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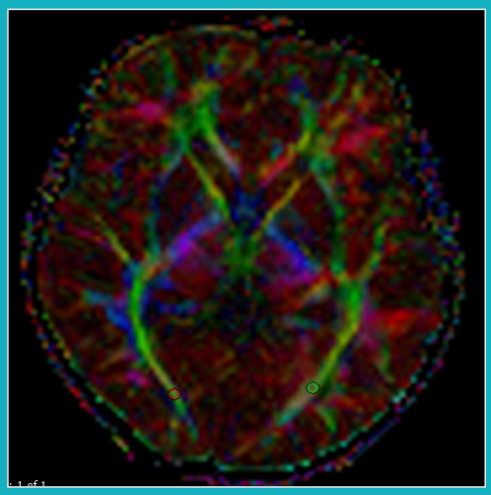

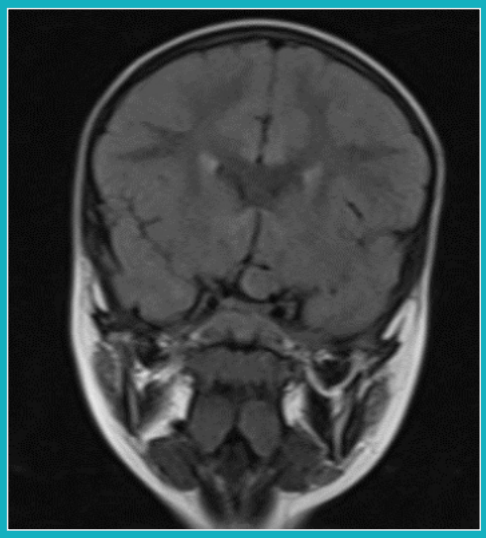



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# CONTENTS

## Commentary



## Original Articles

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BEZMİÂLEM science

# CONTENTS

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# EDITORIAL

**Dear readers,**

We are with you again in the 4th issue of 2021 of our journal. In these days when we have returned to face-to-face training with the beginning of autumn, our scientific studies, academic activities and partially congresses have entered our agenda in a new format in the new normalization process. I would like to give you the good news that the number and quality of articles in our journal have reached the highest level this year. Due to increasing number of articles and in order to increase our quality of our journal, we decided to innovate in our system with our publisher company and we closed our old system as of the end of August, but we continued to evaluate the articles in the system from our old site. We also started to accept submission of articles in the new system. Every innovation brings with it some challenges. This bilateral situation will continue until the new year and if our company agreement is renewed in the new year, we will continue with this system.

In this issue, I would like to talk about our cover image and selected article; "Evaluation of Optical Radiation from Visual Pathways with Diffusion Tensor Imaging in Patients with Neurofibromatosis Type 1" by Dilek Hacer Çeşme.

We are very happy to be together once again with beautiful topics in this issue: "Evaluation of Optical Radiation from Visual Pathways with Diffusion Tensor Imaging in Patients with Neurofibromatosis Type 1" by Dilek Hacer Cesme, "The Status of Iron Stores in the Women with Beta Thalassemia Minor" by Karaaslan et al., "Longitudinal Changes in the Eating Habits of Patients with Cancer Receiving Palliative Care" by Çeltek et al., "Relationships among Increasing Age, Sexual Dysfunction, and Sexual Quality of Life in Married Women of Reproductive Age" by Zobar ve Kahyaoğlu Süt., and "Effects of Oral Alprazolam and Oral Tramadol on Anxiety and Analgesia in Patients Undergoing Breast Cancer Surgery" by Ayan and Meynacı Köksal are among our prominent articles.

As the year 2022 approaches, I would like to state that we expect your articles on clinical studies and experimental studies. Since we are a university journal and a multidisciplinary journal, I am announcing in advance that technology-based articles are also on our agenda next year, that we will create our additional issue with a focus on technology, and if you have existing patents, there will be an opportunity to publish them. Our country has to increase its targets and start the national health industry move in this process that the world has come to. Our university has a pioneering mission in this field. With this awareness, I would like to emphasize the importance of the subject once again.

As it is known, each issue of our journal requires a lot of effort. I would like to thank my associate editors for their hard work. I wish you all the best to meet new goals and successes in the New Year with our referees, publisher and you, our esteemed readers.

Kind regards

**Prof. Dr. Adem AKÇAKAYA**
**Editor in Chief**

Commentary

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Bezmialem Science 2021;9(4):380-1

# Method Selection in the Treatment of Achalasia

## Akalazya Tedavisinde Yöntem Seçimi

Adem AKÇAKAYA

Bezmialem Vakıf University Faculty of Medicine, Department of General Surgery, İstanbul, Turkey

**My dear readers,**

Our topic in this article is which method should be preferred in the treatment of achalasia?

Achalasia is a primary esophageal motility disorder. It is a disease that manifests itself as difficulty in swallowing due to the absence of peristalsis in the esophagus and the inability to relax the lower esophageal sphincter. Sir Thomas Willis first described achalasia in 1672. In 1929, Hurt and Rake realized that the disease was caused by an inability to relax the lower esophageal sphincter (LES). They used the term achalasia which meaned inability to relax.

It is seen in 1.8 to 12.6 people per 100,000 in the population. Although it is shown that the gender distribution is equal in some publications, it is accepted that it is slightly more common in women. Although the age distribution varies between 20-60 years, it is most commonly seen in the 35-45 age group (1).

The primary etiology of achalasia is believed to be selective inhibitory neuronal loss in the myenteric plexus of the distal esophagus and lower esophageal sphincter, resulting in a neuronal imbalance in excitatory and inhibitory activity. Excitatory neurons secrete acetylcholine, while inhibitory neurons mainly secrete vasoactive intestinal peptide and nitric oxide. This imbalance ultimately results in a hypertensive lower esophageal sphincter that cannot relax (1,2). The thickness of the muscles in the esophageal wall and the lower end valve may reach 2-3 times the normal. Due to this situation, the lid at the lower end does not allow the passage of foods, as it cannot relax during swallowing and because the muscle thickness increases excessively.

**What are the Symptoms of Achalasia?**

Since the symptoms of the disease appear gradually, its recognition is often delayed. Dysphagia is the most important symptom of achalasia. The patient has difficulty swallowing both solid and liquid foods. Regurgitation is the return of food residues accumulated in the esophagus to the mouth and is the second most common symptom. This condition can be confused with reflux disease. If the regurgitation happens at night, food residues escaping back can block the trachea. Chest pai**n** is another common symptom in achalasia. Patients with achalasia eat slowly. They usually have water with them and drink water immediately after the bite. Patients are afraid to eat in public. Frequent pulmonary complications can be seen and accordingly their general condition deteriorates over time. Another common complication is damage to the esophagus. Bleeding and anemia may occur due to this. Although rare, rhythm disturbances in the heart and rupture in the esophagus can be seen. The most important problem is the risk of developing cancer. Cancer may develop in 2 to 7% of patients due to prolonged achalasia or food irritation and esophagitis.

**How is Achalasia Diagnosed?**

Achalasia should be considered in patients with swallowing difficulties. These patients should first undergo endoscopy. Thus, achalasia is differentiated from other diseases that cause swallowing difficulties such as esophageal cancer, stomach cancer

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and esophageal strictures. If necessary, a biopsy is taken and sent for analysis. Barium esophagogram is a valuable method in diagnosis. The esophagus appears enlarged and the tip of the esophagus is thinned and has the appearance of a bird's beak in barium esophagogram. However, if the esophagus is not enlarged yet in early-stage patients, there may be errors in the diagnosis. Examination of the contraction movements of the esophagus during swallowing with a device which we call Esophageal Manometr**y** is the most important examination method for diagnosis. Loosening and contraction of the lids may be observed. In manometry, the contraction disorder in the esophagus muscles can be easily seen and the lower lid does not open during swallowing. The high pressure here during swallowing is diagnostic. High resolution manometry is accepted as the current gold standard test in the diagnosis of achalasia (3,4).

**How is Achalasia Treated?**

**Dear readers,**

I always advise my students to rank the diagnosis and treatment from simple to complicated, from inexpensive to expensive, from non-invasive to interventional methods. Here we apply the same rule. The Chicago Classification helps us in determining the treatment (5,6). It is recommended to apply an algorithm as follows: (1) Patients with suspected symptomatic achalasia should undergo upper endoscopy to exclude another pathology and pseudoachalasia. High-resolution manometry (HRM) and barium esophagogram are performed to confirm the diagnosis. After the diagnosis is finalized, the treatment method is selected according to the manometric subtypes of achalasia (Chicago classification), patient preference and the experience of the doctor. In type I and II achalasia, balloon dilation should be done gradually. If there is no response to this, surgical myotomy should be performed. Appropriate treatment for type III achalasia may be surgical myotomy or POEM (Peroral Endoscopic Myotomy). Surgical myotomy can be performed either openly or laparoscopically. It is mostly performed laparoscopically and laparoscopical myotomy is the most effective method that we use today in the treatment of achalasia. It is preferred in patients younger than 40 years of age, patients with recurring symptoms after endoscopic balloon dilatation, patients with esophageal folds, diverticulum, very dilated (greater than 8 cm) or previous esophageal surgery. The effectiveness of surgical treatment is higher than other treatment methods. We perform our operations laparoscopically in our center and simultaneously check the effectiveness of the operation and whether there is any damage to the mucosa with gastroscopy. The basic procedure here is to cut the muscles that cannot relax, namely myotomy. During the procedure, we usually add one of the antireflux procedures to prevent gastroesophageal reflux that may develop after the surgery. In this way, the patient has a more comfortable follow-up period than other procedures, as the reflux complication after the intervention is reduced.

After the intervention, patients should be followed up with barium esophagogram and endoscopy for symptom recurrence and reflux complications. In patients in whom the disease recurs, balloon dilatation, surgical myotomy or POEM can be applied again, depending on the availability.

If patients are not suitable for definitive treatment for some reason, if they have comorbidities, smooth muscle relaxants such as calcium channel blocker (Nifedipine) or nitrate (Isosorbide dinitrate) and botulinum toxin can be used. The effect of botulinum toxin injection is temporary and can last for 6 to 12 months.

**My dear readers,**

To summarize; most diseases of the esophagus are associated with motor function. I would like to emphasize once again how important the function of eating and swallowing is for a healthy life. In patients with swallowing difficulties, it is necessary to exclude life-threatening diseases such as cancer. For this reason, achalasia should be considered in patients with any dysphagia and gastroesophageal reflux disease who do not benefit from drug treatment. Before treatment, gastroscopy and high-resolution manometry should be performed. Although each patient is evaluated individually, surgery is the most effective treatment method in these patients. Another thing that patients should not forget is that they will not have the opportunity to eat whatever they want, like in the pre-disease period. After the treatment, they will learn over time what and how much they should eat with their own experiences. The success of the treatment is directly proportional to the experience of the center and the physician. As one of the centers that perform the most of the achalasia surgeries in Istanbul, our experience has shown that if there are complaints of difficulty in swallowing, feeling of being stuck, waking up like choking at night, a specialist should definitely be consulted and necessary examinations should be made.

All the best, I wish you a healthy day...

## References


1. Vaezi MF, Pandolfino JE, Yadlapati RH, Greer KB, Kavitt RT. ACG Clinical Guidelines: Diagnosis and Management of Achalasia. Am J Gastroenterol 2020 Sep;115:1393-411.
2. Gyawali CP. Achalasia: new perspectives on an old disease. Neurogastroenterol Motil 2016;28:4-11.
3. Pandolfino JE, Gawron AJ. Achalasia: a systematic review. JAMA 2015:1841-52.
4. Kahrilas PJ, Bredenoord AJ, Fox M, et al. The Chicago classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil 2015;27:160-74.
5. Pandolfino JE, Kwiatek MA, Nealis T, et al. Achalasia: A new clinically relevant classification by high-resolution manometry. Gastroenterology 2008;135:1526-33.
6. Kahrilas PJ, Bredenoord AJ, Fox M, Gyawali CP, Roman S, Smout AJ, et al. The Chicago classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil 2015;27:160-74.

Original Article

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# Evaluation of Optical Radiation from Visual Pathways with Diffusion Tensor Imaging in Patients with Neurofibromatosis Type 1

## Nörofibromatosis Tip 1'li olgularda Görme Yolaklarından Optik Radyasyonun Difüzyon Tensör Görüntüleme ile Değerlendirilmesi

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## ABSTRACT

**Objective:** It was investigated whether patients with neurofibromatosis type 1 (NF1) with and without optic glioma (OG) differed from the healthy control group in terms of diffusion tensor imaging (DTI) parameters obtained from optic radiation.

**Methods:** Eighty three patients and 36 healthy controls followed with the diagnosis of NF1 were included in the study. Routine MRI and DTI were applied to all subjects. Fractional anisotropy (FA), mean diffusity (MD), radial diffusity (RD) and axial diffusity (AD) values were calculated by placing ROI on the right and left optic radiation on colored FA maps. Patients with OG detected by conventional magnetic resonance imaging (n=19) were classified as group 1, patients with NF1 without OG (n=64) were classified as group 2 and they were compared with the healthy control group in terms of DTI parameters.

**Results:** The right and left optic radiation FA values of the patients in group 1 and group 2 were significantly different when compared with the healthy control group. Optical radiation FA values were significantly lower than healthy control group. MD values in group 1 patients with OG were significantly higher than healthy control group. Optic radiation RD values were significantly higher in group 1 and group 2 compared with healthy control group.

**Conclusion:** There appears to be microstructural damage in optic radiation in patients with NF1 with or without OG. The idea that

## ÖZ

**Amaç:** Çalışmamızda, optik gliomu (OG) bulunan ve/veya bulunmayan nörofibromatosis tip 1'li (NF1) olgularda görme yolaklarından optik radyasyondan elde edilen difüzyon tensör görüntüleme (DTG) parametrelerinin sağlıklı kontrol grubu ile farklılık gösterip göstermediğini araştırmayı amaçladık.

**Yöntemler:** NF1 tanısı ile takip edilen 83 olgu ve 36 sağlıklı kontrol çalışmaya dahil edildi. NF1'li olgular ve sağlıklı kontrol grubuna rutin manyetik rezonans görüntüleme ve DTG uygulandı. Renkli FA haritalarında sağ ve sol optik radyasyona ROI yerleştirilerek fraksiyonel anizotropi (FA), mean diffusity (MD), radial diffusity (RD) and axial diffusity (AD) değerleri hesaplandı. Konvasiyonel MRG ile OG saptanan olgular (n=19) grup 1, OG bulunmayan NF1'liler (n=64) grup 2 olarak sınıflandırılarak sağlıklı kontrol grubu ile karşılaştırıldı.

**Bulgular:** Grup 1 ve grup 2 NF1'li olguların sağ ve sol optik radyasyon FA değerleri sağlıklı kontrol grubu ile karşılaştırıldığında anlamlı farklılık saptandı. Grup 1 ve grup 2 optik radyasyon FA değerleri kontrollere göre anlamlı derecede düşüktü. OG bulunan olgularda MD değerleri kontrollere göre anlamlı yüksekti. Grup 1 ve grup 2 olgularda optik radyasyon RD değerleri kontrollere göre anlamlı yüksekti. Grup 1 ile grup 2 arasında optik radyasyon FA değerleri açısından anlamlı farklılık saptanmadı.

**Sonuç:** NF 1'li olgularda OG bulunsun veya bulunmasın görme

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changes in FA values detected in optic radiation in visual pathways in patients with NF1 can be predicted in the early period of visual impairment is promising in terms of treatment planning and management.

**Keywords:** Neurofibromatosis type 1, optic gliom, diffusion tensor imaging, fractional anisotropy

yolaklarından optik radyasyonda mikroyapısal düzeyde hasarlanma mevcuttur. NF1'li olgularda görme yollarında özellikle optik radyasyonda tespit edilen FA değerlerindeki değişikliklerin gelecekteki görme bozukluğunu erken dönemde tahmin edilebileceği öngörüsü tedavi planlanması ve yönetimi açısından umut vericidir.

**Anahtar Sözcükler:** Nörofibromatos tip 1, optik gliom, difüzyon tensör görüntüleme, fraksiyonel anizotropi

## Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominant disease that results in decreased production of neurofibromin, a tumor suppressor protein, due to mutation or deletion in the NF1 gene on chromosome 17. NF1 affects almost all organs and systems in the body. Pigment abnormalities (café-au-lait macules, skinfold frecklings, Lisch nodules), peripheral and central nervous system tumors (neurofibromas and gliomas), learning and attention problems, autism spectrum disorders, bone abnormalities (long bone dysplasias, scoliosis), seizures, sleep disorders, and vasculopathies (moyamoya syndrome, renal artery stenosis) are common in affected patients (1,2).

The incidence of optic glioma (OG) in children with NF1 is approximately 15-20%, and vision loss accompanies up to 35-50% (1-4). OGs are usually seen in children younger than 7 years old. Determining the timing of treatment of NF1-associated OGs appears to be a clinical challenge. Visual symptoms include loss of visual acuity, proptosis, strabismus, and nystagmus. NF1-related OGs are infiltrative and tend to progress along the optic nerves, optic chiasm, optic tract, and optic radiations (5-7). OGs that develop in the optic pathway after the optic chiasm tend to exhibit more aggressive clinical behavior than those involving the optic nerve or chiasm. In patients in whom the optic tract and radiation are affected, visual acuity deficiency is mostly seen. Surgical resection is not very suitable because of the irregular tumor margins of OGs and the risk of vision loss.

A reliable criterion predicting future vision loss in patients requiring treatment has not been defined yet (1-3,8). It is not possible to predict the development of vision loss in patients with NF1 with conventional MRI. There is no relationship between tumor size on MRI and visual impairment (2,7). Diffusion tensor imaging (DTI), an advanced neuroimaging method, shows the relationship between white matter structures and neural functions. Both mean diffusity (MD) and fractional anisotropy (FA) values provide information about microstructural changes in white matter. There are studies advocating that future visual acuity loss can be predicted in NF1-related OG with DTI (2).

In our study, we aimed to investigate whether patients with NF1 with and without OG differed from the healthy control group in terms of DTI parameters in optical radiation of the visual pathways.

