurdles. In the end, there is no resolution. None at all. Knowing that there would be no [legal] outcome, I prefer to remain silent and focus on my work [when faced with verbal violence in the room].[…] It's just an extensive workload. I feel perturbed when I have a subpoena in my hand, and the memories of the case resurface each time I encounter it."

**Participant C from the interview**

Similarly, Participant D noted that local prosecutors dismissed charges for the 20 Beyaz Kod incidents that occurred in 2023 at his teaching hospital. According to his further statement, when he shared the news of the dismissal of charges related to Beyaz Kod incidents with the physicians working in the same hospital, he observed a gradual decline in the use of those codes by the medical staff.

By including these real-world insights and experiences, the units in the training program aims to demonstrate how culture plays a significant role in shaping legal and administrative tasks and motivate healthcare workers to take proactive measures in the first instance. Through practical examples and case studies, the program highlights the cultural nuances that can impact legal processes and administrative decisions, encouraging healthcare professionals to develop a more culturally aware approach to managing workplace violence. This proactive stance not only enhances their legal and administrative judgment but also fosters a more resilient and responsive healthcare environment.

## CONCLUSION

The development of a culturally-responsive training program to address workplace violence against physicians in Türkiye represents a crucial step toward improving the safety and wellbeing of healthcare professionals. This program, grounded in empirical evidence and enriched by cultural sensitivity, equips Turkish physicians with the knowledge, skills, and tools necessary to recognize, manage, and mitigate violence in their workplaces.

One of the most significant aspects of the training program is its integration of main cultural characteristics to the Turkish healthcare environment. By acknowledging the hierarchical nature of Turkish society, the importance of family ties, and the high value placed on respect and honor, the program ensures that its content is relevant and relatable to the participants. Real-life scenarios based on actual incidents reported in Turkish hospitals provide a practical framework for understanding and addressing workplace violence, enabling healthcare professionals to apply learned strategies in real-world situations.

The program's structure, comprising 17 modules, covers various facets of workplace violence, from recognizing early warning signs to implementing de-escalation techniques and navigating legal and administrative procedures. Each module is designed to be interactive and engaging, incorporating practical suggestions, legislative guidelines, and hands-on experiences that are crucial for effective learning and application.

One of the program's strengths is the use of real-life scenarios specific to Turkish healthcare settings. These scenarios are drawn from actual incidents reported in Turkish hospitals, reflecting the types of violence physicians are likely to encounter. By presenting these scenarios, the program helps participants to understand the cultural context of workplace violence, including common triggers and effective responses. For example, a scenario might involve a patient's family member becoming aggressive due to long waiting times, a common issue in Turkish hospitals. The training would then guide physicians on how to manage such situations effectively, using culturally sensitive communication techniques and de-escalation strategies.

Despite the program's comprehensive approach, it is important to acknowledge the limitation regarding the absence of a full-scale evaluation stage. Although the evaluation process began

after the program's implementation, the limited number of participants (53 people completed the online program as of August 2024) made it difficult to gather extensive feedback. Despite this, the effectiveness of the training program is continuously assessed through participant feedback and evaluations of their performance in real-life situations as this paper is being written. Originally, the ongoing feedback loop is planned for ensuring that the program remains relevant and responsive to the evolving needs and challenges faced by Turkish physicians. By actively incorporating feedback from participants and monitoring their practical application of the training, the program aims to adapt and enhance its content and methodologies, ensuring it effectively addresses the complexities of healthcare practice in Türkiye.

Through this initiative, the researcher hopes to foster a safer, more compassionate healthcare system where physicians can perform their duties without the fear of violence, and where the cultural values and dynamics of Turkish society are respected and understood. This training program serves as a model for other countries facing similar challenges, demonstrating the importance of cultural responsiveness in developing effective strategies for managing workplace violence in healthcare settings.

In conclusion, the culturally responsive training program for dealing with workplace violence against physicians in Türkiye is a comprehensive and well-structured initiative. By integrating cultural sensitivity into its design and delivery, the program addresses the unique challenges and needs of Turkish healthcare professionals. It equips them with the knowledge, skills, and tools necessary to effectively manage and prevent workplace violence, ultimately improving the safety and well-being of both physicians and patients. Through continuous evaluation and refinement, the program remains dynamic and adaptable, ensuring its long-term success and impact..

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was obtained from Çanakkale Onsekiz Mart University Research Ethics Committee (Date: 25.08.2022, Decision No: 15/25).

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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# Evaluation of the Relationship Between Iron Load, Age, and Cardiac Function in Children and Young Adults with Thalassemia Major

## Talasemi Majorlü Çocuk ve Genç Yetişkinlerde Demir Yükü, Yaş ve Kardiyak Fonksiyonların İlişkisinin Değerlendirilmesi

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## Abstract

**Aim**: To determine the structural and functional cardiac differences in children and young adults with thalassemia major (TM) compared to healthy subjects using pulsed-wave Doppler and tissue Doppler imaging methods and determine the relationship between iron overload and these differences.

**Material and Method**: We analyzed the data of pediatric and young adult TM patients (n = 44) aged 4–22 years and an age- and gender-matched control group (n = 40) in our hospital data system between Oct.01.2023 and Oct.01.2024. Height, weight, body mass index (BMI), systolic–diastolic blood pressure measurements, complete blood count, ferritin, cardiac T2* magnetic resonance imaging (MRI) values, and echocardiography results were recorded. Comparison of echocardiographic measurements between the two groups was performed. In addition, correlation analysis was performed between ferritin, cardiac T2*MRI, age and echocardiographic parameters of TM patients.

**Results**: Our study showed growth retardation (low height standard deviation score (SDS), low weight SDS and low BMI SDS), dilatation of the left cavities (high left ventricular internal diameter end diastole (LVIDd)), increased left ventricular muscle mass (high left ventricular mass index (LVMI)), cardiac distinctive diastolic (restrictive pattern: left ventricular (LV) peak early diastolic flow (E)/peak late diastolic flow (A) and E/early diastolic myocardial peak flow (E') high), and subclinical systolic (LV peak systolic flow low and LV Tei index high) dysfunction. In addition, iron load (ferritin and cardiac T2* MRI) was correlated with LVMI, and cardiac diastolic and systolic function indicators. As age increased, ferritin value did not change, but cardiac T2* MRI value decreased and diastolic–systolic parameters worsened.

**Conclusion**: Periodic cardiac T2* MRI and Doppler echocardiography examinations of patients with TM may detect subclinical myocardial dysfunction at an early stage, thus providing a window of opportunity for intervention.

**Keywords**: Thalassemia, cardiac functions, iron overload, cardiac T2 MRI, Doppler echocardiography

## Öz

**Amaç**: Darbeli dalga Doppler ve doku Doppler görüntüleme yöntemleri kullanılarak talasemi majorlu (TM) çocuk ve genç yetişkinlerde sağlıklı kişilere göre kardiyak yapısal ve fonksiyonel farklılıklarının belirlenmesi; demir yükünün bu farklılıklar ile olan ilişkisinin ortaya konması amaçlanmıştır.

**Gereç ve Yöntem**: Çalışmamızı yaşları 4-22 arasında olan çocuk ve genç yetişkin TM lü hastaların (n=44) ve yaş-cinsiyet uyumlu kontrol grubunun (n=40) hastanemiz veri sistemindeki 01.10.2023 ile 01.10.2024 tarihleri arasındaki verilerinin incelenmesiyle oluşturduk. Hastaların boy, kilo, vücut kitle indexi (VKI), sistolik-diyastolik kan basıncı ölçümleri ile tam kan sayımı, ferritin, kardiyak T2*MRI değerleri ve ekokardiyografi kayıtları kaydedildi. İki grup arasında ekokardiyografik ölçümlerin karşılaştırılması yapıldı. Ek olarak TM hastaların ferritin, kardiyak T2*MRI,yaş ve ekokardiyografik parametreleri arasında korelasyon analizi yapıldı.

**Bulgular**: Çalışmamızda TM hastalarında büyüme gelişme geriliği (boy SDS, kilo SDS ve VKI SDS düşük), sol boşluklarda dilatasyon (LVIDd yüksek), sol ventrikül kas kitlesinde artış (LVMI yüksek), kardiyak aşikar diyastolik (restriktif özellikte olan: LV tepe erken diyastolik akımı (E)/tepe geç diyastolik akımı (A) ve E/erken diyastolik miyokardiyal tepe akımı (E') yüksek) ve subklinik sistolik (LV tepe sistolik akımı (Sm) düşük ve LV Tei indexi (TX) yüksek) fonksiyon bozukluğu olduğunu tespit ettik. Bununla birlikte demir yükü (ferritin ve kardiyak T2*MRI) ile LVMI, kardiyak diyastolik ve sistolik fonksiyon göstergeleri arasında ilişki mevcuttu. Yaş arttıkça ferritin değeri değişmezken kardiyak T2*MRI değerinin azaldığı; diyastolik ve sistolik parametrelerde kötüleşmelerin olduğu tespit edildi.

**Sonuç**: TM lü hastaların periyodik olarak kardiyak T2*MRI ile doppler ekokardiyografi incelemelerinin yapılmasıyla subklinik myokardiyal disfonksiyon erken dönemde tespit edilebilir; bu da bize gerekli müdahelelerin yapılması açısından fırsat penceresi sunabilir.

**Anahtar Kelimele**r: Talasemi, kardiyak fonksiyonlar, aşırı demir yükü, kardiyak T2 MRI, Doppler ekokardiyografi

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## INTRODUCTION

Thalassemia major (TM) is an autosomal recessive disorder that causes chronic hemolytic hypochromic microcytic anemia due to a defect in the synthesis of one or more of the hemoglobin chains. TM patients need frequent and regular blood transfusions from an early age. Due to extramedullary hematopoiesis, bone marrow expansion and iron overload, various life-threatening complications occur. Endocrine system problems, including hypogonadism, growth retardation, hypoparathyroidism, hypothyroidism, glucose intolerance-diabetes susceptibility, adrenal insufficiency, decreased bone mineral density, and increased risk of bone fracture, are frequently encountered in patients with TM.[1] Complications that develop due to frequent blood transfusions include heart failure, pulmonary hypertension, impaired renal and hepatic functions, restrictive lung diseases, thrombosis, hepatosplenomegaly, leg ulcers, urinary system stones, depression-like psychiatric disorders, and viral infections.[2]

Frequent transfusions inevitably lead to iron accumulation in the body as ferritin binds iron up to a certain level; however, free plasma iron species such as labile iron, which increase in plasma, cause the production of reactive oxygen species and damage cells and organs. In addition, labile iron is directly cardiotoxic. The most common cause of life-threatening morbidity in TM patients is heart failure and arrhythmias due to iron accumulation in the heart (6.8% and 5.7% respectively);[3] this occurs mostly in adulthood. Therefore, close cardiac follow-up of the patients is very important for timely interventions. It is possible to detect subclinical cardiac dysfunction with methods such as pulsed-wave Doppler and tissue Doppler imaging in childhood before distinctive heart failure develops.[4] In our study, we aimed to determine structural and functional cardiac differences in children and young adults with TM compared to healthy subjects by using pulsed-wave and tissue Doppler echocardiography methods and to reveal the relationship between iron load and these differences.