## Method

Eighty three patients (43 men and 40 women, mean age; 10.51±5.63) followed with the diagnosis of NF1 and 36 age-matched healthy controls (18 men and 18 women, mean age; 10.69±5.48) were included in the study and evaluated retrospectively. Routine MRI and DTI were applied to all patients with NF1 and healthy control group. The following parameters were used in the imaging protocol; axial and sagittal T2 images (TR/TE: 4.280/91ms matrix: 384×211; NSA: 1; slice thickness 5 mm), axial T1 images (TR/TE: 500/87 ms; matrix: 256×125; NSA: 1; slice thickness 5 mm), axial and coronal FLAIR images (TR/TE/TI: 8,000/118/23.687 ms; NSA: 1; slice thickness 5 mm), axial and coronal T1 images with contrast (TR/TR: 448/ 87; matrix: 256x134; NSA: 1), and 3DT1 postcontrast sagittal images (TR/TE: 476/86; matrix: 256x154; NSA: 1; slice thickness 1mm). The protocol determined by obtaining DTIs in the axial plane was applied (TR=6,000 ms, TE=89 ms, 30 directions, b=1,000 s/mm$^2$, 5-mm section thickness, 230 mm FOV and matrix: 128x128). FA, MD, RD (radial diffusity) and AD (axial diffusity) values were calculated by placing ROI on right and left optical radiation on colored FA maps on a Siemens Leonardo workstation (Figure 1). Patients with NF1 with OG detected by conventional MRI (n=19) constituted group 1, those with NF1 without OG (n=64) constituted group 2; and healthy control group (n=36) were compared in terms of DTI parameters (Figure 2a, b).

### Statistical Analysis

All statistical analyzes were performed with IBM SPSS 19.0. The normal distribution of the groups was evaluated with the Kolmogirov-Smirnov test. Comparisons between patients with NF1 with and without OG and healthy controls were analyzed using the Mann-Whitney U test. A p value less than 0.05 was considered statistically significant.

## Results

Optical radiation FA, MD, AD and RD values in patients with NF1 with and without OG and in healthy control group are presented in Table 1.

When group 1 and healthy control group were compared;

1- When the right and left optical radiation FA values were compared with the healthy control group, a significant difference

was found (p=0.0001 for each). Optic ratio FA values were significantly lower in patients with NF1 with OG compared to healthy controls.

2- Right and left optical radiation MD values were significantly higher than the control group (p=0.02 and p=0.01, respectively).

3- When the optical radiation AD values were compared with the healthy control group, no significant difference was found.

4- Right and left optical radiation RD values were significantly higher than the healthy control group (respectively; p=0.01, p=0.0001).

When group 2 and healthy control group were compared;

1- When the FA values of the right and left optic radiation were compared with the healthy control group, there was a significant difference (p=0.0001 for each). Optic ratio FA values were significantly lower in patients with NF1 without OG compared to healthy controls.

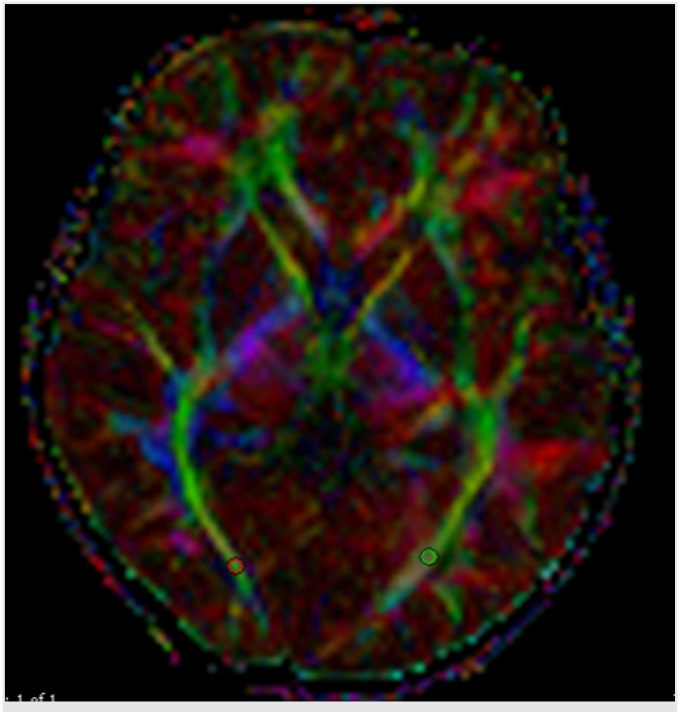

**Figure 1.** FA value is measured by placing ROI on bilateral optical radiation on the color FA map

ROI: Region of interest, FA: Fractional anisotropy

2- When the right and left optical radiation MD and AD values were compared with the control group, no significant difference was found.

3- Right and left optical radiation RD values were significantly higher than the healthy control group (respectively; p=0.001, p=0.002).

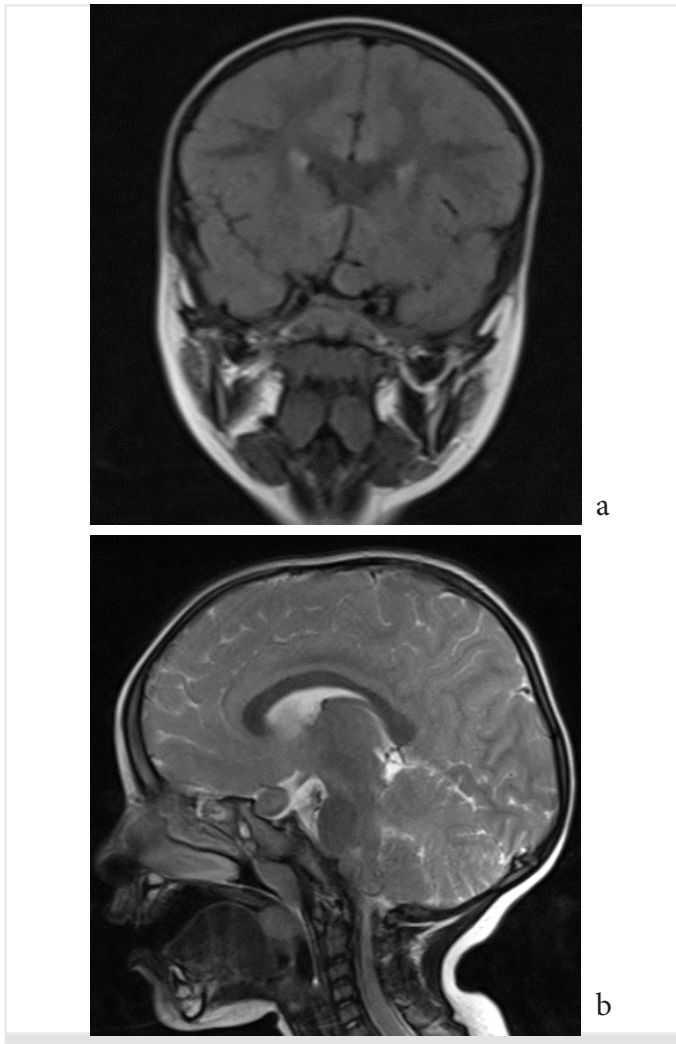


**Figure 2.** A seven-year-old patient with NF1 with optic glioma. Optic glioma is observed on the left side of the optic chiasm in coronal FLAIR (a) and sagittal T2 (b) images

**Table 1.** Optical radiation FA, MD, AD and RD values in patients with NF1 with and without optic glioma and in the healthy control group are presented in Table 1

| | OR FA | | OR_MD | | OR AD | | OR RD | |
|---|---|---|---|---|---|---|---|---|
| | Right | Left | Right | Left | Right | Left | Right | Left |
| Group 1 | 0.485±0.93 | 0.474±0.102 | 0.898±0.99 | 0.929±0.152 | 1.456±0.236 | 1.467±0.363 | 0.619±0.132 | 0.660±0.088 |
| Group 2 | 0.506±0.80 | 0.516±0.80 | 0.851±0.92 | 0.880±0.102 | 1.408±0.196 | 1.462±0.218 | 0.572±0.098 | 0.589±0.120 |
| Control | 0.612±0.79 | 0.602±0.82 | 0.842±0.90 | 0.854±0.77 | 1.523±0.190 | 1.533±0.158 | 0.502±0.089 | 0.514±0.102 |

OR: Optical radiation, Group 1: NF cases with optic glioma, Group 2: NF1 cases without optic glioma, FA: Fractional anisotropy, MD: Mean diffusity ($x10^{-3}$ $mm^2/s$), AD: Axial diffusity ($x10^{-3}$ $mm^2/s$), RD: Radial diffusity ($x10^{-3}$ $mm^2/s$)

When group 1 and group 2 were compared;

1- No significant difference was found in terms of optical radiation FA values.

2- Right and left optical radiation MD values were higher in group 1 (p=0.02 and p=0.05, respectively).

3- No significant difference was found in terms of AD values.

4- Left RD values were significantly higher in Group 1 (p=0.003).

## Discussion

Although OGs have a histologically benign nature, low proliferative potential and excellent survival results, they can cause serious problems that may result in irreversible blindness (5). It may affect the optic nerve or prechiasmatic area unilaterally or bilaterally in approximately one third of children with NF1 under the age of seven (6,9,10). Symptoms may not be evident in the early stages of the disease. Findings such as obstructive hydrocephalus, sudden unexplained visual loss, nystagmus, visual field loss, and diencephalic syndrome may not always be observed in children with OG. The diagnosis is made in the early period by clinical and radiological findings (5,6).

It is thought that the visual impairment observed in OG may be related to perineural or intraneural tumor growth and damage in the nerve's inner structure. Perineural growth occurs as a result of proliferation of astrocytes with some neural intra-tumor components without cystic changes, and fibrovascular arachnoidal trabeculae, mucinous and microcystic degeneration. Intraneural growth represents interaxial astrocytic proliferation and enlargement of fibrovascular trabeculae (5).

Management of OG is possible with careful evaluation of tumor-related parameters, including histological subtype, tumor location and extension, age, and presence of predisposing conditions, especially NF1 (5). Among the treatment options are observation, surgery and chemotherapy aimed at controlling tumor growth. Timing of treatment depends on tumor location and clinical features of other critical functional areas, visual disturbances due to OG, and treatment-related visual risks (5,10-12). Clinical follow-up and treatment decisions in children with NF1-related OG are made by MRI follow-up and ophthalmological examination (8). Vision loss in OGs can probably be explained by direct infiltration or pressure on the visual pathways by the tumor (8).

Although conventional MRI findings do not correlate with tumor size and visual loss, direct measurements of the integrity of the white matter tracts in the optic tract can better show visual loss. DTI can show the identification of all white matter tracts, including optic nerves, optic chiasm, optic tracts, and optic radiations, and whether they are affected at the cellular level (8).

DTI is an advanced imaging method that noninvasively evaluates cerebral white matter integrity and microstructural changes. Tissue anisotropy provides important information about axonal packaging, water-dependent membrane permeability, internal axon structure, degree of myelination, and general tissue water content (13,14). The degree of tissue anisotropy is measured by FA. Axial diffusivity (AD, $\lambda 1$) measures the diffusion of water molecules parallel to the main axis of the axons and radial diffusivity (RD) (mean of $\lambda 2$ and $\lambda 3$) measures the diffusion of water molecules perpendicular to the main axis of the fibers. Increased AD indicates axonal damage, and increased RD is thought to be associated with myelin deficiency or damage (28,29). Myelin loss and axonal damage occur as a result of a long-term disease process. Increased MD values in hamartomatous lesions in the brain seen in NF1 have been associated with histopathologically reported increased water accumulation, myelin vacuolation and spongiotic changes. Decreased FA and increased AD and RD values occur as a result of myelin and axonal damage (13,14).

Evaluation of visual pathways using DTI is important in terms of analyzing the potential risk of visual loss (15). In recent years, it is thought that DTI parameters can be used as a biomarker in the evaluation of pathologies affecting the visual pathways such as optical radiation (15). Optical radiations transmit visual information from the lateral geniculate nucleus to the primary visual cortex. FA in the visual pathways have been associated with visual acuity or disorders such as optic neuritis, visual pathway tumors, prematurity, and optic neuropathy.

There are opinions that FA values can be used as a radiological biomarker in the evaluation of visual acuity in children with OG and can guide treatment (15). In a study, it was reported that there was a correlation between FA values and visual acuity loss in optical radiations of patients with NF1-related OG (8). Optical radiation FA values in subjects with abnormal visual acuity but no tumor involvement were significantly lower than those with normal visual acuity (8). Low FA values in optical radiations were associated with decreased visual acuity. In that study, it was emphasized that microstructural white matter integrity was more important than the number and density of fibers in the visual pathways (8). While white matter tract integrity in optic radiations was associated with loss of visual acuity, no changes in white matter integrity were observed in optic nerves and optic tract. Changes in optic radiation were reported in patients with OG in the anterior visual pathways (8,16,17). In another study, decreased FA values in optic nerve and optic radiation were reported in patients with NF1 compared to healthy controls (8,16). Lober et al. (17), on the other hand, found a decrease in the number of visual tracts in their study with a small number of patients, but they did not find a relationship between this decrease and visual acuity (18). In our study, optical radiation FA values in patients with NF1 with OG showed a significant decrease compared to the healthy control group, while MD and RD values were higher. Decreased FA and increased MD and RD values in the visual pathways in patients with NF1 were thought to be associated with the impairment of optic radiation at the microstructural level and myelin loss and demyelination. In addition, the increase in MD values in optic radiation in patients with NF1 with OG compared to healthy controls may be related to myelin vacuolation and spongiotic changes due to increased water accumulation reported in the histopathology

of hamartomatous lesions. In patients with NF1 without OG, decreased FA and increased RD values were detected in optical radiation. These findings support the hypothesis that NF1 may be associated with microstructural damage in visual pathways independent of the presence of OG. There was no difference between the patients with NF1 with and without OG in terms of optical radiation FA values. This supports the hypothesis that changes similar to the myelin disorder reported in hamartomatous lesions seen in NF1 also develop in the visual pathways.

### Study Limitations

Among the limitations of our study, first of all, small white matter structures of visual pathways such as optic nerves, optic chiasm, and optic tract were difficult to isolate on DTI maps due to the partial volume effect, and these regions were excluded from the study because these pathways were exposed to sensitivity artifacts. Our second limitation was the small number of patients with NF1 with OG. Our third limitation was that examination findings such as visual field and visual acuity in patients with NF1 were not included in our study.

## Conclusion

As a result, it is obvious that there is microstructural damage in optic radiation, which is one of the visual pathways, in patients with NF1 with or without OG. Optical radiation FA values are thought to be related to the decrease in visual acuity during the follow-up period (8). Despite the variability in DTI parameters, extensive prospective studies are needed to determine the FA threshold value associated with visual loss and decreased visual acuity. The idea that changes in FA values detected in optical radiation in the visual pathways in patients with NF1 can be predicted in the early stages of visual impairment is promising in terms of treatment planning and management.

### Ethics

**Ethics Committee Approval:** 2020-10288.

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## References

1. Campen CJ, Gutmann DH. Optic Pathway Gliomas in Neurofibromatosis Type 1. J Child Neurol 2018;33:73-81.
2. Hales PW, Smith V, Dhanoa-Hayre D, O'Hare P, Mankad K, d'Arco F, et al. Delineation of the visual pathway in paediatric optic pathway glioma patients using probabilistic tractography, and correlations with visual acuity. Neuroimage Clin 2017 Oct 11;17:541-8.
3. Avery RA, Mansoor A, Idrees R, Trimboli-Heidler C, Ishikawa H, Packer RJ, et al. Optic pathway glioma volume predicts retinal axon degeneration in neurofibromatosis type 1. Neurology 2016;87:2403-27.
4. Ho CY, Deardorff R, Kralik SF, West JD, Wu YC, Shih CS. Comparison of multi-shot and single shot echo-planar diffusion tensor techniques for the optic pathway in patients with neurofibromatosis type 1. Neuroradiology 2019;61:431-41.
5. Dotto PF, Berezovsky A, Cappellano AM, da Silva NS, Sacai PY, Adolfo F, et al. Visual function assessed by visually evoked potentials in optic pathwaylow-gradegliomaswithand with outneuro fibromatosis t33ype 1. DocOphthalmol2018;136:177-89.
6. Friedrich RE, Nuding MA. Optic Pathway Glioma and Cerebral Focal Abnormal Signal Intensity in Patients with Neurofibromatosis Type 1: Characteristics, Treatment Choices and Follow-up in 134 Affected Individuals and a Brief Review of the Literature. Anticancer Res 2016;36:4095-121.
7. Segal L, Darvish-Zargar M, Dilenge ME, Ortenberg J, Polomeno RC. Optic pathway gliomas in patients with neurofibromatosis type 1: follow-up of 44 patients. J AAPOS 2010;14:155-8.
8. deBlank PM, Berman JI, Liu GT, Roberts TP, Fisher MJ. Fractional anisotropy of the optic radiations is associated with visual acuity loss in optic pathway gliomas of neurofibromatosis type 1. Neuro Oncol 2013;15:1088-95.
9. GuerreiroStucklin AS, Tabori U, Grotzer MA. The changing landscape of pediatric low-grade gliomas: clinical challenges and emerging therapies. Neuropediatrics 2016;47:70-83.
10. Fried I, Tabori U, Tihan T, Reginald A, Bouffet E. Optic pathway gliomas: a review. CNS Oncol 2013;2:143-59.
11. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 2016;131:803-20.
12. Khafaga Y, Hassounah M, Kandil A, Kanaan I, Allam A, El Husseiny G, et al. Optic gliomas: a retrospective analysis of 50 cases. Int J Radiat Oncol Biol Phys 2003;56:807-12.
13. Ertan G, Zan E, Yousem DM, Ceritoglu C, Tekes A, Poretti A, et al. Diffusion tensor imaging of neurofibromatosis bright objects in children with neurofibromatosis type 1. Neuroradiol J 2014;27:616-26.
14. Van Engelen SJPM, Krab LC, Moll HA, Goede-Bolder A de, Pluijm SMF, Catsman-Berrevoets CE, et al. Quantitative differentiation between healthy and disordered brain matter in patients with neurofibromatosis type I using diffusion tensor imaging. AJNR Am J Neuroradiol 2008;29:816-22.
15. De Blank P, Fisher MJ, Gittleman H, Barnholtz-Sloan JS, Badve C, Berman JI. Validation of an automated tractography method for the opticradiations as a biomarker of visual acuity in neurofibromatosis-associated optic pathway glioma. Exp Neurol 2018;299:308-16.
16. Filippi CG, Bos A, Nickerson JP, Salmela MB, Koski CJ, Cauley KA. Magnetic resonance diffusion tensor imaging (MRDTI) of the optic nevre and optic radiations at 3T in children with neurofibromatosis type I (NF-1). Pediatr Radiol 2012;42:168-74.
17. Lober RM, Guzman R, Cheshier SH, Fredrick DR, Edwards MS, Yeom KW. Application of diffusion tensor tractography in pediatric optic pathway glioma. J Neurosurg Pediatr 2012;10:273-80.

Original Article

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# The Status of Iron Stores in the Women with Beta Thalassemia Minor

## Beta Talasemi Minörlü Kadınlarda Demir Depolarının Durumu

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## ABSTRACT

**Objective:** Patients with beta-thalassemia minor are often exposed to unnecessary iron replacement therapies due to hypochrome microcytic change in erythrocyte morphology. However, in these patients, ineffective erythropoiesis may increase iron absorption in the intestines and excessive iron accumulation in the body. In this study, retrospectively, we aimed to show the iron storage status in our patients with beta-thalassemia minor with both biochemical parameters and bone marrow examinations.

**Methods:** Fifteen beta-thalassemia minor patients, who underwent bone marrow aspiration and biopsy for any reason in our hospital but had no additional diagnosis except thalassemia, were detected from the hospital records. Their related laboratory values were examined retrospectively. The pathological materials were reevaluated for erythroblast, and sideroblast.

**Results:** The median age was 43 [interqurtile range (IQR): 27-54] years and the median ferritin values was 24 (IQR: 14.1-84.8) ng/mL. The ferritin values was 15 ng/mL in four cases. Sideroblast values were under the normal limit in all but one case. The median sideroblast value was 6% (IQR: 1.5-15.0%). Transferrin saturation was less than 20% in only one case. There was a moderate positive correlation between ferritin and sideroblast (r=+0.598; p=0.032) while there was not any positive or negative significant correlation between other parameters.

## ÖZ

**Amaç:** Beta talasemi minörlü hastalar eritrosit morfolojilerindeki hipokrom mikrositer değişiklik nedeniyle sıklıkla demir eksikliği anemisiyle karışarak gereksiz demir replasman tedavilerine maruz kalmaktadırlar. Halbuki bu hastalarda var olan inefektif eritropozisden dolayı bağırsaklarda demir emilimi artabilir ve vücutta aşırı demir birikimi oluşabilir. Bizde kendi hastane verilerimizi retrospektif olarak inceleyerek, bizim hasta grubumuzdaki demir depo durumunu hem biyokimyasal parametreler hem de kemik iliği incelemeleri ile göstermeyi amaçladık.

**Yöntemler:** Herhangi bir sebeple hastanemizde kemik iliği aspirasyon ve biyopsisi yapılmış ancak talasemi dışında ek bir tanı almamış, 15 beta-talasemi minör hastası sistemden tespit edilip ilgili laboratuvar değerleri retrospektif olarak incelendi. Ayrıca hastalara telefon ile ulaşılarak gerekli ek bilgiler sorgulandı. Arşivden çıkartılan patolojik materyaller durumdan habersiz bir patoloğa gönderildi ve ilgili kemik iliği preparatları eritroblast, sideroblast ve ring sideroblast açısından yeniden değerlendirildi.

**Bulgular:** Hastaların mediyan yaş: 43 [çeyrekler açıklığı (IQR): 27-54] yıl, medyan ferritin düzeyi ise 24 ng/mL (14,1-84,8) idi. Dört olguda ferritin 15 ng/mL'nin altındaydı. Bir olgu dışında tüm olgularda sideroblast değeri normalin altında tespit edildi. Medyan sideroblast değeri % 6 (1,5-15,0) idi. Transferrin satürasyonu sadece

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**Conclusion:** In this study, where iron storage status was examined both biochemically and histopathologically, 66% of cases with iron deficiency could have been overlooked if the iron status of the patients was evaluated only by the serum iron panel. The examination of bone marrow aspiration with prussian blue is a gold standard method for determining iron storage status.

**Keywords:** Thalassemia minor, ferritin, sideroblast, iron stores

bir olguda %20'nin altında bulundu. Ferritin ile sideroblast arasında orta derecede pozitif bir korelasyon vardı (r=+0,598; p=0,032). Diğer parametreler arasında ise pozitif veya negatif herhangi anlamlı bir korelasyon yoktu.

**Sonuç:** Rutin günlük pratikte demir depolarını ferritin, transferritin satürasyonu ve serum demiri ile değerlendirmekteyiz. Demir depo durumunun hem biyokimyasal hem de histopatolojik olarak incelendiği bu çalışmamızda, sadece serum demir paneline bakarak hastaların demir durumu değerlendirilmiş olunsaydı demir eksikliği olan olguların %66'sı gözden kaçmış olacaktı. Kemik iliği aspirasyonun prusya mavisi ile incelenmesi demir depo durumunu gösteren altın standart bir yöntemdir.

**Anahtar Sözcükler:** Talasemi minör, ferritin, sideroblast, demir depoları

## Introduction

The term "thalassemia" defines a group of diseases that are generally characterized by hypochromic microcytic anemia due to a decrease in the synthesis rate, without showing a structural disorder of one or more polypeptide chains of hemoglobin as a result of an inherited defect (1). While hemolysis is prominent in alpha thalassemia, ineffective erythropoiesis is more prominent in beta thalassemia (2,3).

β-thalassemia is caused by point mutations in the *β-globin* gene. It is common in the Mediterranean population and its frequency is up to 10%. β-thalassemia resulting from an inherited defect of one of the beta genes presents as "β-thalassemia minor" clinically, and although the defect in erythrocyte morphology is evident in these patients, anemia is mild or absent (3). Clinically, it is usually asymptomatic. These patients are often confused with iron deficiency anemia due to the defect in erythrocyte morphology and are exposed to unnecessary iron replacement therapy (3,4).

Unlike iron deficiency anemia, the presence of prominent erythrocytosis besides deep microcytosis stands out. The Mentzer index, which is the ratio of the mean erythrocyte volume (MCV) to the erythrocyte count, is found to be less than 13. This ratio is generally greater than 13 in iron deficiency (5). Peripheral smear shows hypochromic microcytosis as well as basophilic spotting, Heinz bodies and target cells. Again, a red cell distribution volume (RDW) of less than 16 is considered in favor of β-thalassemia minor (6). In addition, β-thalassemia minor is diagnosed by detecting hemoglobin (HbA2) over 3.5% in Hb electrophoresis.

While excessive iron accumulation occurs in the body due to frequent transfusions in patients with thalassemia major, iron accumulation may be evident in thalassemia intermedia even though there is no transfusion. This has been attributed to increased intestinal iron absorption due to ineffective erythropoiesis (7,8). It has been shown that hepcidin is suppressed due to increased erythropoiesis in patients with β-thalassemia minor, resulting in increased intestinal iron absorption (9,10). In addition to studies reporting that the frequency of iron deficiency is lower in these individuals than in the normal population (11-13), there are also publications suggesting that this frequency does not change (14-17). However, it is a fact that these patients are often misdiagnosed as having iron deficiency anemia due to the similarities in erythrocyte morphology and are frequently exposed to unnecessary iron therapy (3,4). Only female patients were included in our study since iron deficiency was observed more frequently in women and they were exposed to iron treatment more frequently. In some previous studies, there were studies stating that iron absorption increased and less iron deficiency was observed in thalassemia carriers. In fact, if such a situation existed in thalassemia carriers, we would have found less iron deficiency in this study, and even we would find a little higher iron level in individuals without iron loss. Based on this theory, this study was designed. Various studies were done with this theory before, but unlike biochemical iron indicators in our study, bone marrow aspiration and biopsy materials were also used. Thus, we aimed to show whether iron absorption actually increased or not, and to have the chance to compare the biochemical parameters and the results of aspiration and biopsy among themselves.

## Methods

Patients with β-thalassemia minor who underwent bone marrow aspiration and biopsy in our hospital for any reason in the last 5 years, but did not receive any additional diagnosis other than thalassemia, were detected in the system, and their examinations and related laboratory values [hemoglobin and hematocrit levels, MCV, mean erythrocyte volume) hemoglobin (MCH), erythrocyte count (RBC), MCV/erythrocyte count ratio (Mentzer index), reticulocyte count, morphological features of erythrocytes in hemoglobin electrophoresis and peripheral smear, serum iron values, bone marrow aspiration and biopsy reports] were analyzed retrospectively. Fifteen patients diagnosed as having β-thalassemia minor were selected for this study. Required additional information (number of pregnancies/births, menstrual

status, use of aspirin and other nonsteroidal anti-inflammatory drugs, iron intake and bleeding) was asked by phone call. None of the patients had a history of blood transfusion, gastrointestinal bleeding, frequent use of nonsteroidal anti-inflammatory drugs, and chronic diarrhea. Again, none of them had a history of abortion, miscarriage or delivery within one year before the relevant bone marrow biopsy. Verbal information was given to the patients in the phone calls made with the patients and necessary medical information was noted down. The study was approved by the relevant ethics committee (2019/12-120).

All bone marrow biopsies were evaluated by staining with Prussian blue. The relevant laboratory tests and pathology preparations of 2 patients could not be accessed. Relevant pathology materials were removed from the files and sent to an unaware pathologist, and the relevant bone marrow preparations were re-evaluated in terms of erythroblast, sideroblast and ring sideroblast.

### Statistical Analysis

Descriptive statistical methods were used. Spearman correlation analysis was used for correlation analysis because the number of patients was small. All assessments were performed using SPSS software (version 17.0 for Windows; SPSS Inc., Chicago, USA) and $p<0.05$ was considered significant for all statistical analyses.

## Results

The general demographic characteristics and laboratory values of the patients are shown in Tables 1 and 2. To summarize shortly; the median age of 15 patients was 43 [interqurtile range (IQR): 27-54] years. Bone marrow aspiration and biopsy results of two patients could not be reached. In four patients, ferritin was below 16 ng/mL, the lower limit for iron storage. The median ferritin level was 24 (IQR: 14.1-84.8) ng/mL. Again, except for one patient, the sideroblast value was below normal. The median sideroblast value was 6 (IQR: 1.5-15) (Table 2).

When we compared ferritin used in routine practice with other values, there was a moderately positive correlation between ferritin and sideroblast ($r=+0.598$; $p=0.032$). There was no significant positive or negative correlation between ferritin and iron ($r=-0.04$; $p=0.884$), iron and sideroblast ($r=-0.21$; $p=0.480$), total iron binding capacity (TIBC) and ferritin ($r=+0.281$; $p=0.310$), TIBC and sideroblast ($r=-0.197$; $p=0.518$), TIBC and iron ($r=-0.214$; $p=0.444$), ferritin and transferrin saturation ($r=-0.05$; $p=0.869$), and sideroblast and transferrin saturation ($r=-0.127$; $p=0.680$).

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

| Paient no | Age (year) | Number of pregnancies/births | Menstruation status | Aspirin use | Iron replacement |
|---|---|---|---|---|---|
| 1 | 54 | 0/0 | Menopause | No | No |
| 2 | 22 | 0/0 | Absence of menstruation | No | No |
| 3 | 18 | 0/0 | Regular | No | No |
| 4 | 43 | 6/3 | Regular | No | No |
| 5 | 56 | 13/5 | Menopause | Yes | No |
| 6 | 68 | 4/4 | Menopause | Yes | Oral/irregular |
| 7 | 37 | 3/2 | Regular | No | 3 months oral +10 amp parenteral |
| 8 | 45 | 7/2 | Regular | Yes | No |
| 9 | 31 | 2/2 | Regular | No | Oral/irregular |
| 10 | 30 | 4/2 | Regular | No | 1 tablet per day for 1 month |
| 11 | 43 | 2/2 | Regular | No | 1 tablet per day for 1 month |
| 12 | 25 | 0/0 | Irregular | No | No |
| 13 | 44 | 3/3 | Menopause | Yes | No |
| 14 | 54 | 4/3 | Menopause | No | No |
| 15 | 27 | 1/0 | Irregular | No | No |

* The patient with Rokitansky-Küster-Hauser syndrome

**Table 2.** Relevant laboratory values of all patients (n=15)

| Patient no | Hb/Htc (g/dL)/% | RBC (x10$^6$/mm$^3$) | MCV (fL) | MCH (pg/RBC) | MCHC (g/dL) | MCV/RBC (Mentzer) | Ret. (%) | HbA2 (%) | HbF (%) | SerumFe (µg/dL) | TIBC (µg/dl) | TrSAT (%) | Ferritin (ng/ml) | Erythroblast (%) | Sideroblast (%) | Ring sideroblast (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Normal values (18) | 12-15.3/ 36-45 | 4.6-5.1 | 80-96 | 28-33 | 33-36 | 13 | 14±0.5 | 1.8-3.2 | <2% | 50-175 | 250-410 | >20 | 11-120 | | >25-30% | 0% |
| 1 | 13.4/42.3 | 6.09 | 69.5 | 22 | 31.8 | 11.4 | 2.2 | 4.1 | 0 | 105 | 330 | 32 | 31.8 | 98 | 2 | 0 |
| 2 | 10.3/32.7 | 5.45 | 60 | 18.9 | 31.5 | 11 | 1.6 | 5.6 | 0 | 70 | 390 | 18 | 24.5 | 96 | 4 | 0 |
| 3 | 12.3/35.8 | 5.54 | 68.7 | 23.6 | 34.3 | 12.4 | 2.0 | 3.9 | 0 | 115 | 315 | 36 | 31.3 | 99 | 1 | 0 |
| 4 | 11.8/39.9 | 5.61 | 71 | 21 | 29.5 | 12.6 | 0.8 | 5 | 0 | 85 | 330 | 26 | 17.9 | 94 | 6 | 0 |
| 5 | 10/37 | 5.51 | 68 | 18 | 27 | 12.3 | 2.6 | 3.7 | 0 | 95 | 345 | 28 | 84.8 | 93 | 7 | 0 |
| 6 | 11.4/42 | 5.70 | 73.8 | 20 | 27 | 12.9 | 4 | 5.1 | 0 | 110 | 330 | 33 | 98.3 | 89 | 11 | 0 |
| 7 | 10.4/30.6 | 4.94 | 62 | 21.1 | 34 | 12.5 | 1.8 | 3.7 | 0 | 140 | 300 | 46 | 170 | 35 | 60 | 0 |
| 8 | 13/43 | 5.51 | 78 | 23 | 30 | 14.1 | 2.2 | 5.4 | 0 | 180 | 375 | 48 | 20.9 | 98 | 2 | 0 |
| 9 | 10/30 | 4.92 | 62 | 20 | 34 | 12.6 | 2.4 | 4.1 | 0 | 130 | 255 | 51 | 108.2 | 87 | 23 | 0 |
| 10 | 8.2/31.3 | 5.82 | 76 | 19.8 | 28.1 | 13 | 2.2 | 4.9 | 0 | 140 | 285 | 49 | 5.1 | 99 | 1 | 0 |
| 11 | 11.4/37.1 | 5.98 | 62.1 | 19.1 | 30.8 | 10.3 | 2.0 | 6 | 0 | 135 | 285 | 47 | 9.7 | 100 | 0 | 0 |
| 12 | 10.3/32.9 | 5.48 | 60 | 18.8 | 31.3 | 10.9 | 2.6 | 4.3 | 0 | 85 | 300 | 28 | 23.9 | - | - | - |
| 13 | 11.9/41 | 6.17 | 66.5 | 19.2 | 28.9 | 10.8 | 2.2 | 5.6 | 0 | 60 | 270 | 22 | 12.1 | 88 | 12 | 0 |
| 14 | 12/39.3 | 5.63 | 69.8 | 21.2 | 30.4 | 12.4 | 4.2 | 5.2 | 3.6 | 105 | 315 | 33 | 24 | 82 | 18 | 0 |
| 15 | 8.5/29.3 | 4.62 | 63.5 | 18.4 | 29 | 13.7 | 5.2 | 5.5 | 0 | 145 | 285 | 51 | 14.1 | - | - | - |

Hb/Htc: Hemoglobin/hemotocrit, RBC: Red blood cell, MCV: Mean corpuscular volume, MCH: Mean cell hemoglobin, MCHC: Mean cell hemoglobin concentration, Ret.: Reticulocyte percentage, HbA2: Hemoglobin A2, HbF: Hemoglobin F: Serum Fe: Serum iron, TIBC: Total iron binding capacity, TrSAT: Transferrin saturation

## Discussion

The status of iron stores in people with β-thalassemia minor has been a matter of interest for years, and many studies have been conducted on this subject. The first study on iron storage status was conducted in 1978 by measuring ferritin in women with β-thalassemia minor. Various erythrocyte indices are used for screening in the differential diagnosis of β-thalassemia minor and iron deficiency anemia. England and Fraser's discriminant function, MCV/RBC ratio (Mentzer index), Shine & Lal index, Green & King index, RDW index, Ricerca index, Srivastava index, Bessman index, and Ehsani formula are the main indexes used in differential diagnosis (19-21). In patients in whom β-thalassemia minor is considered as a result of these tests, the diagnosis can be confirmed by HbA2 and/or DNA analyzes measured using paper chromatography. Bone marrow biopsy has no place in the diagnosis. Therefore, bone marrow examination of these patients is not a method used in routine practice. We aimed to retrospectively evaluate and document the blood values together with these bone marrow aspiration and biopsy results of our patients who were followed up with the diagnosis of β-thalassemia minor in our clinic, who underwent bone marrow aspiration and biopsy for any reason, but in whom no additional disease was detected as a result of the biopsy.