## MATERIAL AND METHOD

We conducted this retrospective study by examining the data of pediatric and young adult patients with TM aged 4–22 years between Oct.01.2023 and Oct.01.2024 in the data system of our tertiary university hospital where patients with TM are regularly followed up and treated. Patients had been receiving blood transfusions at regular intervals of two to four weeks for at least three years and were receiving oral iron chelation therapy. Height, weight, body mass index (BMI), systolic–diastolic blood pressure measurements, complete blood count, ferritin, cardiac T2* magnetic resonance imaging (MRI) values, and echocardiography records were included. The control group consisted of healthy individuals of similar age and gender to the patient group. We selected the control group from subjects who had a complete blood count. Ferritin and cardiac T2* MRI examinations were not performed in the control group. Patients with chronic systemic disease, congenital or acquired cardiac disorders, and those taking medications that may affect cardiac function were excluded.

### Magnetic Resonance Imaging

Cardiac T2* MRI scans were performed using a single-breath-hold multiecho T2* protocol on a 1.5-T scanner (Magnetom Aera, Siemens Healthcare). The parameters were as follows: slice thickness, 8 mm; flip angle, 20°; matrix, 128x256; field of view, 400 mm; time to echo 2.6–16.7 ms with 2.0 ms increments; repetition time 20 ms; and sample bandwidth, 810 Hz/pixel. Mid-ventricular single-slice short-axis T2* maps were obtained. Images were analyzed using SyngoVia software. Measurements were taken from the septum, as measurements from the septum are a good indicator of global iron in the heart.[5] Since iron is preferentially deposited in the epicardium compared to the endocardium, a homogeneous region of interest is defined covering both epicardial and endocardial regions. The degree of cardiac iron overload was categorized as mild (15 ms<T2*<20 ms), moderate (10 ms<T2*<15 ms) and severe (T2*<10 ms).[6]

### Echocardiographic Evaluation

Echocardiographic evaluation was performed by the same pediatric cardiologist using a Vivid S60N (GE Vingmed Ultrasound AS Strandpromenaden 45, 3191 Horten, NORWAY) and 3Sc-Rs sector probes. Three measurements were performed and averaged. Left ventricular (LV) M-mode measurements were obtained from the parasternal long axis window. LVMI was obtained by dividing LVM calculated by Devereoux formula by body surface area.[7]

To evaluate diastolic function, pulsed-wave Doppler measurements were obtained from the four-chamber window by placing mitral leaflets in the sample volume. Inflow peak early diastolic velocity (E) and inflow peak late diastolic velocity (A) measurements were performed. Tissue Doppler measurements were obtained by placing the sample volume on the left lateral wall through a four-chamber window. Annulus early diastolic myocardial peak velocity (E'), annulus late diastolic myocardial peak velocity (A') and peak systolic velocity (Sm) values were recorded. Myocardial performance index (Tei index (TX)) was obtained by dividing the sum of isovolumetric relaxation time and isovolumetric contraction time by ejection time.[8]

### Statistical Analysis

The Statistical Package for the Social Sciences for Windows ver. 26.0 package program was used to conduct the study's statistical analysis. The term n (%) was utilized for categorical variables, whereas mean ± standard deviation was utilized for continuous variables when a normal distribution was followed, and median and inter-quantile range values were used when a normal distribution was not met. Analysis of the data's distribution and frequency was done using descriptive techniques, and the Kolmogorov–Smirnov test was done to check normal distribution. Two independent groups that fit the normal distribution were compared using the Student's t-test. When comparing two

independent groups that did not meet the normal distribution, the Mann–Whitney U test was employed. By using the Spearmann correlation coefficient (rho=r), the relationship between serum ferritin and cardiac T2* MRI values and echocardiographic parameters was determined. The Spearmann correlation coefficient was classified as follows: 0.00–0.19 = "extremely weak", 0.20–0.39 = "weak", 0.40–0.59 = "moderate", 0.60–0.79 = "strong", and 0.80–1.0 = "very strong". In all statistical studies, the significance level was determined to be less than 0.05.

Our study was approved by the ethics committee of our hospital with the date Oct.02.2024 and number 2024-16/8.

## RESULTS

Our study consisted of 44 TM patients with a median age of 13.5 years (min 4, max 22) and 40 completely healthy controls with median age of 14 (4–22) years old. Patients had lower height standard deviation score (SDS), weight SDS and BMI SDS values than the control group (all three p<0.001). Systolic–diastolic blood pressure and heart rate did not differ between the two groups. The hematocrit value of the patients was 25.49±2.67%, while it was 38.1±2.53% in the control group (p<0.001). The median ferritin value of TM patients was 1,581 (220–6,214) ng/mL and cardiac T2* MRI value was 22.61±6.13 ms (**Table 1**).

**Table 1. Comparison of basic demographic and clinical findings between groups.**

| | Thalassemia (n=44) | Control (n=40) | p |
|---|---|---|---|
| Age, years/Median (Min-Max) | 13.5 (4-22) | 14 (4-22) | 0.795 |
| Height, cm | 141.43±22.04 | 151.65±23.64 | 0.044 |
| Height, SDS | -1.2±0.58 | 0.23±0.53 | <0.001 |
| Weight, kg/Median (Min-Max) | 45.5 (14-57) | 54.5 (18-77) | 0.004 |
| Weight, SDS | -0.97±0.67 | 0.17±0.53 | <0.001 |
| BSA, $m^2$ | 1.23±0.33 | 1.4±0.37 | 0.031 |
| BMI, $kg/m^2$ | 18.49±2.5 | 19.78±2.92 | 0.032 |
| BMI, SDS | -0.43±0.63 | 0.06±0.47 | <0.001 |
| SBP, mm Hg | 102.73±9.8 | 107±11.48 | 0.163 |
| SBP, SDS | -0,02±0.36 | 0.1±0.25 | 0.521 |
| DBP, mm Hg | 60.77±4.57 | 62.53±4.04 | 0.067 |
| DBP, SDS | -0,05±0.29 | 0,2±0,25 | 0.097 |
| HR, beats per minute | 72.7±7.1 | 70.4±6.6 | 0.127 |
| Hb, g/dL | 8.7±0.85 | 12.78±0.86 | <0.001 |
| Hct, (%) | 25.49±2.67 | 38.1±2.53 | <0.001 |
| Ferritin, ng/mL/Median (Min-Max) | 1581 (220-6214) | | |
| Cardiac T2*MRI, ms | 22.61±6.13 | | |

BSA, body surface area; BMI, body mass index; SPB, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; Hb, hemoglobin; Hct, haematocrit; T2*MRI, magnetic resonance imaging.

LVMI value was higher in patients with thalassemia major [95.57 (50.71–159.23)] compared to the control group [76.16 (34.67–93.91), p<0.001]. While the ejection fraction (EF), one of the indicators of systolic function, was similar in both groups (p = 0.583), LV Sm value was lower in TM patients (p<0.001). LV E/A and LV E/LV E' ratios, which are diastolic function indicators, were found to be higher in patients with thalassemia major (p<0.001 in both groups). However, LVTX value, which shows systolic and diastolic function together, was found to be high in TM patients (0.44±0.02 - 0.36±0.01, p<0.001) (**Table 2**).

**Table 2. Comparison of M-mode, pulsed and tissue Doppler echocardiographic parameters between groups.**

| | Thalassemia (n=44) | Control (n=40) | p |
|---|---|---|---|
| EF, % | 69.66±3.68 | 70.1±3.64 | 0.583 |
| FS, % | 39.02±3.05 | 39.33±3.12 | 0.654 |
| IVSd, cm | 0.85±0.19 | 0.8±0.16 | 0.264 |
| IVSs, cm | 0.97±0.18 | 0.92±0.16 | 0.337 |
| LVIDd, cm | 4.51±0.66 | 4.19±0.47 | 0.011 |
| LVIDs, cm | 3.08±0.62 | 3±0.49 | 0.529 |
| LVPWd, cm | 0.81±0.2 | 0.78±0.17 | 0.455 |
| LVPWs, cm | 0.94±0.19 | 0.940.17 | 0.873 |
| LVM g | 137.66 (32.36-245.68) | 120.87 (27.42-168.45) | 0.040 |
| LVMI $g/m^2$ | 95.57 (50.71-159.23) | 76.16 (34.67 (93.91) | <0.001 |
| LV E, m/s | 105.98±8.91 | 87.23±5.9 | <0.001 |
| LV A, m/s | 61.93±2.77 | 62.82±2.61 | 0.133 |
| LV E/A | 1.71±0.19 | 1.39±0.11 | <0.001 |
| LV Sm, cm/s | 7.21±0.73 | 8.15±0.80 | <0.001 |
| LV E', cm/s | 13.68±0.83 | 13.28±1.06 | 0.053 |
| LV E/E' | 7.78±0.89 | 6.62±0.78 | <0.001 |
| LVTX | 0.44±0.02 | 0.36±0.01 | <0.001 |

EF, ejection fraction; FS, fractional shortening; IVSd, interventricular septal end-diastolic dimension, IVSs, interventricular septal end-systolic dimension, LVIDd, left ventricle end-diastolic dimension; LVIDs, left ventricle end-systolic dimension; LVPWd, left ventricle posterior wall end-diastolic dimension; LVPWs, left ventricle posterior wall end-systolic dimension; LVMI, left ventricle mass index, E, inflow peak early diastolic velocity; A, inflow peak late diastolic velocity; Sm, peak systolic velocity; E', annulus early diastolic myocardial peak velocity; TX, Tei index (myocardial performance index)

T2* MRI <10 ms was present only in one TM patient, who was aged 21 years. The mean age of patients with T2* MRI >20 ms was 11.29±5.36 years. The mean ferritin level was 3,200 ng/mL in patients with T2* MRI <10 ms and 1,154 (220–2,530) ng/mL in patients with T2* MRI >20 ms (**Table 3**).