The frequent confusion between β-thalassemia minor and iron deficiency anemia, frequent iron replacement without diagnosis, and the knowledge that intestinal iron absorption will increase due to the suppression of hepcidin hormone caused by ineffective erythropoiesis in these patients have brought to mind the hypothesis that iron excess may be present in this group of individuals (3,4,9,10). Starting from this point, we wanted to show the iron storage status both biochemically and histopathologically in this study. Thus, we thought that we would learn more about iron deficiency especially in the prelatent period.

Looking at the patient data, as expected, all our evaluated patients had low MCV, Mentzer index <13, and HbA2 ≥3.7%. Again, an erythrocytosis that was not compatible with the Hb value was noted in all of our patients. Mean erythrocyte count of the patients was $5.5x10^6$. This erythrocytosis supported the diagnosis of β-thalassemia minor (22). MCV values were also found to be ≤70 fL in our patients. In only four patients, the MCV was between 73-78 fL and was lower than normal. Mean MCV values were 67.4 fL. Considering this decrease in MCV values and erythrocytosis, the suspicion of β-thalassemia minor was strengthened. This was in agreement with the results previously written by Jhon N. Lukens in Wintrobe's Clinical Hematology (3).

Ferritin levels were below the normal value (less than 16 ng/mL) (23) in 4 of our patients. In 2 of these 4 patients, serum iron and TIBC were normal, and tranferrin saturation was in the upper limit of normal, due to the iron treatment they received. So the iron stores weren't full yet. In the bone marrow aspirations of these patients, the percentages of sideroblasts were found to be 1%, 0% and 12%. More than half of the erythroblasts in a normal person are made up of sideroblasts, each of which contains fewer than five iron granules. The rate of sideroblasts falls below 30% in iron deficiency (24). In this study, if the bone marrow was not evaluated and only the transferrin saturation and ferritin were evaluated, we would have said that there was iron deficiency in only 4 patients; however, with the evaluation of bone marrow, we found that this situation was different, except for these 4 patients, all of the patients who underwent biopsy had iron deficiency, except for one patient. In patient 7, transferrin saturation was 46% and ferritin level was significantly high (170 ng/mL). This patient had received long-term oral and parenteral iron therapy before admitting to us. Sideroblasts were detected in 60% of this patient's bone marrow aspiration. These values were above normal. When the patient was evaluated together with his/her anamnesis, it was determined that there was iron accumulation in his/her body since this patient was given iron replacement therapy considering only the erythrocyte morphology, without diagnosis of thalassemia. This patient supported the hypothesis that if thalassemia awareness did not develop sufficiently, iron overload might occur in these patients due to unnecessary iron replacement. These patients were similar to the 4 patients shown by Hussein et al. (17) in their 1976 study who received unnecessary iron replacement therapy and subsequently developed high ferritin levels.

Although serum iron, TIBC and ferritin values were normal in our other patients, sideroblast rate was found below 12% in 8 patients and around 20% in 2 patients in the bone marrow aspirate. That is, if we were to interpret the iron storage status in these patients only by looking at the biochemical values, we would interpret the iron storage status as normal, however, it was observed that the iron stores were insufficient in this group with the bone marrow examination. In previous studies, controlled with serum ferritin and erythrocyte ferritin, it was stated that the iron balance of patients with β-thalassemia minor was better than the control group, and the frequency of iron deficiency was lower in patients with β-thalassemia minor. Researchers attributed this to increased iron absorption due to the ineffective erythropoiesis present in patients with β-thalassemia minor (25-27). Considering the studies conducted by researchers who stated that iron absorption was increased in thalassemia, we should have found the ferritin values of our patients to be normal or even above normal values. However, in our patients, ferritin values were generally in the lower limit of normal, and when we evaluated bone marrow aspiration smears, we found that all patients were in the iron deficiency period, except for one patient. Based on these findings, we can say that iron absorption is not increased in patients with β-thalassemia minor, which is consistent with the work of Hussein et al. (15-17). This result shows that the theory that an increase in ineffective erythropoiesis will cause a decrease in hepcidin molecule and as a result increase iron absorption from the intestine is not true for β-thalassemia minor.

When we compared ferritin used in routine practice with other values, there was a moderately positive correlation between ferritin and sideroblast (r=+0.598; p=0.032). There was no significant

positive or negative correlation between ferritin and iron (r=-0.04; p=0.884), iron and sideroblast (r=-0.21; p=0.480), total iron binding capacity (TIBC) and ferritin (r=+0.281; p=0.310), TIBC and sideroblast (r=-0.197; p=0.518), TIBC and iron (r=-0.214; p=0.444), ferritin and transferrin saturation (r=-0.05; p=0.869), and sideroblast and transferrin saturation (r=0.127; p=0.680). This showed us once again that the second laboratory value to be evaluated together with ferritin when evaluating iron deficiency was sideroblast. In addition, if we had evaluated only TrSAT and ferritin, we could have missed the diagnosis of iron deficiency in 66% of the patients. In this case, it can be said that the threshold value of ferritin used in the diagnosis should be kept at higher levels in order not to miss these patients, and larger prospective, case-control studies are needed to make a definite conclusion.

Iron is found in the bone marrow in the form of hemosiderin in the cytoplasm of macrophages. Iron stores can be easily evaluated under the microscope at 20x and 40x magnifications. Prussian stain is used in the iron staining process and the cells having blue granules are considered as positive cells. The presence of more than two positive cells in each (x40) magnification area indicates that the iron stores are increased, and the average of less than one positive cell in each area indicates that the iron stores are decreased. When we examined the bone marrow biopsies based on these criteria, all patients had zero iron in the bone marrow. Iron molecule is filtered during the decalcification stage in the iron staining process of the bone marrow biopsy. Therefore, evaluation of bone marrow iron stores by biopsy may give false negative results. In addition, biopsy is evaluated relatively. Although there is a correlation between biopsy and aspiration in showing iron stores, we could not detect this correlation. In our cases, we found that aspiration smear was a more sensitive method than bone marrow biopsy in assessing iron stores, consistent with the literature (28).

Although the number of patients whose bone marrow biopsy was scanned was high, the number of our patients remained low because bone marrow examination did not have a routine place in the diagnosis/follow-up of thalassemia and those with systemic disease affecting the bone marrow and/or additional blood disease were excluded from the study. The small number of patients (15 patients in total) and the retrospective design were the main limitations of our study. In this analysis, we were not only limited to the measurement of serum iron level, TIBC, and ferritin levels, but also had the opportunity to examine in detail the existing bone marrow aspirations and biopsies of these patients. Thus, in addition to investigating the status of iron stores in women with β-thalassemia minor, we had the chance to compare the diagnostic accuracy of ferritin, bone marrow aspiration smears and bone marrow biopsies.

## Conclusion

In conclusion, we did not find any findings showing increased iron absorption in our patients. Examination of bone marrow aspiration in the evaluation of iron stores gives much better results than biochemical parameters, but the invasiveness of the procedure limits its use in the clinic.

### Ethics

**Ethics Committee Approval:** The study was approved by the relevant ethics committee (2019/12-120).

**Informed Consent:**

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

### Authorship Contributions

Concept: T.K., H.K., K.Ç., Design: T.K., H.K., K.Ç., Data Collection or Processing: T.K., Analysis or Interpretation: T.K., Literature Search: T.K., Writing: T.K., H.K.

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

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## References

1. Dinçol G. Beta ve Delta-Beta talasemi tiplerinin ayrılmasında hemoglobin analiz sonuçlarının değeri, in İstanbul Tıp Fakültesi İç Hastalıkları, Hematoloji Kliniği. İstanbul Üniversitesi, 1977.
2. Benz EJ. Clinical manifestations and diagnosis of the thalassemias. Aug 19 2019. Available from: www.uptodate.com/MusePath/contents/clinical-manifestations-and-diagnosis-of-the-thalassemias?search.
3. Borgna-Pignatti C, Galanello Thalassemias R. Related Disorders:Quantitative Disordersof Hemoglobin Synthesis, in Wintrobe's Clinical Hematology, J.P. Greer, J. Foerster, and J.N. Lukens, Editors. LippincottWilliams&WilkinsPublishers 2004.p.42:1078-118.
4. Bessman JD, Feinstein DI. Quantitative anisocytosis as a discriminant between iron deficiency and thalassemia minor. Blood 1979;53:288-93.
5. Ansari S, Rashid N, Hanifa A, Siddiqui S, Kaleem B, Naz A, et al. Laboratory diagnosis for thalassemia intermedia: Are we there yet? J Clin Lab Anal 2019;33:e22647.
6. Massey AC. Microcytic anemia. Differential diagnosis and management of iron deficiency anemia. Med Clin North Am 1992;76:549-66.
7. Musallam KM, Cappellini MD, Wood JC, Motta I, Graziadei G, Tamim H, et al. Elevated liver iron concentration is a marker of increased morbidity inpatients with β thalassemia intermedia. Haematologica 2011;96:1605-12.
8. Musallam KM, Cappellini MD, Daar S, Karimi M, El-Beshlawy A, Graziadei G, et al. Serum ferritin level and morbidity risk in transfusion-independent patients with β-thalassemia intermedia: the ORIENT study. Haematologica 2014;99:218-21.
9. Jones E, Pasricha SR, Allen A, Evans P, Fisher CA, Wray K, et al. Hepcidin is suppressed by erythropoiesis in hemoglobin E beta-thalassemia and beta- thalassemia trait. Blood 2015;125:873-80.

10. Huang Y, Lei Y, Liu R, Liu J, Yang G, Xiang Z, et al. Imbalance of erythropoiesis and iron metabolism in patients with thalassemia. Int J Med Sci 2019;16:302-10.
11. Aghai E, Shabbad E, Quitt M, Froom P. Discrimination between Iron Deficiency and Heterozygous beta-thalassemia in children. AJCP 1986;85:710-2.
12. Crosby WH, Conrad ME. Iron Balance In Thalassemia Minor. A Preliminary Report. Ann N Y Acad Sci 1964;119:616-23.
13. Halliday JW, Powell LW. Iron overload. Semin Hematol 1982;19:42-53.
14. Bannerman RM, Callender ST, Hardisty RM, Smith RS. IRON ABSORPTION IN THALASSAEMIA. Brit J Haematol 1964;10:490-5.
15. Economidou J, Augustaki O, Georgiopoulou V, Vrettou H, Parcha S, Loucopoulos D. Assessment of Iron Stores in Subjects Heterozygous for β-thalassaemia Based on Serum Ferritin Levels. Acta Haematol 1980;64:205-8.
16. Hegde UM, Khunda S, Marsh GW, Hart GH, White JM. Thalassaemia, iron, and pregnancy.Br Med J 1975;3:509.
17. Hussein S, Hoffbrand AV, Laulicht M, Attock B, Letsky E. Serum ferritin levels in beta-thalassaemia trait. Br Med J 1976;2:920.
18. Leung, L.L. Approach to the adult with anemia. 2019; Available from: https://www.uptodate.com/contents/approach-to-the-adult-with-anemia.
19. Sonati Mde F, Grotto HZ, Kimura EM, Costa FF. Diferenciação entre talassemia beta-heterozigótica e anemia ferropriva [Differentiation between heterozygotic beta-thalassemia and iron deficiency anemia]. Rev Assoc Med Bras (1992) 1993;39:221-3.
20. Mentzer WC Jr. Differentiation of iron deficiency from thalassaemia trait. Lancet 1973;1:882.
21. Maskoen,A.M.,etal., Shine&Lalindex asapredictorforearlydetectionof beta-thalassemiacarriers inalimitedresourceareainBandung,Indonesia. BMCMedGenet
22. Aslan D. Automated blood counts and identification of thalassemia carriers. J Postgrad Med 2008;54:242-3.
23. Michael A. Causes and diagnosis of Iron deficiency and Iron deficiencyanemiainadults.2019; Available from: https://www.uptodate.com/contents/causes-and-diagnosis-of-iron-deficiency-and-iron-deficiency-anemia-in-adults.
24. Andrews NC. Iron Deficiency and Related Disorders, in Wintrobes Clinical Hematology. 2003. p. 794-812.
25. Cermák J, Brabec V. Význam vysetrení hladiny feritinu v cervených krvinkách [The importance of determination of ferritin levels in erythrocytes]. Cas Lek Cesk 1990;129:1357-60.
26. Crosby W, Conrad M. Iron balance in thalassemia minor. Problems of Cooley's Anemia: Academy, Ann NY Acad Sci, 1964.
27. Lyberatos C, Chalevelakis G, Platis A, Stathakis N, Panani A, Gardikas C. Erythrocyte content of free protoporphyrin in thalassaemic syndromes. Acta Haematol 1972;47:164-7.
28. Bucley PJ. Examination and interpretation of bone marrow biopsies and aspirate smears. In: Hofman R, Jr. EJB, Shattil SJ, eds. Hematology Basic Principles and Practice, 1993; 2214-2222.

Original Article

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# Longitudinal Changes in the Eating Habits of Patients with Cancer Receiving Palliative Care

## Hastalık Sürecinde Palyatif Bakım Hastalarında Yeme Alışkanlığı Değişimi

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### ABSTRACT

**Objective:** Nutritional changes are frequently observed in patients with cancer because of multiple symptoms. This study aimed to determine food types most preferred by the patients and most suitable to them and to identify methods to enrich these food options in the future.

**Methods:** This cross-sectional, descriptive study was conducted on 151 patients at Tokat Gaziosmanpaşa University Palliative Care Center. Demographic data, nutritional habits, and food preferences were obtained using a questionnaire. The Karnofsky performance scale (KPS) was also used.

**Results:** Of the 151 patients, 53.6% (n=81) were male, and the mean patient age was 62.7±14.7 years. Moreover, 47% (n=71) of the patients were bothered by the food odor; specifically, 27.8% reported that the food had a disturbing smell. The average KPS score was 63.9±15.0 points. The mean KPS scores were significantly higher in the eating group (p=0.043). Patients most preferred yayla (39.7%) among soups and yogurt (28.8%) among milk products. Only 36.4% (n=55) of the patients stated that they could continue to use enteral nutrition products at the recommended dosage regularly, but 38% (n=21) have been consuming enteral nutrition products.

### ÖZ

**Amaç:** Çeşitli semptomlar nedeniyle kanser hastalarında beslenme değişiklikleri sıklıkla görülür. Bu çalışmayı hastalarımız tarafından en çok tercih edilen, onlar için en uygun gıda seçeneklerini ve bu seçenekleri gelecekte nasıl zenginleştirebileceğimizi belirlemek amacıyla planladık.

**Yöntemler:** Kesitsel ve tanımlayıcı tipteki bu çalışma Tokat Gaziosmanpaşa Üniversitesi Palyatif Bakım Merkezi'ndeki 151 hasta üzerinde gerçekleştirilmiştir. Demografik veriler, beslenme alışkanlıkları ve gıda tercihleri verileri anket ile elde edildi. Karnofsky Performans Ölçeği katılımcılara aynı anda uygulanmıştır.

**Bulgular:** Toplam 151 hastanın %53,6'sı (n=81) erkekti ve hastaların yaş ortalaması 62,7±14,7 idi. Hastaların %47'sinin (n=71) kokudan rahatsız olduğu ve özellikle gıda kokusunun (%27,8) hastaları etkilediği bulunmuştur. Karnofsky Performans Ölçeği (KPS) ortalama puanı 63,9±15,0 olarak tespit edildi. Ortalama KPS puanları yemek yiyebilen grupta anlamlı olarak yüksekti (p=0,043). Çorba çeşitlerinden yayla çorbası (%39,7), süt ürünleri çeşitlerinden yoğurt (%28,8) hastalar tarafından en çok tercih edilen gıdalardı. Hastaların yalnızca %36,4'ü (n=55) enteral beslenme ürünlerini düzenli olarak, önerilen dozda kullanmayı sürdürebileceklerini, ancak bu hastaların dahi yalnızca %38'i (n=21) enteral ürünleri severek tükettiklerini ifade etmişlerdir.

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**Conclusion:** When offering healthy food options, patients should have sufficient calorie intake and consume foods that they think are delicious. Starting enteral nutrition products early is recommended to avoid malnutrition.

**Keywords:** Palliative care, eating habits, food preferences

**Sonuç:** Hastalara sağlıklı gıda seçenekleri sunmaya çalışırken, yeterli kalori aldıklarından emin olmak ve lezzetli olduğunu düşündükleri yiyecekleri tüketmelerine yardımcı olmak önemlidir. Hastalarda malnütrisyondan kaçınmak için enteral beslenme ürünlerine başlamada geç kalınmaması gerektiğini düşünüyoruz.

**Anahtar Sözcükler:** Palyatif bakım, yeme alışkanlıkları, gıda tercihleri

## Introduction

Palatal delight, food preferences, and diet patterns of patients change during cancer treatment (1). Many patients with cancer experience significant weight changes according to the type and stage of the tumor. Oral feeding is diminished or completely stopped because of various factors like smell or taste changes, loss of appetite, nausea, vomiting, dysphagia, mouth sores, and pain (2). The anorexia-cachexia syndrome in cancer is a clinical state characterized by decreased appetite, weight loss, metabolic disorders, and inflammatory events. The etiology of anorexia in cancer is unknown. However, it causes performance loss, decreases quality of life, and results in high morbidity and mortality rates (3).

Studies have reported impaired taste function and reduction in flavor perception in patients with cancer. Malnutrition leads to impaired immune function and failure to cope with the physical stress of radiotherapy, chemotherapy, and surgery, so treatment procedures are interrupted. Many studies have focused on the prevention of malnutrition (4). To maintain the optimal health level of patients with cancer, diet regimens are changed according to their preferences (3,4). Many nutritional support products were created for specific patients. However, the consumption of these products is sometimes extremely difficult because patients developed a high sensitivity to odor and experienced changes in taste perception (5).

This study aimed to understand the food preferences, feeding habits, and attitudes of patients with cancer receiving palliative care related to nutrition.

## Methods

This cross-sectional and descriptive study was conducted on patients with cancer receiving palliative care, between April and November 2016. In our university, palliative care started in 2010 as a voluntary group (palliative care study group) comprising of professionals from different disciplines including surgical oncology, internal medicine, family medicine, public health and nurses, social workers, dieticians, and psychologists.

Initially, the palliative care center accepted patients in the outpatient clinic in November 2015 and started to provide inpatient care in November 2017. The palliative care study group met regularly once a week and organize multidisciplinary research, education, and patient care. The palliative care center is under the responsibility of a family practitioner together with a nurse. Other disciplines were consulted during the treatment when needed.

Ethical committee approval was obtained before the study (16-KAEK-088). Patients aged >18 years with cancer diagnosis followed in our palliative care unit and agreed to participate in the study were included in the study. Patients aged <18 years who had mental illnesses, communication difficulties, and malignant bowel obstruction and were not unwilling to participate in the study were excluded.

A questionnaire was developed to elucidate the feeding habits of patients receiving palliative care by the palliative care study group during several meetings. First, the themes were identified until redundancy. Then, the themes were reduced and related questions were formed. The answer styles and answers were created. The questionnaire consisted of three parts that contain 15 open-ended questions assessing the demographic data of the patients, two open-ended questions and 13 close-ended questions assessing nutritional habits, and six Likert-type questions assessing food preferences. The questions were revised after a pilot test was applied to 20 patients who had similar characteristics with the target group in the palliative care center. Tools used in our palliative care unit such as the Karnofsky performance scale (KPS), Katz daily living activities scale, and basic daily living activities scale were completed during the first admission by a palliative care doctor. The questionnaire was delivered by a service secretary in the outpatient unit and completed in 20 min by face-to-face interview method.

### Statistical Analysis

Descriptive statistics were presented as mean, standard deviation, median, percentile 25 (Q1), percentile 75 (Q3), and minimum and maximum values for numerical variables. The conformity of the variables to normal distribution was examined by using Kolmogorov-Smirnov/Shapiro-Wilk tests. The chi-square test was used for binary and multiple comparisons between categorical variables. The Mann-Whitney U test was used in binary group comparisons of variables that did not disperse normally. Data were analyzed with SPSS v20 software package (IBM Corp., Armonk, NY, USA). For evaluation of demographic data, descriptive statistics (such as percentage, average, standard deviation) were used, and chi-square and Student's t-test were used for comparisons between groups. $P<0.05$ was considered significant.

## Results

### Demographic and Clinical Features of Patients

A total of 151 patients were included in the study, of which 53% (n=81) were male. The mean age was 62.7 (±14.7) years. Details of the demographic features are presented in Table 1.

The most common cancer diagnoses were gastrointestinal tumors. In addition, 119 (78.8%) patients had decreased weight, and 38.7% (n=46) stated that they had lost ≥10 kg during the disease period. The mean KPS score was 63.9 (±15.0) points. As regards the disease duration after diagnosis, 57% of the patients had a disease duration of <1 year. Regarding treatment, 94 (62.3%) and 70 (46.4%) patients received chemotherapy and radiotherapy, respectively.

### Nutritional Status

The questionnaire on the nutritional habits of the patients showed that 94.7% (n=143) were able to eat, 68.2% (n=103) could not enjoy the food as before, and 36.4% (n=55) can use enteral nutrition products at the given dose regularly. However, 38% (n=21) of these patients have been eating the enteral products enjoyably.

In addition, 58.3% of the patients stated that they managed to complete three meals daily with difficulty. Moreover, 47% (n=71) of the patients were intolerant to the smell, and 27.8% reported that the food had a disturbing smell. Furthermore, 98 (64.9%) patients stated that they could eat for nutritional purposes even though they did not enjoy it. The most common symptoms during cancer diagnosis and treatment were loss of appetite (62.9%), nausea and vomiting (47.7%), and taste changes (29.8%). Sour foods (35.1%) are the most preferred flavor by the patients, and 14 (9.3%) patients used herbal treatment products for a period after diagnosis.

Patients consumed mostly soup (64.9%), of which 39.7% most preferred yayla soup (a regional soup made from yogurt and rice). The food preferences are presented in Table 2.

**Table 1.** Demographic and clinical features of the patients with cancer receiving palliative care

| Sociodemographic features | n | % |
|---|---|---|
| **Age groups (mean age, 62.7±14.7)** | | |
| <50 | 27 | 17.9 |
| 50-59 | 35 | 23.2 |
| 60-69 | 39 | 25.8 |
| 70-79 | 32 | 21.2 |
| ≥80 | 18 | 11.9 |
| **Gender** | | |
| Male | 81 | 53.6 |
| Female | 70 | 46.4 |
| **Place of living** | | |
| Urban region (province, district center) | 100 | 66.2 |
| Rural region (little town, village) | 51 | 33.8 |
| **Education level** | | |
| Illiterate | 52 | 34.4 |
| Primary school | 71 | 47.0 |
| Secondary school and upper | 28 | 18.5 |
| **Economic status** | | |
| Income is less than the expenses | 38 | 25.2 |
| Income equal to the expenses | 97 | 64.2 |
| Income is more than the expenses | 16 | 10.6 |
| **Diagnosis** | | |
| Lung cancer | 25 | 16.6 |
| Stomach cancer | 28 | 18.5 |
| Column cancer | 21 | 13.9 |
| Breast cancer | 14 | 9.3 |
| Rectum cancer | 14 | 9.3 |
| Pancreas cancer | 5 | 3.3 |
| Others | 44 | 29.1 |

**Table 2.** Food preferences of the patients with cancer receiving palliative care

| Food preferences | n | % |
|---|---|---|
| **Soup** | | |
| Yayla | 60 | 39.7 |
| Lentil | 26 | 17.2 |
| Tarhana | 12 | 7.9 |
| Others | 53 | 35.2 |
| **Dough products** | | |
| Breads | 39 | 25.8 |
| Patty | 35 | 23.2 |
| Katmer | 23 | 15.2 |
| Others | 54 | 35.8 |
| **Sweets** | | |
| Baked sweet | 42 | 27.8 |
| Honey | 28 | 18.5 |
| Milky sweet | 27 | 17.9 |
| Others | 54 | 35.8 |
| **Meat** | | |
| Red meat | 95 | 62.9 |
| Fish | 24 | 15.9 |
| Chicken | 12 | 7.9 |
| Others | 20 | 13.3 |
| **Milk products** | | |
| Yogurt | 43 | 28.8 |
| Milk | 36 | 23.8 |
| Cheese | 31 | 20.5 |
| Others | 41 | 26.9 |
| **Oil** | | |
| Flower oil | 67 | 44.4 |
| Butter | 53 | 35.1 |
| Olive oil | 25 | 16.6 |
| Others | 6 | 3.9 |
| **Total** | 151 | 100.0 |

**Relationship Between Nutritional Status and KPS Score**

During the interview, most of the patients (94.7%) were able to eat. The median KPS score of the eating group was significantly higher than that of the non-eating group [60 (60-80) vs. 55 (35-60); p=0.043]. Patients who were dependent on enteral nutrition had significantly lower KPS scores [60 (50-70)]. Significant differences were found between the median KPS scores according to the use of enteral nutrition products (formula) during the treatment (KPS scores [60 (50-70) vs. 70 (60-80); p=0.022].

## Discussion

This study of patients with cancer in the palliative care unit showed that a large proportion of the patients were able to eat during the study period. Moreover, the majority of the patients had weight loss >10 kg, and two-thirds did not enjoy food as before. Approximately one-third of the patients were able to consume enteral nutrition products, and only one-third who started the product could have used the given dose regularly. The participants were uncomfortable most with the smell of food. Among the food groups they could consume for nutritional purposes, patients most preferred soup. Regionally, yayla was the most preferred soup. Other frequently preferred foods were bread, baked desserts, meat dish, yogurt, and flower oil.

One of the most common problems in patients with cancer is related to nutrition. Oral feeding of patients is reduced or ceased completely because of symptoms such as nausea, dysphagia, loss of appetite, constipation, mouth sores, and pain. During the initial phases of the disease, loss of appetite and weight loss are observed in one of the two patients, while more than 75% of the patients experienced these problems in the terminal period, (5) as we also observed in our patients. Enig et al. (1) found that patients experienced anorexia and inadequate nutrition as well as food disgust. The lack of appetite and some other symptoms in patients with cancer might have been caused by malnutrition (2,6). Treatments such as radiotherapy and chemotherapy and the disease process increase the severity of the symptoms and impair the palatal delight of the patients (7). Interestingly, one-third of the patients experienced severely impaired taste sensation. Many authors have investigated the olfactory changes during the progress and treatment of cancer (2,7-11). In the present study, half of the patients had increased odor sensitivity and considered many odors "unbearable or malodorous". Although they were affected by various smells such as cigarettes, detergents, perfumes, and hospital odors, patients are uncomfortable most with food odors. It worsened the nutritional status of the patient since they had already serious problems with eating due to both physical and psychological symptoms such as anorexia and depression. Consequently, malnutrition in patients with cancer, whatever the reason, led to decreased performance, reduced quality of life, and increased morbidity and mortality (3).

We also found a significant relationship between KPS scores and the eating status of the patients. Patients with a high KPS score, which means good physical performance, consume few enteral nutrition products. The possible reason was that formula was started when the general condition of the patient deteriorates or the patient does not use enteral products as long as he/she can consume other foods.

It is extremely important to identify enjoyable foods during this period because leisure experienced during food intake will strong contribute to the well-being of the patients. For the first time, we tried to elucidate in this group of patients (namely, patients with cancer in palliative care) the most preferred food in terms of both taste and nutritional value. Food disgust is frequently seen in patients with cancer receiving active treatment. Dietary regimens are largely altered or allowed to be fed as preferred to maintain the health of these patients at an optimal level (3,4). Our patients preferred soup as food during the diseased state, which quite corresponds with our culture because a strong belief about the nutritional power of soup for diseases is evident in many sayings written in our language, such as "The soup was not asked to the patient-hastaya çorba sorulmaz-, prepare soup for patient-hastaya çorba hazırlamak, hasta çorbası-soup for sick". Yayla soup was the most preferred soup**,** a well-known soup in our country prepared with rice and yogurt. It can be easily prepared and can be potentially enriched with herbs, vegetables, and meat broths. Worldwide, soup is considered an easy meal for patients who experience difficulty with eating. Indeed, Berhardson et al. (7) presented that patients preferred soup more because it can be consumed more easily and quickly. To improve the psychological well-being and nutrition of the patients, the staff in palliative care centers have ordered food and drinks for patients with cancer. However, there is little research on which foods and beverages these patients like during clinical visits (4). In particular, few or no studies have examined the traditional food types preferred by these patients. The sense of taste, i.e., taste perception, is a subject that varies with each person, ethnic origin, and culture and needs to be investigated worldwide. Traditional foods that patients desired need to be evaluated to provide them with food rich in protein, lipid, carbohydrate, and vitamins. The results of these studies will improve the quality of life of patients receiving palliative care, not only because of proper nourishment but also of the ethnic and cultural effects of foods.

As regards feeding management, patients with cancer should receive enough calories while they keep their palatal delight. The food should have a familiar taste and contain nutritious elements to keep up their metabolic balance. The provision of nutritional support, such as enteral feeding solutions, was not considered food intake because they were treated like drugs. Although various taste options with these enteral solutions are present, the patients refuse to drink them, as also shown in our study (5). Therefore; the industrial market tries to overcome the human perception of enteral solutions as well as different taste selections. It is tempting to suggest the enrichment of a well-known, eatable or drinkable, and easily prepared soup with supportive nutritional supplements such as vegetable/meat broths, whey powder, etc., within acceptable changes in the taste. Therefore, the present study suggests a novel approach of initially identifying the preferred food of patients with cancer in palliative care settings. This approach is the use of a patient-

specific nutritional plan that considers the cultural and ethical meanings of foods and their nutritional values, and the most important part is the food preference of the patients. A review on nutrition in patients with cancer emphasized the importance of a patient-specific nutrition plan approach (12). The subject is covered in the ESPEN guide published in 2017 (13). Subsequent studies are expected to develop a nutritionally rich food built on a culturally acknowledged diet. This approach could help these patients overcome at least some of the nutritional problems encountered in the course of their disease.

### Study Limitations

The study limitations include the single-center setting and the small number of patients. Similarly, the nature of the food preferences makes the study more local than universal. However, this weakness could be considered a study strength because this emphasizes the cultural aspects of palliative care.

## Conclusion

In conclusion, Hippocratic aphorisms regarding "food as medicine" should be considered for these patients during nutrition management in palliative care settings. This study shows the nutritional preferences of patients in palliative care. We recommend starting enteral nutrition products early to avoid malnutrition. Subsequent studies should examine the nutritional value of enriched foods and their impact on patient feeding.

### Ethics

**Ethics Committee Approval:** Ethical committee approval was obtained before the study (16-KAEK-088).

### Informed Consent:

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

### Authorship Contributions

Concept: N.Y.Ç., İ.O., M.S., Design: N.Y.Ç., İ.O., M.S., Data Collection or Processing: N.Y.Ç., U.Ü., R.Ç., Y.Ö., Analysis or Interpretation: R.Ç., Y.Ö., Literature Search: U.Ü., N.Y.Ç., M.S., Writing: U.Ü.

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## References

1. Enig B, Petersen HN, Smith DF, Larsen B. Food preferences, nutrient intake and nutritional status in cancer patients. Acta Oncol 1987;26:301-5.
2. Bernhardson BM, Tishelman C, Rutqvist LE. Chemosensory changes experienced by patients undergoing cancer chemotherapy: a qualitative interview study. J Pain Symptom Manage 2007;34:403-12.
3. Barrera R. Nutritional support in cancer patients. JPEN J Parenter Enteral Nutr 2002;26(5 Suppl):S63-71.
4. Danhauer SC, Keim J, Hurt G, Vitolins M. A survey of cancer patient preferences: which types of snacks do they prefer during treatment? Eur J Cancer Care (Engl) 2009;18:37-42.
5. Yılmaz B, Erdem D, Kemal Y. Nutrition Support Treatment in Cancer. İç Hastalıkları Dergisi 2011;18:133-43.
6. McQuestion M, Fitch M, Howell D. The changed meaning of food: Physical, social and emotional loss for patients having received radiation treatment for head and neck cancer. Eur J Oncol Nurs 2011;15:145-51.
7. Bernhardson BM, Olson K, Baracos VE, Wismer WV. Reframing eating during chemotherapy in cancer patients with chemosensory alterations. Eur J Oncol Nurs 2012;16:483-90.
8. Hutton JL, Baracos VE, Wismer WV. Chemosensory dysfunction is a primary factor in the evolution of declining nutritional status and quality of life in patients with advanced cancer. J Pain Symptom Manage 2007;33:156-65.
9. Brisbois TD, de Kock IH, Watanabe SM, Baracos VE, Wismer WV. Characterization of chemosensory alterations in advanced cancer reveals specific chemosensory phenotypes impacting dietary intake and quality of life. J Pain Symptom Manage 2011;41:673-83.
10. Bernhardson BM, Tishelman C, Rutqvist LE. Self-reported taste and smell changes during cancer chemotherapy. Support Care Cancer 2008;16:275-83.
11. Bernhardson BM, Tishelman C, Rutqvist LE. Olfactory changes among patients receiving chemotherapy. Eur J Oncol Nurs 2009;13:9-15.
12. Muhsiroglu O. Medical nutrition treatment in cancer patients. Gülhane Med J 2017;59:79-88.
13. Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, et al. ESPEN guidelines on nutrition in cancer patients. Clin Nutr 2017;36:11-48.

Original Article

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# Relationships among Increasing Age, Sexual Dysfunction, and Sexual Quality of Life in Married Women of Reproductive Age

## Üreme Çağı Evli Kadınlarında Artan Yaş, Cinsel İşlev Bozukluğu ve Cinsel Yaşam Kalitesi Arasındaki İlişki

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### ABSTRACT

**Objective:** This study aimed to examine the relationship among increasing age, sexual dysfunction, and sexual quality of life (SQL) in married women of reproductive age.

**Methods:** This cross-sectional study was implemented between July 2015 and April 2016. Married women aged 18-49 years (n=1,004) were stratified according to age groups (18-19, n=138; 20-24, n=153; 25-29, n=144; 30-34, n=157; 35-39, n=149; 40-44, n=135; 45-49, n=128). Data were collected using an information questionnaire, the Arizona Sexual Experiences Scale-Female (ASEX-F) questionnaire, and the Quality of Sexual Life Questionnaire-Female (SQLQ-F) questionnaire.

**Results:** Sexual dysfunction (SD) was detected in 68% of the women. The prevalence of SD increased significantly (p<0.001) from 51.4% in the 18-19 age group to 85.2% in the 45-49 age group. In the 45-49 age group, the sexual of quality life was at its lowest (29.7%) (p<0.001). Among married women of reproductive age with increasing age and in women in the 45-49 age group, the level of SD increased (p=0.021), whereas the sexual of quality life decreased (p<0.001). Furthermore, in all age groups, as SD increases, the SQL decreases significantly (p<0.001).

**Conclusion:** The prevalence of SD among married women of reproductive age is quite high and increases with age. The highest prevalence of SD is observed in women aged 45-49 years. In all age groups, as SD increases, the SQL decreases.

**Keywords:** Married women, reproductive age, sexual dysfunction, sexual quality of life

### ÖZ

**Amaç:** Üreme çağı evli kadınlarında artan yaş, cinsel işlev bozukluğu ve cinsel yaşam kalitesi (CYK) arasındaki ilişkiyi incelemek.

**Yöntemler:** Kesitsel tipte bu çalışma Temmuz 2015 ile Nisan 2016 tarihleri arasında yürütüldü. 18-49 yaşlarındaki (n=1,004) evli kadınlar yaş gruplarına (18-19, n=138; 20-24, n=153; 25-29, n=144; 30-34, n=157; 35-39, n=149; 40-44, n=135; 45-49, n=128 kadın) göre sınıflandırıldı. Veriler bir bilgi formu, Arizona Cinsel Yaşantılar Ölçeği-Kadın Formu (ACYÖ-K) ve CYK Ölçeği-Kadın Formu (CYKÖ-K) kullanılarak toplandı.

**Bulgular:** Kadınların %68'inde cinsel işlev bozukluğu (CİB) saptandı. CİB prevalansının 18-19 (%51,4) ile 45-49 (%85,2) yaş aralığında anlamlı derecede arttığı (p<0,001) gözlendi. Kırk beş-49 yaş aralığında, CYK en düşük düzeydeydi (%29,7) (p<0,001). Evli kadınlarda yaş arttıkça ve 45-49 yaş grubundaki kadınlarda CİB artmış (p=0,021), CYK azalmıştır (p<0,001). Ayrıca tüm yaş gruplarında CİB arttıkça, CYK önemli ölçüde azalmaktadır (p<0,001).