**Table 3: Age and ferritin levels of patients according to T2*MRI values**

| | T2*MRI <10 ms, (n=1) | T2*MRI 11-14 ms, (n=3) | T2*MRI 15-19 ms, (n=9) | T2*MRI >20 ms, (n=31) | Total (n=44) |
|---|---|---|---|---|---|
| Age, years | 21 | 18.67±2.89 | 18±3.67 | 11.29±5.36 | 13.5 (4-22) |
| Age>18 years, n (%) | 1 (10) | 1 (10) | 5 (50) | 3 (30) | 10 (100) |
| Age 4-17 years, n (%) | 0 (0) | 2 (5.9) | 4 (11.8) | 28 (82.3) | 34 (100) |
| Ferritin, ng/mL | 3200 | 2350 (2227-6214) | 1860 (522-3600) | 1154 (220-2530) | 1581 (220-6214) |

The T2* MRI value of TM patients age>18 years was 17.5 (8–25), while that of patients aged 4–17 years was 25 (11–29) ms (p<0.001). Ferritin value of TM patients aged>18 years was 1,855 (422–3,200) ng/mL, while that of patients aged 4–17 years was 1,489 (220–6,214) ng/mL (p<0.001) (**Table 4**).

**Table 4: T2*MR and Ferritin levels of patients under and over 18 years of age**

| | Age >18 years, (n=10) | Age 4-17 years, (n=34) | Total, (n=449 | p |
|---|---|---|---|---|
| T2*MRI, ms | 17.5 (8-25) | 25 (11-39) | 22.61±6.13 | <0.001 |
| Ferritin, ng/mL | 1855 (422-3200) | 1489 (220-6214) | 1581 (220-6214) | <0.001 |

Hematocrit and EF were not associated with any echocardiographic parameters. Ferritin was weakly associated with LVMI; and moderately associated with E/A, E/E', LVTX and LV Sm. Cardiac T2* MRI associated strongly with LVMI, E/E', LVTX, LV Sm; and very strongly with E/A (**Table 5**, **Figure 1**). Ferritin was not associated with age, whereas cardiac T2* MRI was strongly associated with age (**Table 5**, **Figure 2**).

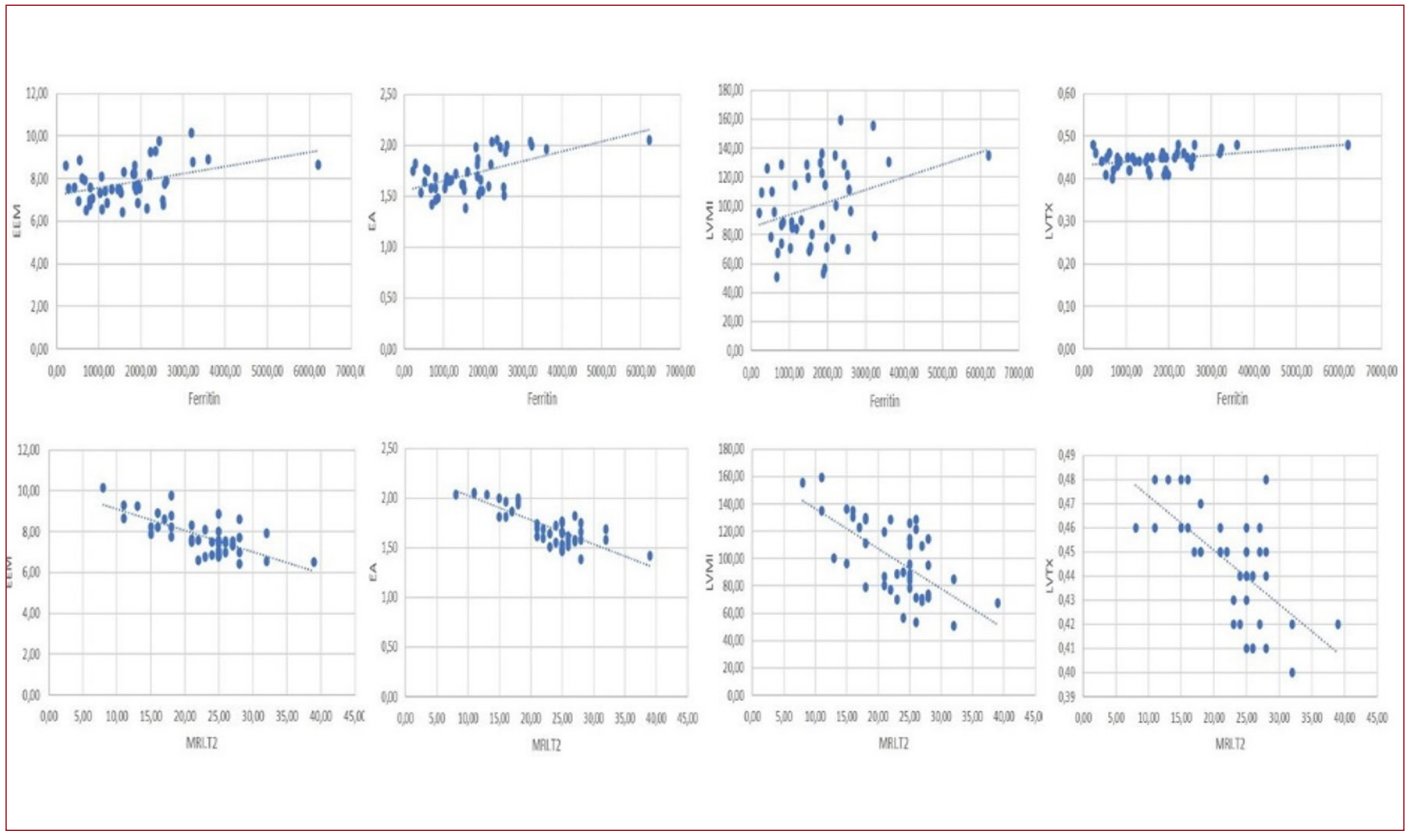


**Figure 1.** Spearmann correlation of ferritin, cardiac T2*MRI and echocardiographic parameters.
LVMI, left ventricle mass index, E, inflow peak early diastolic velocity; A, inflow peak late diastolic velocity; E', annulus early diastolic myocardial peak velocity; TX, Tei index (myocardial performance index).

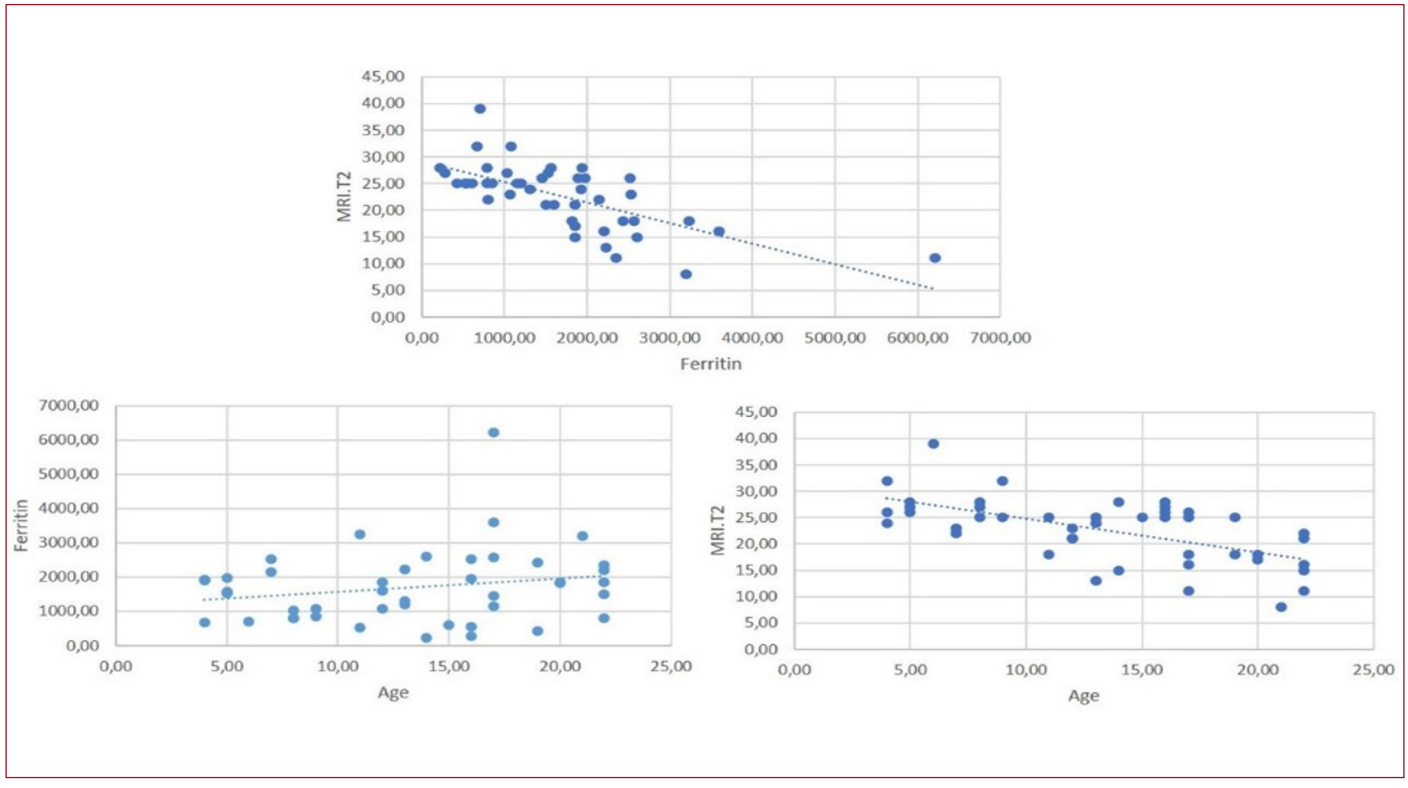


**Figure 2.** Spearmann correlation of ferritin and T2*MRI each other; and ferritin and T2*MRI with age.
T2*MRI, magnetic resonance imaging