**Sonuç:** Üreme çağındaki evli kadınlar arasında CİB prevalansı oldukça yüksektir ve yaş arttıkça artmaktadır. En yüksek CİB prevalansı 45-49 yaş grubundaki kadınlarda görülür. Tüm yaş gruplarında, CİB arttıkça, kaliteli yaşamın cinsiyeti azalır.

**Anahtar Sözcükler:** Evli kadın, üreme çağı, cinsel işlev bozukluğu, cinsel yaşam kalitesi

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## Introduction

Sexual dysfunction (SD) in women is a multidimensional problem that has a negative influence on holistic well-being (1). It is described as a recurrent or permanent lack of sexual drive and sexual arousal, pain during sexual intercourse, and difficulties or a permanent difficulty in achieving orgasm (2). SD expresses the difficulties that occur during the sexual reaction cycle that prevent the individual from achieving satisfaction during sexual activity (3). SD is a problem that increases with age and affects 30%-50% of women; its prevalence in women of reproductive age is quite high (4,5). Social and cultural restrictions, as well as cultural taboos, make it quite difficult to precisely determine the prevalence of SD among women. Previous studies have reported that the prevalence of SD in women of reproductive age was 52% in Iran, 63% in Nigeria, and 45.6% in Egypt (1,6,7). In Turkey, studies have observed that the prevalence of SD varied between 45.0% and 69.8% (8-10).

Sexual quality of life (SQL) speaks to the existence of a general level of well-being regarding sexuality and sexual satisfaction (11). SD can negatively affect the SQL of married women (12). In married life, which embodies spiritual, emotional, and sexual elements, the happiness of couples is heavily dependent on a healthy relationship and SQL (13). As a negative effect on the SQL of married women, SD can destroy the relationship between partners (14).

Multidimensional, cultural, and ethnic factors that dominate all societies have influenced the prevalence of SD (15). In all societies, the most effective common factor for SD in women is age. Throughout the woman's life, the prevalence of SD increases with age. In Jordan, the prevalence of SD was at its lowest levels among women aged <18 years and at its highest levels among women aged >40 years, with age seen as the most significant risk factor (16). In married Turkish women, studies have also reported increases in the prevalence of SD with age (8,17). In Iran, the prevalence of SD increases with age; SD affects 26% of women in the 20-39 age group and 39% of those aged >50 years (18).

Women's sexual life is influenced by psychological, interpersonal, and physiological factors. In married women of reproductive age, aging associated with sexuality led to a decline in interactions between married couples and an increase in sexual problems (12). Thus, for the general health of marital relationships, married women should share any aging-related SD problems with healthcare professionals and subsequently seek treatment. To the best of our knowledge, no studies have examined the relationship among increasing age, SD, and SQL in married women.

Thus, this study aimed to examine the relationship among increasing age, SD, and SQL of married women of reproductive age.

## Methods

This cross-sectional study was implemented between July 2015 and April 2016 among married women residing in the city centers of the Edirne and Kirklareli provinces of Turkey. The study population consisted of 89,372 and 77,330 women residing in Edirne and Kırklareli, respectively, all aged 18-49 years (Turkish Statistical Institute, 2014). The sample size was determined as 980 women based on the effect of 21 possible independent factors on the scores of the SQL scale, with a $R^2$ of 0.03, alpha of 5%, and power of 80%. However, 1004 women were included in the study considering the probability of missing data. As per data from the Turkish Statistical Institute (2014), 1,004 people were weighted according to their city population. The sample included 537 married women from Edirne City and 467 from Kırklareli City. Using a stratified sampling method (n=1,004), women were stratified by age groups: 18-19, n=138; 20-24, n=153; 25-29, n=144; 30-34, n=157; 35-39, n=149; 40-44, n=135; 45-49, n=128. The address of married women in the 18-49 age group was obtained from their neighborhood official, and in the final stage, a simple random sampling method was used. Women who were married, healthy, sexually active, not pregnant, non-menopausal, and willing to participate in the study were included.

Ethical approval for the study was obtained from the Trakya University Scientific Research Ethics Committee. The participants were informed about the study, and they signed the informed consent form accompanying the questionnaire.

Data were collected through a data questionnaire, Arizona Sexual Experiences Scale-Female (ASEX-F) questionnaire, and SQL Questionnaire-Female (SQLQ-F) form. First, volunteer participants were informed about the purpose of the study and how to fill out the data form. Then, they were left alone for approximately 20 min to complete the data questionnaire. The survey questionnaire, which was prepared by the researchers after an examination of the literature, consisted of 11 questions, of which seven were about the women's attributes and four were about their sexual lives (8,13,17,19,20).

ASEX-F: This tool was developed in 2000 by McGahuey et al. (21) for the assessment of SD in women. The ASEX-F was adapted in 2004 to Turkish by Soykan (22). The scale consists of five items and is evaluated using a six-point Likert scale. The scale has the following five subdimensions: sexual drive, arousal, vaginal lubrication, sexual satisfaction, and orgasm. Each scale item is scored from 1 to 6 points (ranging from 1 indicating hyperfunction to 6 presenting hypofunction). The lowest and highest scores are 5 and 30 points, respectively. A low score demonstrates that SD is not evident, whereas a high score demonstrates the presence of SD. According to Soykan, the cutoff score for the scale to detect sexual symptoms was 11 points (22). The Cronbach's alpha value of the scale was 0.90 according to Soykan (22), and in the current study, it was 0.92.

The SQLQ-F was developed in 2005 by Symonds et al. (23), and the Turkish adaptation was performed by Tuğut and Gölbaşı (24) in 2010. The scale consists of 18 items with a six-point Likert scale and can be applied to all women aged >18 years. Women are expected to answer each item by reflecting on their sexual lives over the previous 4 weeks. The score ranges from 18 to 108

points. A high score received from the scale demonstrates that the SQL level is also high. Its Cronbach's alpha value according to Tuğut and Gölbaşı (24) was 0.83. In the present study, its Cronbach's alpha value was 0.94, and the cutoff point of the SQLQ-F total score was >62.2 by using the receiver operating characteristics (ROC) analysis. The area value under the ROC curve (AUC =0.890) was quite high and significant (p<0.001). At this cutoff point, very high predictive values (sensitivity, 93.3%; specificity, 75.4%; positive predictive value, 93.3%; negative predictive value, 70.9%) were obtained (Figure 1). Accordingly, in the present study, those with an SQLQ-F cutoff score >62 were assessed to have a good SQL.

**Statistical Analysis**

In the data analysis, SPSS 20.0 software package (IBM Corp., Armonk, NY, USA) was used. The normality distribution of quantitative data was tested by the one-sample Kolmogorov-Smirnov test. For the comparison of the ASEX-F and SQLQ-F scores according to age categories, a one-way analysis of variance test was used. A chi-square test was used to compare categorical data. Spearman correlation analysis was used to analyze the relationship between ASEX-F and SQLQ-F scores. With the ROC analysis, the cutoff value of the SQLQ-F total average score was found, and according to this cutoff value, the sensitivity, specificity, and positive predictive values were calculated. The results are shown as mean ± standard deviation or number (%), and p<0.05 was accepted as the limit value of significance.

## Results

The background personal attributes of married women of reproductive age are shown in Table 1. The distribution of the participants according to the age groups was as follows: 13.7%, 18-19 age group; 15.3%, 20-24 age group; 14.3%, 25-29 age group; 15.7%, 30-34 age group; 14.8%, 35-39 age group; 13.5%, 40-44 age group; 12.7%, 45-49 age group. Edirne was home to 53.4% of the women, and 46.6% of the women resided in Kırklareli. Moreover, 56.8% of the participants had attended high school or obtained tertiary-level education. Additionally, 83.4% of the women were members of nuclear families, 51.6% were employed, and 63.9% had income levels equal to expenditure levels. The duration of their marriages was 10.4±9.2 years (Table 1).

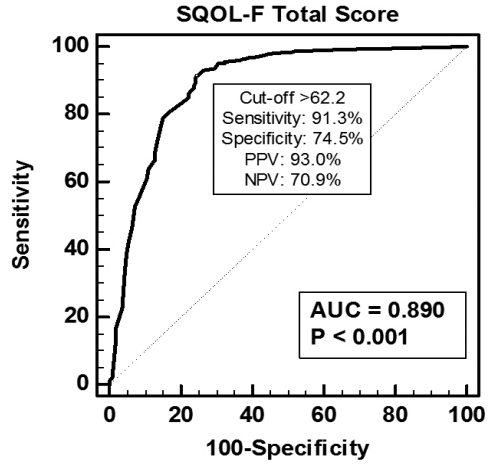


**Figure 1.** Quality of sexual life questionnaire-female cutoff score calculation according to the receiver operating characteristics analysis

In this study, the attributes of the sexual lives of all age groups (18-19, 20-24, 25-29, 30-34, 35-39, 40-44, and 45-49) were compared. Moreover, 78.1% (n=1004) of the participants were satisfied with their sexual lives; women in the 20-24 age group (86.9%) had the highest level of satisfaction, whereas those in the 45-49 age group (50.8%) had the lowest level of satisfaction. Moreover, 41.8% of the women who most frequently regarded sexuality as a "natural need" belonged to the 20-24 age group, and 28.9% who least frequently regarded sexuality as a "natural need" were part of the 45-49 age group. Women who most

**Table 1.** Personal attributes of married women of reproductive age (n=1.004)

| | n | % |
|---|---|---|
| Age | | |
| 18-19 | 138 | 13.7 |
| 20-24 | 153 | 15.3 |
| 25-29 | 144 | 14.3 |
| 30-34 | 157 | 15.7 |
| 35-39 | 149 | 14.8 |
| 40-44 | 135 | 13.5 |
| 45-49 | 128 | 12.7 |
| Place of residence | | |
| Edirne/center | 536 | 53.4 |
| Kırklareli/center | 468 | 46.6 |
| Education level | | |
| Primary and lower | 434 | 43.2 |
| High school and higher | 570 | 56.8 |
| Family structure | | |
| Nuclear family | 837 | 83.4 |
| Extended family | 167 | 16.6 |
| Employment status | | |
| Not working | 486 | 48.4 |
| Working | 518 | 51.6 |
| Income status | | |
| Income level less than expenditure level | 230 | 22.9 |
| Income level equal to expenditure level | 642 | 63.9 |
| Income level higher expenditure level | 132 | 13.1 |
| | Â ± SD | |
| Marriage year | 10.4±9.2 | |

Mean (Â), SD: Standard deviation

frequently regarded sexuality as "the most important bond with their partners" belonged to the 25-29 age group (56.3%), and the women who least frequently regarded sexuality in this way were part of the 45-49 age group (36.7%). Sexuality was regarded as "unnecessary except for reproductive purposes" most frequently by women in the 45-49 age group (18.0%) (p<0.001). The frequency of daily sexual intercourse was highest (24.6%) in the 18-19 age group, whereas women in the 20-24 age group had sexual intercourse 3-4 times a week (64.1%), and those in the 40-44 age group had sexual intercourse 1-2 times a week (53.3%). In addition, 46.1%, 16.4%, and 5.5% of the women in the 45-49 age group had sexual intercourse 1-2 times a week, 1-2 times a month, and 1-2 times every 3 weeks, respectively (p<0.001). In this study, 96.5% of the women in the 25-29 age group most frequently stated that foreplay before sexual intercourse was important, and 75.8% of the women who least frequently expressed the same sentiments belonged to the 45-49 age group (p<0.001) (Table 2).

In this study, the average ASEX-F score of married women of reproductive age was 13.4±5.4. The ASEX-F average score of women in the 45-49 age group (16.6±5.9) was significantly higher than that of women in the other age groups (18-19, 20-24, 25-29, 30-34, 35-39, and 40-44) (p=0.021). According to ASEX-F, SD was found in 68% of the women. Based on age range, the prevalence of SD was significantly increased from 51.4% in the 18-19 age group [(subsequent age groups: 20-24 age group (51.6%), 25-29 age group (64.6%), 30-34 age group (71.3%), and 40-44 age group (81.5%)] to 85.2% in the 45-49 age group (p<0.001). The average SQLQ-F score of the women was 74.2±21.0. Following a comparison between age range and the average SQLQ-F score of the women, the average SQLQ-F score of women in the 45-49 age group (60.9±23.7) was significantly lower than that of the women in the other age groups (18-19, 20-24, 25-29, 30-34, 35-39, and 40-44) (p<0.001). According to the average SQLQ-F score, where the cutoff value was ≤62, the SQL of 23.3% of the women was poor, and with the cutoff value of >62, the SQL of 76.7% of the women was good. In

**Table 2.** Comparison of attributes of women's sexual lives according to age group (n = 1004)

| | Age groups | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 18-49 (n=1004) | 18-19 (n=138) | 20-24 (n=153) | 25-29 (n=144) | 30-34 (n=157) | 35-39 (n=149) | 40-44 (n=135) | 45-49 (n=128) | p* |
| | n % | n % | n % | n % | n % | n % | n % | n % | |
| Satisfaction from sexuality | | | | | | | | | |
| Yes | 784 (78.1) | 111 (80.4) | 133 (86.9) | 124 (86.1) | 126 (80.3) | 116 (77.9) | 109 (80.7) | 65 (50.8) | <0.001 |
| No | 220 (21.9) | 27 (19.6) | 20 (13.1) | 20 (13.9) | 31(19.7) | 33 (22.1) | 26 (19.3) | 63 (49.2) | |
| Viewpoint on sexuality | | | | | | | | | |
| Natural need | 355 (35.4) | 42 (30.4) | 64 (41.8) | 53 (36.8) | 61 (38.9) | 50 (33.6) | 48 (35.6) | 37 (28.9) | <0.001 |
| The most important bond between me and my partner | 486 (48.4) | 68 (49.3) | 73 (47.7) | 81 (56.3) | 87 (55.4) | 68 (45.6) | 63 (45.9) | 47 (36.7) | |
| Unnecessary outside reproductive purposes | 82 (8.2) | 5 (3.6) | 8 (5.2) | 5 (3.5) | 4 (2.5) | 20 (13.4) | 17 (12.6) | 23 (18.0) | |
| Shame/sin | 48 (4.8) | 20 (14.5) | 5 (3.3) | 5 (3.5) | 2 (1.3) | 4 (2.7) | 2 (1.5) | 10 (7.8) | |
| I detest it | 25 (2.5) | 3 (2.2) | 2 (1.3) | 0 (0.0) | 2 (1.3) | 7 (4.7) | 3 (2.2) | 8 (6.3) | |
| It has no place in my life | 8 (0.8) | 0 (0.0) | 1 (0.7) | 0 (0.0) | 1 (0.6) | 0 (0.0) | 3 (2.2) | 3 (2.3) | |
| Sexual intercourse frequency | | | | | | | | | |
| Every day | 82 (8.2) | 34 (24.6) | 22 (14.4) | 9 (6.3) | 6 (3.8) | 5 (3.4) | 3 (2.2) | 3 (2.3) | <0.001 |
| 3-4 times a week | 434 (43.2) | 84 (60.9) | 98 (64.1) | 70 (48.6) | 76 (48.4) | 57 (38.3) | 29 (21.5) | 20 (15.6) | |
| 1-2 times a week | 336 (33.5) | 15 (10.9) | 21 (13.7) | 54 (37.5) | 55 (35.0) | 60 (40.3) | 72 (53.3) | 59 (46.1) | |
| 1-2 times every 2 weeks | 72 (7.2) | 2 (1.4) | 7 (4.6) | 5 (3.5) | 10 (6.4) | 9 (6.0) | 21 (15.6) | 18 (14.1) | |
| 1-2 times every 3 weeks | 27 (2.7) | 3 (2.2) | 2 (1.3) | 1 (0.7) | 4 (2.5) | 8 (5.4) | 2 (1.5) | 7 (5.5) | |
| 1-2 times a month | 53 (5.3) | 0 (0.0) | 3 (2.0) | 5 (3.5) | 6 (3.8) | 10 (6.7) | 8 (5.9) | 21 (16.4) | |
| Importance of foreplay before sexual intercourse | | | | | | | | | |
| Yes | 896 (89.2) | 128 (92.8) | 143 (93.5) | 139 (96.5) | 142 (90.4) | 133 (89.3) | 113 (83.7) | 98 (75.8) | <0.001 |
| No | 108 (10.8) | 10 (7.2) | 10 (6.5) | 5 (3.5) | 15 (9.6) | 16 (10.7) | 22 (16.3) | 30 (23.4) | |

*Pearson chi-square test

the 25-29 age group (6.9%), the SQL was at its lowest level. In the 45-49 age group (29.7%), the decline in the SQL was at its highest (p<0.001) (Table 3).

In this study, a significant negative relationship was detected between the ASEX-F scores for all age groups (18-19, 20-24, 25-29, 30-34, 35-39, 40-44, and 45-49); their average scores for the subdimensions sexual drive, arousal, vaginal lubrication, sexual satisfaction, and orgasm; and their SQLQ-F score average (p<0.001) (Table 4).

## Discussion

In this study, we found that the prevalence of SD among married women of reproductive age is high; in all age groups, the prevalence of SD increases as age increases, and as the level of SD increases, the SQL decreases.