**Table 5: Spearmann correlation coefficient matrix of serum Hct, Ferritin levels, T2*MRI and echocardiographic parameters (rho=r).**

| | Hct | Ferritin | T2*MRI | EF | LVMI | E/A | E/E' | LVTX | Age | Sm |
|---|---|---|---|---|---|---|---|---|---|---|
| Hct (r) | - | -0.258 | 0.222 | -0.081 | -0.290 | -0.180 | -0.216 | -0.126 | -0.180 | 0.212 |
| (p) | - | 0.091 | 0.148 | 0.602 | 0.056 | 0.243 | 0.159 | 0.415 | 0.243 | 0.166 |
| Ferritin (r) | -0.258 | - | -0.681 | 0.222 | 0.341 | 0.560 | 0.408 | 0.417 | 0.203 | -0.501 |
| (p) | 0.091 | - | <0.001 | 0.148 | 0.023 | <0.001 | 0.006 | 0.005 | 0.187 | 0.001 |
| T2*MRI (r) | 0.222 | -0.681 | - | -0.078 | -0.648 | -0.801 | -0.716 | -0.648 | -0.605 | -0.617 |
| (p) | 0.148 | <0.001 | - | 0.614 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| EF (r) | -0.081 | 0.222 | -0.078 | - | 0.010 | 0.084 | -0.101 | -0.056 | -0.128 | -0.60 |
| (p) | 0.602 | 0.148 | 0.614 | - | 0.950 | 0.586 | 0.516 | 0.717 | 0.407 | 0.700 |
| LVMI (r) | -0.290 | 0.341 | -0.648 | 0.010 | - | 0.630 | 0.609 | 0.602 | 0.941 | -0.200 |
| (p) | 0.056 | 0.023 | <0.001 | 0.950 | - | <0.001 | <0.001 | <0.001 | <0.001 | 0.192 |
| E/A (r) | -0.180 | 0.560 | -0.801 | 0.084 | 0.630 | - | 0.821 | 0.747 | 0.628 | -0.709 |
| (p) | 0.243 | <0.001 | <0.001 | 0.586 | <0.001 | - | <0.001 | <0.001 | <0.001 | <0.001 |
| E/E' (r) | -0.216 | 0.408 | -0.716 | -0.101 | 0.609 | 0.821 | - | 0.602 | 0.583 | -0.617 |
| (p) | 0.159 | 0.006 | <0.001 | 0.516 | <0.001 | <0.001 | - | <0.001 | <0.001 | <0.001 |
| LVTX (r) | -0.126 | 0.417 | -0.648 | -0.056 | 0.602 | 0.747 | 0.602 | - | 0.630 | -0.648 |
| (p) | 0.415 | 0.005 | <0.001 | 0.717 | <0.001 | <0.001 | <0.001 | - | <0.001 | <0.001 |
| Age (r) | -0.180 | 0.203 | -0.605 | -0.128 | 0.941 | 0.628 | 0.583 | 0.630 | - | -0.187 |
| (p) | 0.243 | 0.187 | <0.001 | 0.407 | <0.001 | <0.001 | <0.001 | <0.001 | - | 0.224 |
| Sm (r) | 0.212 | -0.501 | -0.617 | -0.60 | -0.200 | -0.709 | -0.617 | -0.648 | -0.187 | - |
| (p) | 0.166 | 0.001 | <0.001 | 0.700 | 0.192 | <0.001 | <0.001 | <0.001 | 0.224 | - |

Hct, haematocrit; T2*MRI, magnetic resonance imaging; LVMI, left ventricle mass index, E, inflow peak early diastolic velocity; A, inflow peak late diastolic velocity; E', annulus early diastolic myocardial peak velocity; TX, Tei index (myocardial performance index); Sm, peak systolic velocity

## DISCUSSION

The incidence of hemoglobinopathies has been reported to be one in 0.1–0.4 million per year worldwide and thalassemias are the most common. It is frequently observed in Mediterranean, Middle Eastern, and Southeast Asian countries.[9] For beta thalassemia major to occur, both parents must be carriers. As in developed countries, screening of men and women for thalassemia before marriage is a legal obligation in Turkey. Although the incidence of TM patients has decreased in recent years, it is still seen as a public health problem due to immigrants relocating to Turkey from other Middle Eastern countries. In our study, 14 of 44 patients (31.8%) were immigrants to Turkey in recent years.

Various endocrinologic problems occur due to iron accumulation in the organs; chronic hypoxia caused by chronic anemia, and growth retardation also occur in TM patients.[1,10,11] In our study, we found low height, weight, and BMI SDS values in TM patients.

Patients with TM have hypertrophy of the heart because of iron accumulation in the heart and enlargement of the cavities due to chronic anemia.[12] Studies have shown LV end-systolic and end-diastolic dilatation and increased LVMI levels in patients with TM.[13-15] Similarly, in our study, we found that high left ventricular internal diameter end diastole (LVIDd) and left ventricular mass index (LVMI) measurements were higher in patients with TM compared to the control group. In addition, LVMI increased with increasing age.

In patients with TM, non-transferrin-bound iron accumulates in the heart as in many organs. It leads to the formation of toxic oxygen metabolites via the Fenton reaction, which damage cell and membrane lipids, proteins, and nucleic acids in mitochondria. In addition, iron accumulation in the heart causes iron overload cardiomyopathy.[16,17] The causes of death of 2,797 TM patients in the United States between 1999 and 2020 were analyzed, and it was reported that the leading cause, with 26%, was cardiovascular diseases.[18] In patients with TM, distinctive heart failure secondary to systolic dysfunction is observed in the late stages of the disease; until then, EF measured by conventional methods remains within normal limits. However, early changes in tissue Doppler Sm and TX values indicating subclinical systolic dysfunction have been shown in studies.[16,19-21] In our study, there was no difference between TM patients and the control group in terms of EF, which is an indicator of systolic function. However, a tissue Doppler imaging study showed that patients with TM had low LV Sm and high LVTX, indicating subclinical systolic dysfunction. In addition, LV Sm decreased and LVTX increased with increasing age.

Studies have shown that patients with TM have diastolic myocardial dysfunction in the early stages. In restrictive myocardial diastolic dysfunction, the E value and E/A ratio is high. Restrictive diastolic myocardial dysfunction also occurs in patients with TM due to iron accumulation in the heart.[16,23-25] In our study, E/A and E/E' ratios indicating restrictive diastolic myocardial dysfunction were high. It was also found that E/A and E/E' ratios increased with increasing age.

The volume of iron load caused by periodic blood transfusions can be detected by MRI in the liver, pancreas, and heart.[26] Silvilariat et al. reported a correlation between ferritin level, cardiac T2* MRI value, and diastolic function parameters in their study of 77 TM patients with a median age of 14 years.[27] El-Shanshory et al. reported that there was a correlation between cardiac T2* MRI value and LVTX; and T2* MRI value decreased with increasing age in their study of 100 children with TM with a mean age of 10.9±3.7 years.[28] Khezri et al. compared ferritin and cardiac T2* MRI results in 1,959 adults

with TM and reported that the ferritin cut-off value for predicting high cardiac iron load (cardiac T2* MRI above 20 ms) was 2,027 ng/mL.[29] Güzelbey et al. reported that cardiac T2* MRI follow-up would be very useful in the evaluation of cardiac iron accumulation in TM patients.[30] In our study, the median ferritin level of TM patients was 1,581 (220–6,214) ng/mL. Severe cardiac iron accumulation (T2* MRI level below 10 ms) was detected in a 21-year-old patient; moderate iron accumulation (11–14 ms) was detected in three patients aged 13, 17 and 22 years. All patients with significant cardiac iron accumulation (T2* MRI below 20 ms) were older than 11 years. There was a strong correlation between ferritin and cardiac T2* MRI levels (rho = -0.681, p<0.001). T2* MRI decreased with increasing age (rho = -0.605, p<0.001), whereas ferritin levels did not change with age (rho = 0.203, p = 0.187).

## CONCLUSION

In our study, we found that TM patients had growth retardation (low height SDS, low weight SDS and low BMI SDS), LV dilatation (high LVIDd), increased LV cardiac muscle mass (high LVMI), distinctive cardiac diastolic dysfunction (restrictive pattern: high LV E/A and E/E') and subclinical systolic (low LV Sm and high LVTX) dysfunction. However, there was a correlation between iron load (ferritin and cardiac T2* MRI) and LV muscle mass, and cardiac diastolic and systolic function indicators. While ferritin value did not change with increasing age, cardiac T2* MRI value decreased, and diastolic and systolic parameters worsened. Ferritin levels were higher and T2* MRI values were lower in patients with TM older than 18 years compared to younger patients. It may be possible to prevent advanced stages of cardiac dysfunction in patients with TM by not interrupting blood collection periods and making iron chelation therapy more disciplined. In addition, periodic cardiac T2* MRI and Doppler echocardiography examinations may detect subclinical myocardial dysfunction at an early stage, which may provide an opportunity for necessary interventions. However, the main principle in the fight against TM is to identify potential parents who are thalassemia carriers and prevent the emergence of individuals with TM from the very beginning.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: Approval for our study was obtained from the Bursa City Hospital Clinical Research Ethics Committee (Date: 02.10.2024, Decision no: 2024-16/8).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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# Views on Sustainable Nutrition Among Nutrition and Dietetics Students, Dietitians, and Healthcare Professionals

## Beslenme ve Diyetetik Öğrencileri, Diyetisyenler ve Sağlık Profesyonellerinin Sürdürülebilir Beslenme Hakkındaki Görüşleri

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## Abstract

**Aim**: In this study, the views of individuals, dietitians and health professionals who are educated in the field of nutrition and dietetics on sustainable nutrition were evaluated.

**Material and Method**: This study, which was designed in the survey model, was conducted on 456 individuals, including Nutrition and Dietetics students, dietitians and health professionals. Sociodemographic characteristics, knowledge and attitudes towards sustainable nutrition were questioned.

**Results**: 34.4% of the participants were nutrition and dietetics students, 13.1% were dietitians and 52.5% were health professionals. The percentage of participants who had previously received education on sustainable nutrition was 36.7%, 26.1% and 2.5% for dietitians, undergraduate students and health professionals, respectively ($p<0.05$). When the level of knowledge about sustainable nutrition was evaluated, 13.3% of dietitians and 3.8% of undergraduate students declared that they had excellent knowledge, while no health professionals declared that they had excellent knowledge (<0.05). The knowledge and approaches of nutrition and dietetics educated individuals about sustainable nutrition, environment and environmental problems, supply and consumption of various foods, and correct information about the products purchased while shopping for food were found to be higher than health professionals ($p<0.05$).

**Conclusion**: This study shows that students in Nutrition and Dietetics are more knowledgeable about sustainable nutrition compared to healthcare professionals; however, their knowledge is not at sufficient levels. The necessity of expanding education on sustainable nutrition is becoming increasingly apparent.

**Keywords**: Dietitian, health professional, nutrition and dietetics students, sustainable nutrition

## Öz

**Amaç**: Bu çalışmada, beslenme ve diyetetik alanında eğitim gören bireylerin, diyetisyenlerin ve sağlık profesyonellerinin sürdürülebilir beslenmeye ilişkin görüşleri değerlendirilmiştir.

**Gereç ve Yöntem:** Tarama modelinde tasarlanan bu çalışma, Beslenme ve Diyetetik öğrencileri, diyetisyenler ve sağlık profesyonelleri olmak üzere 456 kişi üzerinde yürütülmüştür. Bireylerin sosyodemografik özellikleri, sürdürülebilir beslenme konusundaki bilgi ve yaklaşımları sorgulanmıştır.

**Bulgular**: Katılımcıların %34,4'ü beslenme ve diyetetik öğrencisi, %13,1'i diyetisyen ve %52,5'i sağlık profesyoneliydi. Daha önce sürdürülebilir beslenme konusunda eğitim almış olan katılımcıların yüzdesi diyetisyenler, lisans öğrencileri ve sağlık çalışanları için sırasıyla %36,7, %26,1 ve %2,5'tir ($p<0,05$). Sürdürülebilir beslenme konusundaki bilgi düzeyleri değerlendirildiğinde, diyetisyenlerin %13,3'ü ve lisans öğrencilerinin %3,8'i mükemmel düzeyde bilgi sahibi olduğunu beyan ederken, sağlık profesyonellerinden hiç kimse mükemmel düzeyde bilgi sahibi olduğunu beyan etmemiştir (<0,05). Beslenme ve Diyetetik eğitimi alan bireylerin sürdürülebilir beslenme, çevre ve çevre sorunları, çeşitli gıdaların temini ve tüketimi, gıda alışverişi yaparken satın alınan ürünlerle ilgili doğru bilgilendirme konularında bilgi ve yaklaşımları sağlık çalışanlarına göre daha yüksek bulunmuştur ($p<0,05$).

**Sonuç**: Bu çalışma, Beslenme ve Diyetetik eğitimi görenlerin sürdürülebilir beslenme konusunda sağlık profesyonellerine göre daha bilgili olduğunu, ancak bu bilgilerin yeterli seviyelerde olmadığı görülmektedir. Sürdürülebilir beslenme eğitiminin yaygınlaştırılmasının gerekliliği giderek daha fazla anlaşılmaktadır.

**Anahtar Kelimeler**: Beslenme ve diyetetik öğrencileri, diyetisyen, sağlık profesyoneli, sürdürülebilir beslenme

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## INTRODUCTION

The rising global population, combined with climate change, threatens our finite energy resources. One approach to addressing this issue is through managing dietary choices, which has led to the development of the concept of sustainable nutrition.[1,2] Sustainable nutrition involves shifting dietary preferences to reduce excessive consumption, adopting healthier eating habits with lower environmental impacts, and minimizing waste in food production systems.[3]

Current food systems not only fail to support the global population's needs and contribute to chronic nutritional diseases but also place undue stress on natural resources. Climate change, environmental degradation, loss of biodiversity, and pollution are driving the need for a more sustainable nutritional framework.[4,5]

Sustainable nutrition relies on effective systems and policies.[6,7] Dietitians, as health professionals, can influence policy and raise awareness about sustainable nutrition. In Turkey, however, dietitians conduct limited research on sustainability. Studies show that dietitians generally possess higher knowledge of sustainable nutrition and emphasize the importance of continuous development in this area.[8-10] Integrating sustainable nutrition into the nutrition and dietetics curriculum is crucial for shaping future strategies.[11,12]

Given the critical importance of sustainable nutrition for healthy eating, it is essential to assess the knowledge and attitudes of nutrition and dietetics students, dietitians, and other health professionals.[13-15] The aim of this study is to evaluate the opinions on sustainable nutrition among nutrition and dietetics students, dietitians and other health professionals.

## MATERIAL AND METHOD

### Design and Sampling

This study designed as a survey model and performed knowledge and attitudes on sustainable nutrition in nutrition and dietetic undergraduates, dieticians and other health professionals in Ankara. The sample size was determined using G*Power 3.1.9.6, with an effect size of 0.15, an alpha level of 0.05, and 95% power, resulting in a sample size of 450.[16] This research consists of three groups. First groups include Nutrition and Dietetics undergraduates between 18-65 ages who live in Ankara, second groups as dietitians and third is other health professionals (e.g. midwifery, nurse). Totally 456 individuals (Nutrition and Dietetic undergraduates n=157, dietitians n=60, other health professionals n=239) participate of the study.

### Data Collection and Tools

The questionnaire consists of three parts. First part demographic features included 7 questions about gender, date of birth, education, department, class, occupation, and work status. Second part anthropometric measurements calculated by researchers' body weight (kg), body height (m), and third part knowledge and attitudes to sustainable nutrition were collected face-to-face interview method spending about 30 min for each participant to fill the questionnaire. Body Mass Index (BMI) calculated with body weight(kg) divided height(m) square (kg/m²). The data evaluated according to the classification of the World Health Organization (WHO). BMI values were classified as underweight <18.5 kg/m², normal 18.5-24.9 kg/ m², overweight 25-29.9 kg/ m², and obese ≥30 kg/m².[17] The survey consists of 26 questions evaluating participants' knowledge about sustainable nutrition. The questionnaire covers topics such as whether the respondents are educated about sustainable nutrition, their responses to certain statements about sustainable nutrition and their behaviours regarding the consumption of different food items. The section assessing the respondents' attitudes towards sustainable nutrition consists of 19 questions using a two-choice rating scale. The statements related to the participants' purchasing behavior's and attitudes towards food products are related to environmentally friendly sustainable nutrition approaches.

### Statistical Analysis

The data were analyzed with IBM SPSS Statistics 24 (IBM SPSS) program. Descriptive categorical variables were defined with numbers (n) and percentages (%). Descriptive statistics were presented with mean ($\bar{X}$), standard deviation (SD). Relationships between two categorical variables were presented using cross-tables and tested using the Chi-Square test ($\chi 2$). The significance level in the study was set at $p<0.05$.[18]

### Ethical Considerations

This study was approved by the Ankara Yıldırım Beyazıt University Ethics Committee with Decision No: 09 February 14, 2020. After ethical approval was obtained, all participants were given the necessary explanations about the study through the information paragraph in the questionnaire before starting the study and the informed consent form was signed. This study was conducted by the principles of the Declaration of Helsinki.

## RESULTS

The study was completed with a total of 456 participants, disturbing 86.8% (n=396) females and 13.2% (n=60) males. Among the participants, 34.4% (n=157) were nutrition and dietetics students, 13.1% (n=60) were dietitians, and 52.5% (n=239) were other health professionals. The descriptive statistics for age, gender, and BMI of the participants are shown in **Table 1**. The average ages of nutrition and dietetics undergraduates, dietitians, and other health professionals were 21.9±2.12, 26.8±5.26, and 31.0±10.45 years, and female of the participants were found 97.5%,

98.3%, and 77.0% respectively. As seen in **Table 1**, normal BMI was found 71.3%, 68.3%, and %60.7 in graduates, dietitians, and other health professionals; on the other hand, overweight-obese participants distribution were determined 8.9%-1.3%, 8.3%-1.7%, and 27.6%-9.2%, respectively (p<0.05). The average (X̄±SD) BMI were calculated 21.0±4.30, 21.2±5.56, and 24.2±4.23 kg/m² averages for undergraduates, dietitians, and other health professionals, respectively.

**Table 1. Participants' Socio-demographic Characteristics and BMI**

| | Undergraduates (n=157) | | Dietitian (n=60) | | Health Professionals (n=239) | | p* |
|---|---|---|---|---|---|---|---|
| Age (X̄±SD) | 21.9±2.12 | | 26.8±5.26 | | 31.0±10.45 | | |
| | n | % | n | % | n | % | |
| Gender | | | | | | | |
| Male | 4 | 2.5 | 1 | 1.7 | 55 | 23.0 | |
| Female | 153 | 97.5 | 59 | 98.3 | 184 | 77.0 | |
| BMI | | | | | | | |
| Underweight | 29 | 18.5 | 13 | 21.7 | 6 | 2.5 | |
| Normal | 112 | 71.3 | 41 | 68.3 | 145 | 60.7 | <0.05 |
| Overweight | 14 | 8.9 | 5 | 8.3 | 66 | 27.6 | |
| Obese | 2 | 1.3 | 1 | 1.7 | 22 | 9.2 | |
| X̄±SD | 21.0±4.30 | | 21.2±5.56 | | 24.2±4.23 | | |

* Chi-Square

The percentages of participants who have received previously on sustainable nutrition education are found, 36.7%, 26.1%, and 2.5% for dietitians, undergraduates, and other health professionals, respectively (**Table 2**). Statistically significant differences were found among the groups (p<0.05).

In assessing their knowledge levels about sustainable nutrition categorized to 5-pointed Likert scale, 13.3% of dietitians and 3.8% of undergraduates declared that extremely aware, while no one from health professionals' group. Significantly difference found in three groups of participants (p<0.05) (**Table 2**).

**Table 2. Training and Awareness of Sustainable Nutrition**

| | Undergraduates (n=157) | | Dietitian (n=60) | | Health Professionals (n=239) | | p* |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | |
| Training | | | | | | | |
| Yes | 41 | 26.1 | 22 | 36.7 | 6 | 2.5 | <0.05 |
| No | 116 | 73.9 | 38 | 63.3 | 233 | 97.5 | |
| Self-Assess Awareness | | | | | | | |
| Extremely aware | 6 | 3.8 | 8 | 13.3 | - | - | |
| Moderately aware | 54 | 34.4 | 38 | 63.3 | 29 | 12.1 | |
| Somewhat aware | 69 | 43.9 | 13 | 21.7 | 72 | 30.1 | <0.05 |
| Slightly aware | 27 | 17.2 | 1 | 1.7 | 82 | 34.3 | |
| Not at all aware | 1 | 0.6 | - | - | 56 | 23.4 | |

* Chi-Square

Economical contribution perceptions of sustainable nutrition vary among dietitians, undergraduates, and other health professionals, with percentages of those who believe 100%, 99.4%, and 88.3%, respectively (p <0.05).

Regarding the perception of sustainable nutrition as a global issue, the percentages of undergraduates, dietitians, and other health professionals who believe in its global significance are 79.0%, 78.3%, and 66.9%, respectively (p<0.05). In terms of considering sustainable nutrition related to resource conservation, the percentages of those who hold this belief are 98.7%, 98.3%, and 92.1% for undergraduates, dietitians and health professionals, respectively (p<0.05).