This study examined the relationships between increasing age, SD, and SQL in married women of reproductive age. Of the women, 68% reported SD (ASEX-F score ≥11). Significantly, an increased prevalence of SD was observed between those in the 18-19 (51.4%) and 45-49 (85.2%) age groups. An examination of similar studies carried out in different regions in Turkey showed that SD was reported by Ege et al. (25) in 45.6% of women, Öksüz and Malhan (26) in 48.3%, Cayan et al. (8) in 46.9%, Demir et al. (27) in 28.6%, Ozturk et al. (9) in 69.8%, Artune-Ulkumen et al. (28) in 36.8%, and Yilmaz et al. (10) in 45.0% of women. The prevalence of SD among women of reproductive age was 52% in an analysis undertaken in Iran (6). In Nigeria, Fajewonyomi et al. (7) found that 63% of the women of reproductive age had SD. In Egypt, Gabr et al. (29) found that 30% of fertile women had SD, and Mustafaa et al. (1) reported 45.6%. Mishra et al. (30) found that 55.5% of fertile Indian women had SD. In studies based on age range, Özerdoğan et al. (31) found SD in 53.9% of Turkish women in the 40-44 age group and 65.8% in the 45-49 age group. Oksuz and Malhan. (32) found SD in 41% of Turkish women in the 18-30 age group, 53.1% in the 31-45 age group, and 67.9% in the 46-55 age group. Aslan et al. (17) found an age-related increase in the prevalence of SD in Turkish women, with 22%, 39.7%, and 50.2% in the 20-29, 30-39, and 40-49 age groups, respectively. Cayan et al. (8) reported an increase in the prevalence of SD

**Table 3.** Comparison of SD and SQL prevalence and ASEX-F and SQLQ-F score averages by age groups (n=1,004)

| | ASEX-F | SD | SQLQ-F | SQL poor |
|---|---|---|---|---|
| **Age** | **Â ± SD** | **Prevalence (%)** | **Â ± SD** | **Prevalence (%)** |
| 18-19 | 11.1±4.6 | 51.4 | 78.9±20.5 | 11.6 |
| 20-24 | 11.3±4.7 | 51.6 | 79.4±18.5 | 10.5 |
| 25-29 | 12.6±4.9 | 64.6 | 78.8±17.7 | 6.9 |
| 30-34 | 13.4±4.9 | 71.3 | 76.3±18.7 | 9.6 |
| 35-39 | 14.1±5.8 | 73.2 | 71.9±22.5 | 16.8 |
| 40-44 | 14.6±5.2 | 81.5 | 71.4±19.7 | 13.3 |
| 45-49 | 16.6±5.9 | 85.2 | 60.9±23.7 | 29.7 |
| Total | 13.4±5.4 | 68.0 | 74.2±21.0 | 23.3 |
| p | 0.021* | <0.001** | <0.001* | <0.001** |

*One-way ANOVA, **Pearson chi-square test, mean (Â), SD: Standard deviation
ASEX-F: Arizona Sexual Experiences Scale-Female, SQLQ-F: Quality of Sexual Life Questionnaire-Female

**Table 4.** Relation between the ASEX-F total and subdimension score averages and SQLQ-F score averages according to age groups

| | Age groups | | ASEX-F total | Sexual drive | Arousal | Vaginal lubrication | Sexual satisfaction | Orgasm |
|---|---|---|---|---|---|---|---|---|
| SQLQ-F total | 18-19 | r | -0.613* | -0.576* | -0.562* | -0.468* | -0.524* | -0.601* |
| | 20-24 | r | -0.507* | -0.519* | -0.370* | -0.334* | -0.447* | -0.475* |
| | 25-29 | r | -0.460* | -0.401* | -0.338* | -0.362* | -0.408* | -0.355* |
| | 30-34 | r | -0.539* | -0.519* | -0.422* | -0.486* | -0.467* | -0.458* |
| | 35-39 | r | -0.670* | -0.600* | -0.569* | -0.535* | -0.596* | -0.668* |
| | 40-44 | r | -0.628* | -0.542* | -0.480* | -0.569* | -0.452* | -0.603* |
| | 45-49 | r | -0.721* | -0.593* | -595* | -0.651* | -0.583* | -0.717* |

*Spearman correlation analysis, p<0.001 for all
ASEX-F: Arizona Sexual Experiences Scale-Female, SQLQ-F: Quality of Sexual Life Questionnaire-Female

with age in Turkish women, i.e., 21.7% in the 18-27 age group and 92.9% in the 58-67 age group. In Iran, the prevalence of SD in women was reported to increase with age, affecting 26% of women in the 20-39 age range and 39% in those aged >50 years (18). In Jordan, Maita et al. (16) found that the prevalence of SD was at its lowest level among those aged <18 years and the highest level in women aged >40 years. Mishra et al. (30) reported that SD was more common in fertile Indian women aged 26-30 and >41 years. The prevalence of SD is quite high in married women of reproductive age, which increases with age. In the present study, 78.1% of the women stated that they were satisfied with their sexual life, and the possible reason for this high satisfaction rate is that women are unwilling to share their sexual problems because of cultural reasons.

In the present study, 76.7% and 23.3% of married women of reproductive age had high and poor SQL, respectively. Tuncer et al. (33), Taskin Yilmaz et al. (34), Dogan et al. (20), and Yaralı and Hacıalioglu. (35) reported that married Turkish women had good SQL (21). Strizzi et al. (36) found that healthy women had good SQL. Moreover, SQL was good in most married and healthy women of reproductive age. In the present study, the SQL varied according to the age group of married women of reproductive age. Those (29.7%) in the 45-49 age group had poor SQL. Dogan et al. (20) reported a positive relationship between happiness, life satisfaction, and SQL in married Turkish women. They noted that SQL is an indicator of the level of satisfaction that an individual receives from sex (21). In the present study, the 20-24 age group (86.9%) had the highest satisfaction level from sex, and the 45-49 age group (50.8%) presented the lowest level of satisfaction. The incidence of hypoactive sexual desire disorder may increase with advancing age; therefore, women can experience sexual interest and arousal disorder. In women aged 45-49 years, the level of satisfaction derived from sex decreases, and their views related to sexuality became increasingly negative.

In the present study, the level of SD increased, whereas SQL decreased in married women of reproductive age and women aged 45-49 years. Moreover, in all age groups, as SD increases, the SQL decreases, and a significant relationship was found between the two. In their analysis of married women, Sahin et al. found that SD increased with age and women aged ≥45 years had a higher level of SD. In addition, SD is more common in those who had been married between 2 and 9 years (37). Moreover, SD increases with the age of the married Egyptian women and with the age of her partner (1). Again, in married Egyptian women, age was found as a risk factor for SD (38). In Chinese women, a significant relationship was found between age and SD, with SD becoming more frequent with age (39); a decrease in vaginal lubrication and an increase in the frequency of pain during intercourse were also reported (40). Lin et al. (41) found a significant relationship between age and SD, and as age increases, the frequency of SD increases, which negatively affects SQL. Likewise, Shin et al. (42) reported a significant relationship between age and SD, and as age increases, there is a concomitant decrease in vaginal lubrication and an increase in the frequency of pain during sexual intercourse, with SD levels increasing overall and negatively affecting SQL. Sathyanarayana Rao et al. (43) reported an increase in SD in women aged 31-50 years. Fajewonyomi et al. (7) reported that SD most frequently occurred in Nigerian women aged 26-30 years. Zhang et al. (44) found that the increase in sexual symptoms was most common in married women in the 41-49 age group. Regarding studies among Turkish women aged >49 years, Özerdoğan et al. (31) reported that SD was present in 78% of women aged ≥50 years and that there was an increase in the SD/age ratio (32). Kömürcü and Işbilen (45) noted that SD is more widespread in women aged ≥50 years than in other age groups. According to Mishra et al. (30), SD was more common in fertile Indian women aged 26-30 years and aged >41 years, and those with sexual desire dysfunction had severe SD (31). Oniz et al. (46) found that women aged 19-51 years reported an increased number of symptoms if they had been married for >11 years. According to Haghi et al. (12), marital closeness in married Iranian women aged 20-35 years was closely related to SQL and SD. In line with the literature, SD also increases with an increase in age, and as sexual symptoms increase, SQL decreases. Compared with other age groups, women in the 45-49 age group exhibited an increase in hormonal (in women, androgen hormone level decreases with increasing age, which results in decreased sexual interest and arousal) and physical changes due to menopause, decline in sexual closeness between partners, and inability to share sexual problems because of cultural reasons, which resulted in a more severe SD and a poorer SQL.

### Study Limitation

The strengths of this study were related to its inclusion of healthy, sexually active, non-pregnant, non-menopausal, and married women aged 18-49 years. Women were selected by using a stratified sampling method. Women were visited in their homes by the same researcher. However, the study has limited generalizability because it was only conducted in two cities in Turkey.

## Conclusion

The prevalence of SD among married women of reproductive age is quite high and increases with age. SQL was observed to be poorest in women aged 45-49 years. In all age groups, as SD increases, SQL decreases. In women of reproductive age, diagnosing and treating sexual problems through family health policies is important to maintain the holistic well-being of women and mitigate the likelihood of marital conflicts.

### Ethics

**Ethics Committee Approval:** Ethical approval for the study was obtained from the Trakya University Scientific Research Ethics Committee.

**Informed Consent:** The participants were informed about the study, and they signed the informed consent form accompanying the questionnaire.

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

**Authorship Contributions**

Concept: E.Z., H.K.S., Design: E.Z., H.K.S., Data Collection or Processing: E.Z., H.K.S., Analysis or Interpretation: E.Z., H.K.S., Literature Search: E.Z., H.K.S., Writing: E.Z., H.K.S.

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## References

1. Mustafaa AI, El EsawyaFM, Fawzyb I. Female sexual dysfunction among married women from the Nile Delta of Egypt. Int J SexHealth 2019;31:131-141.
2. Bassoon R, Berman J, Burnett A, Derogatis L, Ferguson D, Fourcroy J. Report of the international consensus development conference on female sexual dysfunction: definitions and classifications. J Urol 2000;163:888-93.
3. Chen CH, Lin YC, Chiu LH, Chu YH, Ruan FF, Liu WM, et al. Female sexual dysfunction: definition, classification, and debates. Taiwan J Obstet Gynecol 2013;52:3-7.
4. Berman JR, Adhikari SP, Goldstein I. Anatomy and physiology of female sexual function and dysfunction: classification, evaluation and treatment options. Eur Urol 2000;38:20-9.
5. Basson R, Althof S, Davis S, Fugl-Meyer K, Goldstein I, Leiblum S, et al. Summary of the recommendations on sexual dysfunctions in women. J Sex Med 2004;1:24-34.
6. Ghiasi A, Keramat A. Prevalence of sexual dysfunction among reproductive-age women in Iran: A systematic reviewand meta-analysis. J Midwifery Reprod Health 2018;6:1390-8.
7. Fajewonyomi BA, Orji EO, Adeyemo AO. Sexual dysfunction among female patients of reproductive age in a hospital setting in Nigeria. J Health Popul Nutr 2007;25:101-6.
8. Cayan S, Akbay E, Bozlu M, Canpolat B, Acar D, Ulusoy E. The prevalence of female sexual dysfunction and potential risk factors that may impair sexual function in Turkish women. Urol Int 2004;72:52-7.
9. Ozturk S, Sut HK, Kucuk L. Examination of sexual functions and depressive symptoms among infertile and fertile women. Pak J Med Sci 2019;35:1355-60.
10. Yilmaz BA, Sonmez Y, Sezik M. Prevalence and risk factors for sexual dysfunction in reproductive-aged married women: A cross-sectional epidemiological study. J Obstet Gynaecol Res 2020;46:507-16.
11. Gülsün M, Ak M, Bozkurt A. Marriage and Sexuality From a Psychiatric Point of View. Current Approaches in Psychiatry 2009;1:68-79.
12. Haghi F, Allahverdipour H, Nadrian H, Sarbakhsh P, Hashemiparast M, Mirghafourvand M. Sexualproblems, maritalintimacyandquality of sex life amongmarriedwomen: A studyfrom an Islamiccountry. SexRelationTher 2018;33(3):339-352.
13. Gölbaşı Z, Tuğut N, Şentürk EA, Eroğlu K. Prevalence and some related factor of sexual dysfunction among married women admitted to gynecologicout patient clinic. Cumhuriyet Med J 2014;36:1-10.
14. Morley JE, Kaiser FE. Female sexuality. Med Clin North Am 2003;87:1077-90.
15. Sungur MZ, Bez Y. Cultural factors in the treatment of sexual dysfunction in Muslim clients. Curr Sex Health Rep 2016;8:57-63.
16. Maaita ME, Khreisat BM, Tasso OA, Otom NN, Aljaafreh BM, Abuassaf GM. Prevalence and associated risk factors of female sexual dysfunction among Jordanian women. J Family Med Prim Care 2018;7:1488-92.
17. Aslan E, Beji NK, Gungor I, Kadioglu A, Dikencik BK. Prevalence and risk factors for low sexual function in women: a study of 1,009 women in an outpatient clinic of a university hospital in Istanbul. J Sex Med 2008;5:2044-52.
18. Safarinejad MR. Female sexual dysfunction in a population-based study in Iran: prevalence and associated risk factors. Int J Impot Res 2006;18:382-95.
19. Yilmaz E, Esra Zeytinci I, Sari S, Fatih Karababa I, Savaş Cilli A, Kucur R. Konya Il Merkezi'nde Yaşayan Evli Nüfusta Cinsel Sorunlarin Araştirilmasi [Investigation of sexual problems in married people living in the center of Konya]. Turk Psikiyatri Derg 2010;21:126-34.
20. Dogan T, Tugut N, Golbasi Z. The relationship between sexual quality of life, happiness, and satisfaction with life in married Turkish women. Sex Disabil 2013;31:239-47.
21. McGahuey CA, Gelenberg AJ, Laukes CA, Moreno FA, Delgado PL, McKnight KM, et al. The Arizona Sexual Experience Scale (ASEX): reliability and validity. J Sex Marital Ther 2000;26:25-40.
22. Soykan A. The reliability and validity of Arizona sexual experiences scale in Turkish ESRD patients undergoing hemodialysis. Int J Impot Res 2004;16:531-4.
23. Symonds T, Boolell M, Quirk F. Development of a questionnaire on sexual quality of life in women. J Sex Marital Ther 2005;31:385-97.
24. Tuğut N, Gölbaşı Z. A validity and reliability study of Turkish version of the Sexual Quality of Life Questionnaire-Female. Cumhuriyet Med J 2010;32:172-80.
25. Ege E, Akın B, Arslan SY, Bilgili N. Sağlıklı kadınlarda cinsel fonksiyon bozukluğu sıklığı ve risk faktörleri. TÜBAV J Sci 2010;3:137-44.
26. Öksüz E, Malhan S. Reliability and validity of the Female Sexual Function Index in Turkishpopulation. Sendrom 2005;17:54-60.
27. Demir Ö, Parlakay N, Gök G, Esen AA. Sexual dysfunction in a female hospital staff. Turk J Urol 2007;33:156-60.
28. Artune-Ulkumen B, Erkan MM, Pala HG, Bulbul Baytur Y. Sexual dysfunction in Turkish women with dyspareunia and its impact on the quality of life. Clin Exp Obstet Gynecol 2014;41:567-71.
29. Gabr AA, Omran EF, Abdallah AA, Kotb MM, Farid EZ, Dieb AS, et al. Prevalence of sexual dysfunction in infertile versus fertile couples. Eur J Obstet Gynecol Reprod Biol 2017;217:38-43.
30. Mishra VV, Nanda S, Vyas B, Aggarwal R, Choudhary S, Saini SR. Prevalence of female sexual dysfunction among Indian fertile females. J Midlife Health 2016;7:154-8.

31. Özerdoğan N, Sayıner FD, Köşgeroğlu N, Ünsal A. The Prevalence of Sexual Dysfunction and Depression and Other Factors Associated in Women 40 to 65 YearsOld. Maltepe University J Nurs Sci Art 2009;2:46-59.
32. Oksuz E, Malhan S. Prevalence and risk factors for female sexual dysfunction in Turkish women. J Urol 2006;175:654-8.
33. Tuncer SK, Aydin E, Kasimoğlu N, Ağdemir B, Başkan SA. Investigation of the effects of marital adjustment on sexual life quality of married women. Asian J Pharm Nurs Med Sci 2018;6:31-44.
34. Taskin Yilmaz F, Karakoc Kumsar A, Demirel G. The effect of body image on sexual quality of life in obese married women. Health Care Women Int 2019;40(4):479-92.
35. Yaralı S, Hacıalioğlu N. Evli kadınlarda cinsel fonksiyon bozukluğu ve cinsel yaşam kalitesinin incelenmesi. Int Refereed J Nurs Res 2016;6:108-27.
36. Strizzi J, Landa LO, Pappadis M, Olivera SL, Tangarife ERV, Agis IF, et al. Sexual functioning, desire, and satisfaction in women with TBI and healthy controls. Behavioural Neurology 2015;2015 247479:7.
37. İrer B, Çelikhisar A, Çelikhisar H, Bozkurt O, Demir Ö. Evaluation of Sexual Dysfunction, Lower Urinary Tract Symptoms and Quality of Life in Men With Obstructive Sleep Apnea Syndrome and the Efficacy of Continuous Positive Airway Pressure Therapy. Urology 2018;121:86-92.
38. Arafa AE, Elbahrawe RS, Shawky SM, Mostafa AM, Ahmed SS, El-Houfey AA, et al. Risk factors associated with female sexual dysfunction among married women in Upper Egypt; a cross sectional study. Int J Community Med Public Health 2018;5:449-53.
39. Lou WJ, Chen B, Zhu L, Han SM, Xu T, Lang JH, et al. Prevalence and Factors Associated with Female Sexual Dysfunction in Beijing, China. Chin Med J (Engl) 2017;130:1389-94.
40. Du J, Ruan X, Gu M, Bitzer J, Mueck AO. Prevalence of and risk factors for sexual dysfunction in young Chinese women according to the Female Sexual Function Index: an internet-based survey. Eur J Contracept Reprod Health Care 2016;21:259-63.
41. Lin MC, Lu MC, Livneh H, Lai NS, Guo HR, Tsai TY. Factors associated with sexual dysfunction in Taiwanese females with rheumatoid arthritis. BMC Women's Health 2017;17:2-7.
42. Shin H, Min B, Park J, Son H. A 10-year interval study to compare the prevalence and risk factors of female sexual dysfunction in Korea: the Korean internet sexuality survey (KISS) 2014. Int J Impot Res 2017;29:49-53.
43. Sathyanarayana Rao TS, Darshan MS, Tandon A. An epidemiological study of sexual disorders in south Indian rural population. Indian J Psychiatry 2015;57:150-7.
44. Zhang H, Fan S, Yip P. Sexual dysfunction among reproductive-aged Chinese married women in Hong Kong: Prevalence, risk factors, and associated consequences. J Sex Med 2015;12:738-45.
45. Kömürcü N, İşbilen A. Adaptation of women to sexual life during the postmenopausal period. Turk J Urol 2011;37:326-30.
46. Oniz A, Keskinoglu P, Bezircioglu I. The prevalence and causes of sexual problems among premenopausal Turkish women. J Sex Med 2007;4:1575-81.