Health professionals, compared to dietitians and undergraduates, have higher percentages of those who believe that the Mediterranean diet does not contribute to sustainable nutrition, with values of 22.6%, 3.3%, and 1.9%, respectively (p<0.05). Regarding the concepts of ecological footprint, carbon footprint, and biodiversity, the percentages of those who believe these are related to sustainable nutrition are 95.5%, 95.0%, and 74.5% for undergraduates, dietitians, and health professionals, respectively (**Table 3**).

**Table 3. The Perception Analysis of Sustainable Nutrition**

| Attitudes | Undergraduates (n=157) | | Dietitian (n=60) | | Health Professionals (n=239) | | p* |
|---|---|---|---|---|---|---|---|
| | Yes | No | Yes | No | Yes | No | |
| | n<br>% | n<br>% | n<br>% | n<br>% | n<br>% | n<br>% | |
| It may contribute to the economy | 156<br>99.4 | 1<br>0.6 | 60<br>100.0 | -<br>- | 211<br>88.3 | 28<br>11.7 | <0.05 |
| I think it's a global problem | 124<br>79.0 | 33<br>21.0 | 47<br>78.3 | 13<br>21.7 | 160<br>66.9 | 79<br>33.1 | <0.05 |
| I think it is related to food safety | 150<br>95.5 | 7<br>4.5 | 58<br>96.7 | 2<br>3.3 | 218<br>91.2 | 21<br>8.8 | >0.05 |
| I think it's about saving resources | 155<br>98.7 | 2<br>1.3 | 59<br>98.3 | 1<br>1.7 | 220<br>92.1 | 19<br>7.9 | <0.05 |
| The Mediterranean diet does not contribute | 3<br>1.9 | 154<br>98.1 | 2<br>3.3 | 58<br>96.7 | 54<br>22.6 | 185<br>77.4 | <0.05 |
| I believe that the terms diet and healthy eating are synonymous | 96<br>61.1 | 61<br>38.9 | 37<br>61.7 | 23<br>38.3 | 172<br>72.0 | 67<br>28.0 | >0.05 |
| I think it is related to the concepts of ecological, and carbon footprint and biodiversity | 150<br>95.5 | 7<br>4.5 | 57<br>95.0 | 3<br>5.0 | 178<br>74.5 | 61<br>25.5 | <0.05 |

* Chi-Square

The percentages of undergraduates, dietitians, and other health professionals who believe that the production processes of foods can contribute to greenhouse gas emissions and water pollution are 96.8%, 96.7%, and 74.1%, respectively (p <0.05). Health professionals, compared to undergraduates and dietitians, have higher percentages of those who believe that the production processes of meat, poultry, and derivatives have significant environmental consequences, with values of 43.1%, 26.8%, and 8.3%, respectively (p<0.05).

Health professionals, compared to dietitians and undergraduates, have higher percentages of those who believe that the production processes of fruits and vegetables have significant environmental consequences, with values of 59.0%, 45.0%, and 42.0%, respectively (p<0.05). The percentages of those who believe that the production processes of processed packaged foods have significant environmental consequences are 94.9%, 90.0%, and 80.8% for undergraduates, dietitians, and health professionals, respectively (p<0.05).

Health professionals, compared to dietitians and undergraduates, have higher percentages of those who believe that foods requiring more water consumption are of plant origin, with values of 66.1%, 44.6%, and 28.3%, respectively (p<0.05). Health professionals, compared to dietitians and undergraduates, have higher percentages of those who believe that considering animal rights and welfare is not a concern in meat consumption, with values of 45.6%, 40.0%, and 31.2%, respectively (p<0.05) (**Table 4**).

The percentages of dietitians, undergraduates, and other health professionals who examine the nutritional labels on the products they purchase are 93.3%, 84.7%, and 73.2%, respectively (p<0.05). Dietitians are more likely to prioritize purchasing local products, with percentages of 80.0%, compared to health professionals (69.5%) and undergraduates (51.6%) (p <0.05).

The percentages of dietitians, undergraduates, and other health professionals in avoiding excessive food purchases are 100%, 94.9%, and 87.0%, respectively (p<0.05). Dietitians, undergraduates, and health professionals show percentages of 95.0%, 89.8%, and 77.0%, respectively, in being careful about evaluating food leftovers (p<0.05) (**Table 5**).

Health professionals are more likely to prioritize products with an organic certification, with percentages of 57.3%, compared to undergraduates (42.0%) and dietitians (35.0%) (p<0.05). Undergraduates, dietitians, and other health professionals show preferences for products produced seasonally, with percentages of 94.9%, 93.3%, and 83.7%, respectively (p<0.05). Undergraduates exhibit a higher percentage (98.7%) in paying attention to the price of the products they purchase compared to dietitians (91.7%) and other health professionals (90.0%) (p<0.05) (**Table 5**).

**Table 4. The Distribution of Participants' Approaches Towards the Acquisition and Consumption of Various Foods**

| | Undergraduates (n=157) | | Dietitian (n=60) | | Health Professionals (n=239) | | p* |
|---|---|---|---|---|---|---|---|
| | Yes | No | Yes | No | Yes | No | |
| | n<br>% | n<br>% | n<br>% | n<br>% | n<br>% | n<br>% | |
| Food production procedures have the potential to lead to high greenhouse gas emissions and water pollution | 152<br>96.8 | 5<br>3.2 | 58<br>96.7 | 2<br>3.3 | 177<br>74.1 | 62<br>25.9 | <0.05 |
| I don't think the environmental impact of chicken and its production processes is significant. | 42<br>26.8 | 115<br>73.2 | 5<br>8.3 | 55<br>91.7 | 103<br>43.1 | 136<br>56.9 | <0.05 |
| I think the environmental impact of milk and dairy production processes is significant. | 110<br>70.1 | 47<br>29.9 | 48<br>80.0 | 12<br>20.0 | 161<br>67.4 | 78<br>32.6 | >0.05 |
| I think the environmental impact of vegetable and fruit production processes is significant. | 66<br>42.0 | 91<br>58.0 | 27<br>45.0 | 33<br>55.0 | 141<br>59.0 | 98<br>41.0 | <0.05 |
| I think the environmental impact of bread and cereal production processes is significant. | 75<br>47.8 | 82<br>52.2 | 34<br>56.7 | 26<br>43.3 | 138<br>57.7 | 101<br>42.3 | >0.05 |
| I do not think that the environmental impact of the production processes of dried legumes is high. | 93<br>59.2 | 64<br>40.8 | 33<br>55.0 | 27<br>45.0 | 27<br>53.1 | 12<br>46.9 | >0.05 |
| I think the environmental impact of processed packaged foods production processes is significant. | 149<br>94.9 | 8<br>5.1 | 54<br>90.0 | 6<br>10.0 | 193<br>80.8 | 46<br>19.2 | <0.05 |
| Foods that require more water consumption are of animal origin | 101<br>64.3 | 56<br>35.7 | 46<br>76.7 | 14<br>23.3 | 89<br>37.2 | 150<br>62.8 | <0.05 |
| Foods that require more water consumption are of plant origin | 70<br>44.6 | 87<br>55.4 | 17<br>28.3 | 43<br>71.7 | 158<br>66.1 | 81<br>33.9 | <0.05 |
| I don't care about animal rights when it comes to meat consumption | 49<br>31.2 | 108<br>68.8 | 24<br>40.0 | 36<br>60.0 | 109<br>45.6 | 130<br>54.4 | <0.05 |
| It doesn't matter to me whether the fish comes from a farm or from the sea | 41<br>26.1 | 116<br>73.9 | 16<br>26.7 | 44<br>73.3 | 68<br>28.5 | 171<br>71.5 | >0.05 |

* Chi-Square

**Table 5. The Distribution of Participants' Approaches and Tendencies Towards Grocery Shopping and Environmentally Friendly Practices**

| | Undergraduates (n=157) | | Dietitian (n=60) | | Health Professionals (n=239) | | p* |
|---|---|---|---|---|---|---|---|
| | Yes | No | Yes | No | Yes | No | |
| | n % | n % | n % | n % | n % | n % | |
| I always review the nutritional information provided on the label | 133 84.7 | 24 15.3 | 56 93.3 | 4 6.7 | 175 73.2 | 64 26.8 | <0.05 |
| I pay attention to the brand and manufacturer. | 148 94.3 | 9 5.7 | 55 91.7 | 5 8.3 | 222 92.9 | 17 7.1 | >0.05 |
| I make sure to take into account the recommended expiration date. | 156 99.4 | 1 0.6 | 59 98.3 | 1 1.7 | 230 96.2 | 9 3.8 | >0.05 |
| I make sure it is local product. | 81 51.6 | 76 48.4 | 48 80.0 | 12 20.0 | 166 69.5 | 73 30.5 | <0.05 |
| I make sure it has an organic certificate. | 66 42.0 | 91 58.0 | 21 35.0 | 39 65.0 | 137 57.3 | 102 42.7 | <0.05 |
| I ensure that the food is suitable for seasonal production. | 149 94.9 | 8 5.1 | 56 93.3 | 4 6.7 | 200 83.7 | 39 16.3 | <0.05 |
| I make sure it is in the amount I can consume. | 152 96.8 | 5 3.2 | 57 95.0 | 3 5.0 | 218 91.2 | 21 8.8 | >0.05 |
| I pay attention to the price. | 155 98.7 | 2 1.3 | 55 91.7 | 5 8.3 | 215 90.0 | 24 10.0 | >0.05 |
| I make sure that the products are delicious. | 154 98.1 | 3 1.9 | 58 96.7 | 2 3.3 | 226 94.6 | 13 5.4 | >0.05 |
| I pay attention to its contribution to sustainability. | 96 61.1 | 61 38.9 | 41 68.3 | 19 31.7 | 147 61.5 | 92 38.5 | >0.05 |
| I make sure the packaging can be recycled or redesigned. | 80 51.0 | 77 49.0 | 32 53.3 | 28 46.7 | 132 55.2 | 107 44.8 | >0.05 |
| I take care to have an environmentally friendly logo. | 77 49.0 | 80 51.0 | 31 51.7 | 29 48.3 | 136 56.9 | 103 43.1 | >0.05 |
| I'm willing to pay more for sustainably produced food and drink products. | 84 53.5 | 73 46.5 | 32 53.3 | 28 46.7 | 140 58.6 | 99 41.4 | >0.05 |
| I avoid excessive food purchases. | 149 94.9 | 8 5.1 | 60 100.0 | - - | 208 87.0 | 31 13.0 | <0.05 |
| I take care to use food scraps. | 141 89.8 | 16 1.2 | 57 95.0 | 3 5.0 | 184 77.0 | 55 23.0 | <0.05 |
| I separate my garbage (plastic, glass, paper, batteries, food, etc.). | 85 54.1 | 72 45.9 | 34 56.7 | 26 43.3 | 131 54.8 | 108 45.2 | >0.05 |

*Chi-Square

## DISCUSSION

The expected global population increase, coupled with environmental concerns such as climate change, exerts greater pressure on our planet's limited natural resources. The future food system should meet the nutritional needs for the health of future generations, while also ensuring the sustainability of natural ecosystems in economic, social, and environmentally appropriate ways.[19] Therefore, dietitians need to be adequately equipped to raise awareness in society about sustainable nutrition approaches with low environmental impact, contributing to a healthy life for current and future generations, as well as to food and nutrition security.

When evaluating the participants' status of receiving education on sustainable nutrition, it was found that dietitians and undergraduates had a higher percentage compared to health professionals (p<0.05). However, a significant lack of education on sustainable nutrition was identified. In Akay's study,[12] although the percentage of nutrition and dietetics students receiving education on sustainable nutrition was higher than that of medical faculty students, no statistically significant difference was observed (p>0.05). In contrast to our study's results, Engin and Sevim[20] reported in their study that there was no significant difference between sustainable nutrition behavior and knowledge scores and the field of study (p >0.05). When assessing their knowledge levels on sustainable nutrition, dietitians and undergraduates claimed to be very good at it by 13.3% and 3.8%, respectively, while no one from the health professionals claimed to be very good. Similar to our study results, Ünal Özen[11] stated that 2.9% of dietitians and 0.6% of nutrition and dietetics students expressed themselves as very good in sustainable nutrition. Similarly, there were no individuals from other department students who claimed to be very good.[11] The reason for dietitians and nutrition and dietetics students having such a low percentage of claiming to know sustainable nutrition very well could be due to the lack of mandatory curriculum in sustainable nutrition in undergraduate education. The reason for health professionals' not-very-good statements may indicate a lack of public awareness on this issue.

The percentages of correct answers to the statements 'Sustainable nutrition contributes to the economy, I believe it is a global issue, I believe it is related to resource conservation, the Mediterranean diet has no contribution, I believe it is associated with the concepts of ecological footprint, carbon footprint, and biodiversity' are similar between dietitians and undergraduates (78.3% - 100%), while in the health professionals (77.4% - 92.1%), this rate is significantly lower ($p<0.05$).

Undergraduates and dietitians have answered 'yes' to the statement 'The production processes of foods can cause an increase in greenhouse gases and pollution of waters' compared to health professionals (respectively, 96.8%, 96.7%, 74.1%, $p<0.05$). In a study, medical students stated that foods high in fat and sugar and meat and meat products have a greater impact on greenhouse gas emissions, while undergraduates indicated that foods high in fat and sugar and fruits and vegetables have a greater impact.[12] In our study, health professionals do not believe that the production processes of meat, poultry, and derivatives have significant environmental consequences compared to undergraduates and dietitians (respectively, 43.1%, 26.8%, 8.3%, $p<0.05$). Lentz et al.[21] found that consumers are less aware of the environmental impact of meat consumption compared to other sustainable nutrition behaviors. Health professionals believe that the production processes of vegetables and fruits have significant environmental consequences compared to undergraduates and dietitians (respectively, 59.0%, 45.0%, 42.0%, $p<0.05$). In a study, participants from other departments believed that the production processes of vegetables and fruits have the most environmental impact compared to undergraduates.[11] In another study in the field of sustainable nutrition, it was reported that nutrition and dietetics students exhibit a more environmentally conscious attitude compared to nursing students.[22] The reason why individuals outside the Nutrition and Dietetics group have these thoughts may be due to the absence of courses in their curricula that would affect environmental awareness during their education.

Dietitians and undergraduates predominantly believe that foods requiring more water consumption are of animal origin (76.7%, 64.3%, respectively), while health professionals think that foods requiring more water are of plant origin (66.1%) ($p<0.05$). The higher correct answer rates of dietitians and undergraduates may stem from learning about the Mediterranean diet, which includes a high proportion of plant-based foods with a low water footprint, in their undergraduate courses.[23]

When evaluating participants' approaches to the products they purchase while food shopping, most dietitians, undergraduates, and health professionals examine the nutrition labels on the products they purchase (93.3%, 84.7%, 73.2%, respectively, $p<0.05$). Like our results, a study conducted in 2012 found that the rate of habitually reading food labels among Turkish consumers was 76.5%.[24] Another study showed that nutrition and dietetics students have a higher rate of reading food labels compared to other health science students.[25]

Dietitians and health professionals are more inclined to ensure that the products they purchase are locally produced compared to undergraduates (80.0%, 69.5%, 51.6%, respectively, $p<0.05$). In a study by Engin and Sevim,[20] university students scored the lowest average on the sustainable behavior scale for the item 'I pay attention not to consume imported food.' In the same study, students scored the highest on the item 'I pay attention to taking as much food as I can eat on my plate'.[20] Similarly, in our study, dietitians, undergraduates, and health professionals mostly avoid excessive food purchases (100%, 94.9%, 87.0%, respectively, $p<0.05$).

Health professionals are more inclined to ensure that the products they purchase have an organic certification compared to undergraduates and dietitians (57.3%, 42.0%, 35.0%, respectively, $p<0.05$). In a study conducted on university students, it was found that they prioritize taste, freshness, and price most when buying food, and organic certification is least considered.[26]

Undergraduates, dietitians, and health professionals mostly ensure that the products they purchase are produced in accordance with the season (94.9%, 93.3%, 83.7%, respectively, $p<0.05$). Similar to our study results, Kayak[27] in a study on Family Health Center employees, found that doctors scored the highest on the item of seasonal food consumption in terms of sustainable nutrition awareness ($p<0.05$).

## CONCLUSION

Dietitians and undergraduates have been found to possess greater knowledge and awareness of sustainable nutrition compared to health professionals. However, they express a lack of adequate competence in this area. To promote the widespread adoption of the concept of sustainable nutrition in society, dietitians should be provided with the necessary training, nutritional guidelines should be developed, and policies should be formulated to create awareness. Given the limited studies on sustainable nutrition, there is a need for further research on this topic.

## ETHICAL DECLARATIONS

**Ethics Committee Approval**: The study was obtained from Ankara Yıldırım Beyazıt University Ethics Committee (Date: 14.02.2020, Decision No: 09).

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Review / Derleme


# Comprehensive Mini Review of Pediatric Sleep Disorders: Types, Impact on Health and Current Management Strategies

## Çocuklarda Uyku Bozukluklarının Kapsamlı Mini İncelemesi: Türleri, Sağlık Üzerindeki Etkileri ve Güncel Yönetim Stratejileri

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## Abstract

This mini review explores the health implications of sleep disorders in children and examines current treatment approaches. A comprehensive analysis of recent literature from PubMed and Google Scholar, focusing on studies published between 2019 and 2024, was conducted to assess the types of sleep disorders in children, their impact on health, and effective management strategies. The review details the significant impact of sleep disorders on children's physical, mental, and emotional health, highlighting issues such as impaired glucose control, inflammation, obesity, behavioral problems, and emotional dysregulation. Effective treatment methods and management strategies include sleep hygiene, behavioral therapies, and innovative interventions like bright light therapy combined with cognitive-behavioral therapy. Early detection and comprehensive management of sleep disorders in children are crucial to improving overall child health and well-being.

**Keywords**: Sleep disorders, child health, sleep hygiene, treatment, prevention

## Öz

Bu mini derleme, çocuklarda uyku bozukluklarının sağlık üzerindeki etkilerini incelemekte ve mevcut tedavi yaklaşımlarını değerlendirmektedir. PubMed ve Google Scholar'da 2019-2024 yılları arasında yayınlanmış çalışmalara odaklanarak, çocuklardaki uyku bozukluklarının türleri, sağlık üzerindeki etkileri ve etkili yönetim stratejileri hakkında kapsamlı bir literatür analizi yapılmıştır. Derleme, uyku bozukluklarının çocukların fiziksel, zihinsel ve duygusal sağlığı üzerindeki önemli etkilerini detaylandırmakta olup, glukoz kontrolünün bozulması, inflamasyon, obezite, davranış sorunları ve duygusal düzensizlik gibi sorunları vurgulamaktadır. Etkili tedavi yöntemleri ve yönetim stratejileri arasında uyku hijyeni, davranış terapileri ve bilişsel-davranışçı terapi ile birleştirilen parlak ışık terapisi gibi yenilikçi müdahaleler bulunmaktadır. Çocuklarda uyku bozukluklarının erken tespiti ve kapsamlı yönetimi, genel çocuk sağlığı ve refahını iyileştirmek için büyük önem taşımaktadır.

**Anahtar Kelimeler**: Uyku bozuklukları, çocuk sağlığı, uyku hijyeni, tedavi, önleme

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## INTRODUCTION

The idea that pediatric sleep health is different from adult sleep medicine was first presented decades ago. Since then, researchers have worked to describe normal sleep patterns at different ages and to create treatment plans for various sleep issues in children.[1]

Sleep is essential for children's overall health and development. It plays a crucial role in their physical growth, cognitive abilities, and emotional well-being. Adequate sleep supports the body's growth processes, helps the brain consolidate learning and memory, and regulates mood and behavior. Without sufficient sleep, children can experience a range of health and developmental issues, making the understanding and management of pediatric sleep critical.

Various studies have highlighted the prevalence of sleep disorders in children, underscoring the significance of addressing this issue. In one study, it was found that 39.36% of children experienced one or more sleep-related problems, with a higher prevalence observed among boys compared to girls.[2]

Another review, encompassing several studies, reported that the prevalence of sleep problems in children ranged from 15.3% to 76.3%.[3] These findings highlight that sleep disorders affect a significant portion of the pediatric population, emphasizing the need for effective assessment and intervention strategies. For instance, a recent cross-sectional study conducted in Riyadh, Saudi Arabia, over two months from August to September 2022, identified bed-time resistance as the most prevalent sleep issue at 71.3%. This was followed by sleep-onset delay at 58.1%, difficulty waking up in the morning at 41.3%, and interrupted sleep patterns at 31%. These results align with earlier studies, such as those by Fadime et al., who found bedtime resistance to be the most common sleep problem at 48.1%, and BaHammam et al., who reported a prevalence of 26.2%.[4] These consistent findings across different studies underscore the widespread nature of sleep issues among children and the urgent need for targeted interventions.

Sleep disorders in children can arise from a variety of factors. Medical conditions such as asthma, allergies, and gastrointestinal issues can disrupt sleep patterns. Psychological factors, including anxiety and depression, also play a significant role, as do behavioral issues and irregular sleep routines. Additionally, environmental factors like excessive screen time before bed or an uncomfortable sleep environment can contribute to sleep problems. Understanding these diverse causes is essential for effective diagnosis and treatment of sleep disorders in children.

The purpose of this review is to examine the impact of sleep disorders on child health and to explore various treatment approaches. By highlighting how sleep problems affect overall health and discussing effective strategies for management, this review aims to provide valuable insights for improving pediatric sleep care.

## MATERIAL AND METHOD

A comprehensive review of pediatric sleep disorders was conducted using recent literature from PubMed and Google Scholar. Relevant studies published between 2019 and 2024 were selected based on their focus on sleep disorders, their impact on health, and management strategies. Data were analyzed to summarize the prevalence, health effects, and treatment approaches for pediatric sleep disorders.

### Sleep Disorders and Child Health

Sleep disorders significantly impact children's health and development. According to the International Classification for Sleep Disorders, 3rd Edition (ICSD-3),[5] these disorders are categorized into several groups: insomnia, parasomnias, hypersomnias, sleep-related breathing disorders, circadian rhythm disorders, and sleep-related movement disorders. Common sleep issues in children include insomnia, which may result from factors such as poor sleep habits or behavioral issues. Circadian rhythm disorders, like delayed sleep-wake phase, affect the timing of sleep. Disorders related to breathing, such as obstructive sleep apnea, interfere with normal breathing during sleep. Central hypersomnolence disorders, including narcolepsy, cause excessive daytime sleepiness. Parasomnias, such as sleepwalking and night terrors, involve abnormal behaviors during sleep. Additionally, movement disorders like restless legs syndrome can disrupt sleep. Identifying and understanding these disorders is essential for effective treatment and overall child health improvement.[5]

Sleep disorders can have significant effects on children's physical health. Poor sleep quality and disrupted sleep patterns are linked to problems such as impaired blood glucose control and inflammation. Mixed results have been found regarding the impact of sleep duration on inflammation and blood pressure.[6] Additionally, children with sleep issues are at higher risk for obesity, musculoskeletal pain, and injuries.[6] Addressing these sleep problems is important for maintaining overall physical health in children.[6]

Lack of adequate sleep can have a profound effect on children's mental and emotional well-being. Research indicates that poor sleep, including insufficient duration and quality, is associated with behavioral issues, learning difficulties, and emotional problems.[6] Studies have found that disrupted sleep patterns are linked to an increased risk of depression and anxiety in older children and adolescents.[6] While there is some evidence suggesting that improving sleep may help mitigate these symptoms, the exact relationship between sleep variability and specific emotional disorders remains unclear. Additionally, inadequate sleep can affect emotional regulation, making it harder for children to manage their feelings and behaviors effectively. Addressing sleep issues is crucial for supporting better mental and emotional health in children.[6]

**Treatment Approaches and Management**

Addressing pediatric sleep disorders often begins with enhancing sleep hygiene. This involves setting up an ideal sleep environment—keeping bedrooms dark, quiet, and well-ventilated—and adhering to consistent sleep schedules while avoiding stimulating activities before bedtime. Monitoring and limiting caffeine and substance use are also key factors.

Behavioral and cognitive-behavioral therapies are effective for managing issues such as insomnia and irregular sleep patterns. These approaches focus on changing negative sleep-related thoughts and behaviors and establishing healthy sleep routines. Incorporating these therapies can also benefit children with related conditions like anxiety and ADHD, as they address broader behavioral and cognitive challenges impacting sleep.[7]

For sporadic sleep terrors, reassurance to parents often alleviates anxiety, as most children outgrow the condition. Avoid intervening during episodes to prevent increased confusion and aggression. Ensure good sleep hygiene and an optimal sleep environment, as sleep deprivation can exacerbate terrors. Avoid caffeine and medications that may trigger episodes. Reduce stress and address factors that may disturb sleep, such as discomfort or environmental noises. Safety precautions should be taken to protect the child.[8]

A study on combining morning bright light therapy with cognitive behavioral therapy (CBT) in children with delayed sleep phase disorder (DSPD) found significant improvements in sleep timing, duration, and overall sleepiness. Light therapy, involving exposure to 10,000 lux light boxes each morning, was effective in resetting the circadian rhythm and sustained benefits for six months.[7]

When addressing pediatric sleep disorders, particularly severe cases like sleep terrors, initial medication approaches are crucial. Clonazepam may be prescribed for short-term use to mitigate frequent and severe episodes, ideally administered 90 minutes before bedtime to align with the timing of disturbances. Melatonin has also shown efficacy in managing these disorders. Additionally, tricyclic antidepressants, selective serotonin reuptake inhibitors, mirtazapine, and ramelteon are options, though their success can vary. For frequently occurring sleep terrors, anticipatory awakening—waking the child 30 minutes before the expected episode—can be effective. If underlying psychological issues are suspected, psychotherapeutic interventions should be considered.[8]

For treating pediatric sleep disorders, several medical treatments are being evaluated. Oral iron supplements and alpha-2-delta ligands have shown potential for conditions like Restless Legs Syndrome (RLS) and Periodic Limb Movement Disorder (PLMD),[9] although these treatments lack broad regulatory approval and are primarily supported by case reports rather than large-scale trials. There is a need for further studies, including randomized controlled trials, to confirm their effectiveness and explore other treatments such as behavioral therapies and vitamin D. Additionally, effective strategies must be developed for managing RLS, particularly when it co-occurs with conditions like ADHD or anxiety.[9]

In children with neurodevelopmental disorders (NDDs), the management of sleep disorders begins with sleep hygiene, similar to other pediatric groups. This includes creating a conducive sleep environment, maintaining a consistent sleep schedule, and practicing good sleep habits. Research highlights that children with autism spectrum disorder (ASD) often have low serum ferritin levels, which can negatively impact sleep. Addressing these deficiencies, along with maintaining optimal sleep hygiene, is essential for effective management.[10]

Pharmacological interventions are frequently utilized. Melatonin has shown efficacy in managing sleep disturbances in children with NDDs, particularly those with delayed sleep phase syndrome. Controlled trials have demonstrated that doses of 5-15 mg taken 20-30 minutes before bedtime significantly improve sleep.[10] Additionally, clonidine has been beneficial for treating sleep and behavioral disorders in children with ASD, as evidenced by pilot studies.[10] Clonazepam is another option, particularly effective for children with Williams syndrome who experience movement arousal disorders, providing targeted relief for these specific sleep issues.[10]

Adenotonsillectomy is the first-line treatment for obstructive sleep apnea syndrome (OSAS) in children over two years old with adenotonsillar hypertrophy, significantly improving behavior, quality of life, and polysomnographic findings. The Childhood Adenotonsillectomy Trial (CHAT) confirmed that 79% of surgical patients had normalized polysomnogram results at seven months, compared to 49% in the watchful waiting group.[11]

These emerging approaches highlight the importance of tailored interventions based on individual needs. Continuous research and adaptation of treatment strategies will enhance the effectiveness of managing pediatric sleep disorders.

**Prevention And Intervention Strategies**

Early intervention programs are crucial for the early diagnosis and treatment of sleep disorders in children. Educating and raising awareness among parents and teachers through targeted campaigns can significantly contribute to better sleep health. Implementing sleep-friendly practices and support systems within school and home environments is essential to ensure that children have the proper conditions for healthy sleep routines.

Early detection and intervention for sleep disorders can be seamlessly integrated into regular child health checkups. Despite the high prevalence of these disorders, their underdiagnosis reflects a gap in awareness and access to appropriate care. Enhancing parental education about sleep's importance during these mandated checkups is essential, as primary care providers and pediatricians may often miss these issues.

Education and awareness efforts are critical. In Japan, health checkups for children at various developmental stages can include a two-week sleep log recorded by parents. This data can help identify sleep problems, offer guidance on sleep management, and suggest consultations with pediatricians as needed.[11]

Moreover, adjustments in school and home environments are vital in preventing sleep disorders. An AI-powered application is being developed to assist parents in monitoring their child's sleep quality and alerting them to potential issues. This tool aims to facilitate timely pediatric consultations, which, in turn, can help alleviate postpartum depression and reduce the risk of child abuse by addressing the stress and poor sleep quality that often affect both children and their caregivers.[11]

## DISCUSSION

This mini-review has examined the diagnosis and treatment approaches for sleep disorders in children. Sleep disorders have extensive effects on children's health, impacting their physical, mental, and emotional development. Poor sleep can negatively influence school performance, social relationships, and overall quality of life. Moreover, it can affect parents' mental health, leading to issues in family dynamics. Therefore, early diagnosis and effective management of sleep disorders in children are crucial for their well-being and healthy development.

Despite advancements in understanding and managing pediatric sleep disorders, significant gaps remain. More research is needed to identify specific diagnostic criteria and effective interventions tailored to different age groups and special populations, such as children with neurodevelopmental disorders. Additionally, further studies should explore the long-term effects of various treatment approaches, the role of genetic and environmental factors, and the development of innovative technologies for monitoring and managing sleep disorders. Addressing these gaps will enhance our ability to prevent and treat sleep disorders, ultimately improving children's health outcomes and quality of life.

## CONCLUSION

Sleep disorders significantly impact children's health and development. These disorders, as classified by the International Classification for Sleep Disorders, include insomnia, parasomnias, hypersomnias, sleep-related breathing disorders, circadian rhythm disorders, and sleep-related movement disorders. Effective treatment and improvement of overall child health necessitate the identification and understanding of these disorders. Poor sleep quality and disrupted sleep patterns can lead to issues such as impaired blood glucose control, inflammation, obesity, musculoskeletal pain, and increased risk of injuries. Addressing these sleep problems is crucial for maintaining physical health. Additionally, inadequate sleep can profoundly affect mental and emotional well-being, contributing to behavioral issues, learning difficulties, depression, anxiety, and emotional dysregulation.

Early detection and intervention for sleep disorders are essential. Despite the high prevalence of sleep disorders, healthcare utilization remains low due to poor awareness and access to care. Educating parents and teachers through targeted campaigns is crucial. In Japan, for instance, regular health checkups for children could involve parents recording their child's sleep patterns. This information can help identify sleep problems and provide guidance on sleep management, encouraging timely pediatric consultations. Effective management includes enhancing sleep hygiene, behavioral and cognitive-behavioral therapies, and, when necessary, medication. Advanced approaches, such as combining bright light therapy with cognitive-behavioral therapy, show promising results in treating specific disorders like delayed sleep phase disorder. By addressing sleep disorders, we can alleviate related health issues and improve children's overall well-being..

## ETHICAL DECLARATIONS

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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