Original Article

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# Effects of Oral Alprazolam and Oral Tramadol on Anxiety and Analgesia in Patients Undergoing Breast Cancer Surgery

## Meme Kanseri Cerrahisi Geçirecek Hastalarda Oral Alprazolam ve Oral Tramadol Premedikasyonun Anksiyete ve Analjezi Üzerine Etkileri

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## ABSTRACT

**Objective:** The aim of this study is to determine postoperative pain and anxiety condition of patients undergoing elective breast cancer surgery who recieved preoperative combination of Tramadol and Alprazolam.

**Methods:** One hundred and twenty American Society of Anesthesiologists I-III patients undergoing elective breast surgery were enrolled clinically, randomized, prospectively in the study. Patients separated into Group 1 (Alprazolam 1 mg PO + Tramadol 100 mg PO), Group 2 (Alprazolam 1 mg PO + Tramadol 50 mg PO) and Group 3 (conventional premedication-control group). Alprazolam was given to the patients before the night of the operation. Tramadol was given to the patients before 60 min before the operation. All patients received standard general anesthesia. After extubation, st minute visual analogue scale (VAS) and richmond agitation sedation scale (RASS) values were recorded. In the recovery room, VAS and RASS values were recorded in 20$^{th}$ and 40$^{th}$ minutes and again in 24$^{st}$ hour. For statistical analysis of data, one-way Anova Test, Tukey HSD Test, Tamhane's T2 test were used.

**Results:** In the postoperative period, levels of agitation caused by anxiety were lower in the patients who received preoperative Alprazolam (Group 1-2) than the patients who did not receive Alprazolam (Group 3) (p=0.007). RASS levels were significantly lower in the patients who received preoperative 100 mg Tramadol and 1 mg Alprazolam than the other groups. VAS levels were decreased in time in each group, but there was no difference in VAS levels between groups.

## ÖZ

**Amaç:** Çalışmada amacımız, elektif meme kanseri cerrahisi uygulanacak kadınlarda preoperatif dönemde verilen tramadol-alprazolam kombinasyonunun postoperatif dönemde ağrı ve anksiyete üzerine etkinliğini araştırmaktır.

Yöntem: Çalışmaya elektif meme kanseri cerrahisi uygulanacak 120 hasta klinik, randomize ve prospektif olarak dahil edildi. Hastalar Amerikan Anesteziyoloji Derneği (ASA) sınıflandırmasına göre sınıf 1-3 arasındaydı. Hastalar Grup 1 (Alprazolam 1 mg oral + Tramadol 100 mg oral), Grup 2 (Alprazolam 1 mg oral + Tramadol 50 mg oral), Grup 3 (konvansiyonel premedikasyon-kontrol grubu) olarak 3 gruba ayrıldı. Hastalara operasyondan 1 gece önce alprazolam verildi, operasyondan 60 dakika önce tramadol verildi. Tüm hastalarda standart genel anestezi uygulandı. Ekstübasyon sonrası 1. dakikada vizüel analog skala (VAS) ve richmond ajitasyon sedasyon skalası (RASS) verileri kaydedildi. Postoperatif derlenme odasına alınan hastaların 20. 40. dakika ve 24. saatte VAS ve RASS ölçümleri yinelendi. İstatistiksel analiz için One-Way Anova Test, Tukey HSD Test veTamhane's T2 Test kullanıldı.

**Bulgular:** Preoperatif alprazolam verilen hastaların (Grup 1-2), Alprazolam verilmeyen hastalara (Grup 3) oranla postoperatif dönemde anksiyete ilişkili ajitasyon daha az yaşadığı saptandı (p=0,007). Preoperatif 1 mg alprazolam ve 100 mg tramadol verilen gruptaki hastaların RASS değerlerinin diğer gruplardan anlamlı oranda düşük olduğu görüldü. Grup içi VAS değelerinin zaman içinde düştüğü, ancak gruplar arası VAS değerinde farklılık olmadığı görüldü.

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**Conclusion:** We found that the preoperative combination of oral administered 100 mg Tramadol and 1 mg Alprazolam resulted in decreased anxiety in the postoperative period in patients undergoing elective breast cancer surgery.

**Keywords:** Postoperative analgesia, preemtive analgesia, breast cancer, anxiety

**Sonuç:** Elektif meme cerrahisi uygulanan hastalarda preoperatif oral olarak verilen 1 mg Alprazolam ve 100 mg Tramadol kombinasyonunun, postoperatif dönemde anksiyeteyi azalttığını saptadık.

**Anahtar Sözcükler:** Postoperatif analjezi, preemptif analjezi, meme kanseri, anksiyete

## Introduction

Breast cancers have emotional and psychological implications for the woman beyond the size of the affected tissue or organ (1). While almost half of patients with cancer experience psychiatric disorders, more than one third of female patients with breast cancer experience psychopathological disorders and anxiety during the disease process (2). Anxiety has many negative effects on the organism, one of which is pain (3) .

In recent years, research on controlling postoperative pain starting from the preoperative period has brought the concept of "preemptive analgesia" to the agenda. The aim of preemptive administration of drugs is to prevent the central sensitization process and to achieve a better analgesia quality after surgery (4-7).

Tramadol is a commonly used synthetic opioid derivative analgesic agent. Analgesic efficacy has been demonstrated in many studies (8-10). It is also frequently and effectively used in preemptive analgesia.

Alprazolam is a short-acting benzodiazepine commonly used in the treatment of anxiety disorders. Various studies have mentioned the analgesic properties of alprazolam and its use in preemptive analgesia (11,12). Studies showing the postoperative efficacy of opioid and benzodiazepine combinations in breast surgeries are limited.

Unlike the postoperative pain that occurs after breast surgeries performed for other reasons, the postoperative pain experienced by women undergoing breast cancer surgery deteriorates their quality of life more, and the anxiety they experience during this period also has an effect on this pain. In our study, we aimed to reveal the effectiveness of tramadol and alprazolam combination in the preoperative period on pain and anxiety in the postoperative period in female patients who underwent surgery with the diagnosis of breast cancer.

## Methods

The study was conducted with 120 ASA I-III class women in the 20-80 age group who underwent elective breast surgery between 2012 and 2014 in İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty Monobloc Operating Room after obtaining the approval of the Ethics Committee of İstanbul University-Cerrahpaşa Cerrahpaşa Faculty of Medicine. It was conducted clinically, randomized and prospectively. Before the patients participated in the study, the study was explained to the patients in detail and their written consent was obtained. The study was prepared in accordance with the principles of the Declaration of Helsinki.

A person who was unaware of the study divided the patients into groups by drawing lots. The patients were divided into groups and randomization was achieved in this way.

Patients with a history of drug allergy, decompensated respiratory and circulatory insufficiency, psychiatric disorders, and those requiring follow-up in the postoperative intensive care unit were not included in the study.

The patients were randomly divided into 3 groups:

Group 1: Alprazolam 1 mg orally + Tramadol 100 mg orally were given.

Group 2: Alprazolam 1 mg orally + Tramadol 50 mg orally were given.

Group 3: Midazolam 0.03 mg/kg was administered intravenously (conventional premedication-control group).

One mg tablet of alprazolam (Xanax 1 mg tablet, Pzifer Inc., New York, USA) was given orally to the premedicated patient groups (Group 1 and Group 2) in the surgical ward the night before the scheduled day of surgery. The group that would receive conventional premedication was not given any medication the night before. Patients were taken to the preoperative preparation room 60 minutes before the operation, intravenous access was established with a 20G cannula for all patients, 50 mg/100 mg tramadol (Contramal 50 mg tablet-Contramal Retard 100 mg, Abdi İbrahim, İstanbul, Turkey) was administered to the premedicated groups 60 minutes before the surgery in the recovery unit. The tablet was given orally with 5 mL of water. Conventional premedication was applied to Group 3 (Demizolam 5 mg ampoule, Dem İlaç, Istanbul, Turkey). Then the patients were taken to the operating room. Standard monitoring was done. After the operation, the visual analogue scale (VAS) and richmond agitation sedation scale (RASS) values were recorded at the 1$^{st}$ minute following extubation. After the patients were taken to the postoperative care room, standard monitoring was applied, oxygen was administered at 4 L/min with a simple face mask, and VAS and RASS values were recorded at the 20$^{th}$ and 40$^{th}$ minutes. After the 40$^{th}$ minute, the patients were transferred to the service in accordance with the criteria for leaving the postoperative care room (aldrete score >9). VAS and RASS values

were recorded again at the postoperative 24th hour and additional analgesic requirement, nausea and vomiting were questioned.

At the end of the study, preoperative, intraoperative and postoperative recorded VAS and RASS values of all three groups were statistically compared.

### Statistical Analysis

While evaluating the study data, in addition to descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) in comparison of quantitative data, "One-way Anova Test" in the comparison of groups of three or more with normal distribution and "Tukey HSD" test and "Tamhane's T2" test were used in the determination of the group causing the difference. Kruskal-Wallis test was used in the comparison of groups of three or more that did not show normal distribution, and the "Mann-Whitney U" test was used to determine the group that caused the difference. The Friedman test was used for in-group comparisons of parameters that did not show normal distribution, and the "Wilcoxon Signed Ranks" test was used to evaluate binary comparisons. "Pearson chi-square test" was used in the comparison of qualitative data. Significance was evaluated at $p<0.01$ and $p<0.05$ levels.

## Results

### Demographic Features

There was no significant difference between the groups in terms of demographic findings of the patients. Demographic data of the patients are given in Table 1.

### VAS Scores

No statistically significant difference was observed between the groups in terms of VAS scores at the 1st, 20th, 40th minutes and 24th hour (Table 2) (Figure 1).

The change (decreases) observed at the 20th minute scores compared to the 1st minute VAS scores showed a statistically significant difference between the groups (p=0.032). The changes observed at the 40th minute and 24th hour scores compared to the 1st minute VAS scores did not show a statistically significant difference between the groups. The changes observed at the 40th minute and 24th hour scores compared to the 20th minute VAS scores were not statistically significant between the groups (Table 2). The changes (decreases) observed in the 24th hour scores compared to the 40th minute VAS scores showed a statistically significant difference between the groups (p=0.018).

### RASS Scores

Significant differences were observed in the distribution of RASS scores between the groups (Figure 2). A statistically significant difference was observed between the groups in terms of 1st minute RASS scores (p=0.036) (Table 3). According to the binary comparisons made to determine the group that created the difference; it was observed that the 1st minute RASS scores of Group 1 patients were statistically significantly lower than the scores of both Group 2 patients and Group 3 patients (p=0.041

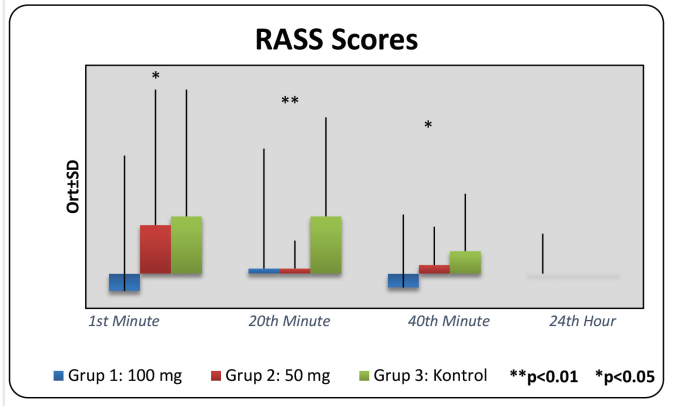


**Figure 1.** Distribution of VAS scores by groups
VAS: Visual analogue scale

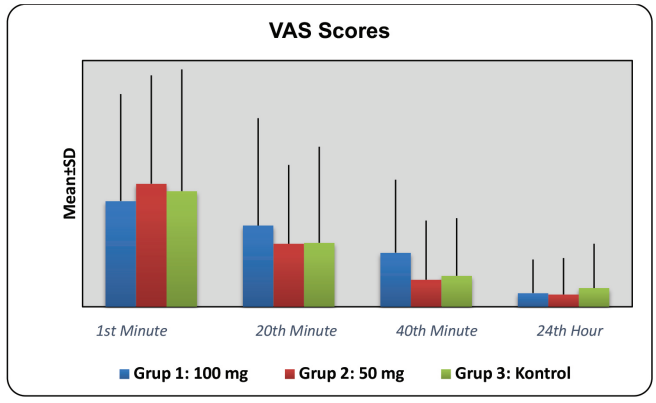


**Figure 2.** Distribution of RASS scores by groups
RASS: Richmond agitation sedation scale

**Table 1.** Demographic data of groups

| n (%) | | Group 1<br>n (%) | Group 2<br>n (%) | Group 3 | p |
|---|---|---|---|---|---|
| ASA | 1 | 25 (62.5) | 25 (62.5) | 27 (67.5) | [a]0.865 |
| | 2 | 15 (37.5) | 15 (37.5) | 13 (32.5) | |
| | | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | |
| Age | | 48.35±12.13 | 44.75±9.97 | 45.85±9.38 | [b]0.299 |
| Height | | 162.05±6.57 | 160.25±7.01 | 160.25±5.94 | [b]0.366 |

SD: Standard deviation

and p=0.017, respectively). No statistically significant difference was observed between Group 2 patients and Group 3 patients (Table 3a).

A statistically significant difference was observed between the groups in terms of 20th minute RASS scores (p=0.007) (Table 3). According to the binary comparisons made to determine the group that created the difference; it was observed that the 20th minute RASS scores of Group 3 patients were statistically significantly higher than the scores of both Group 1 patients and Group 2 patients (p=0.019 and p=0.002, respectively). No statistically significant difference was observed between Group 1 patients and Group 2 patients (Table 3a).

A statistically significant difference was observed between the groups in terms of 40th minute RASS scores (p=0.007) (Table 8). According to the binary comparisons made to determine the group that created the difference; it was observed that the 40th minute RASS scores of Group 1 patients were statistically significantly lower than the scores of Group 3 patients (p=0.020 and p<0.05, respectively). No statistically significant difference was observed between the other groups (Table 3).

It was observed that the changes in the measurements made at the 1st minute, 20th minute, 40th minute and 24th hour in Group 1 patients were not statistically significant (Table 3).

In Group 2 patients, it was observed that the change between the measurements made at the 1st minute, 20th minute, 40th minute and 24th hour was statistically significant (p=0.041). It was observed that the change (decrease) in the RASS scores of the patients in this group at the 20th minute and 24th hour compared to the 1st minute RASS scores were statistically significant (p=0.041 and p=0.033, respectively). It was observed that the changes observed at the 40th minute compared to the 1st minute RASS scores were not statistically significant. It was observed that the changes in the direction of decrease observed at the 40th minute and 24th hour compared to the 20th minute RASS scores were not statistically significant. It was observed that the changes in the direction of decrease observed at the 24th hour compared to the 40th minute RASS scores were not statistically significant (Table 3).

In Group 3 patients, it was observed that the change between the measurements made at the 1st minute, 20th minute, 40th minute and 24th hour was statistically significant (p=0.001). It was observed that the changes in the direction of decrease observed at the 20th and 40th minutes compared to the 1st minute RASS scores in this group were not statistically significant. It was observed that the change in the direction of decrease observed in the 24th hour RASS scores compared to the 1st minute RASS scores was statistically significant (p=0.009). Compared to the 20th minute RASS scores, the changes in the direction of decrease observed at the 40th minute and 24th hour were statistically significant (p=0.005 and p=0.002, respectively). It was observed that the change in the direction of decrease observed at the 24th hour compared to the 40th minute RASS scores was statistically significant (p=0.025) (Table 3).

**Table 2.** Evaluations according to VAS scores

| VAS score | Group 1 | | Group 2 | | Group 3 | | [a]p |
|---|---|---|---|---|---|---|---|
| | Min/max (median) | Mean ± SD | Min/max (median) | Mean ± SD | Min/max (median) | Mean ± SD | |
| [1]1st minute | 0-7 (2.00) | 2.15±2.17 | 0-8 (2.00) | 2.50±2.20 | 0-8 (2.00) | 2.35±2.47 | 0.759 |
| [2]20th minute | 0-8 (0.00) | 1.65±2.18 | 0-6 (0.00) | 1.28±1.60 | 0-8 (0.00) | 1.30±1.95 | 0.775 |
| [3]40th minute | 0-4 (0.00) | 1.10±1.48 | 0-4 (0.00) | 0.55±1.20 | 0-4 (0.00) | 0.63±1.17 | 0.111 |
| [4]24th hour | 0-2 (0.00) | 0.28±0.68 | 0-4 (0.00) | 0.25±0.74 | 0-4 (0.00) | 0.38±0.90 | 0.897 |
| [b]p | 0.001** | | 0.001** | | 0.001** | | |
| Differences | Min/max (median) | [c]p | Min/max (median) | [c]p | Min/max (median) | [c]p | [a]p |
| 1-2 | -4/2 (0.00) | 0.022* | -4/0 (-1.50) | 0.001** | -6/0 (0.00) | 0.001** | 0.032* |
| 1-3 | -4/0 (0.00) | 0.001** | -6/0 (-2.00) | 0.001** | -7/0 (-2.00) | 0.001** | 0.072 |
| 1-4 | -7/0 (-2.00) | 0.001** | -7/0 (-2.00) | 0.001** | -7/0 (-2.00) | 0.001** | 0.618 |
| 2-3 | -4/0 (0.00) | 0.007** | -4/0 (0.00) | 0.001** | -4/0 (0.00) | 0.001** | 0.732 |
| 2-4 | -8/0 (0.00) | 0.001** | -5/0 (0.00) | 0.001** | -6/0 (0.00) | 0.001** | 0.609 |
| 3-4 | -4/0 (0.00) | 0.001** | -3/1 (0.00) | 0.023* | -3/2 (0.00) | 0.119 | 0.018* |

[a]Kruskal-Wallis test, [b]Friedman test, [c]Wilcoxon Signed Ranks test, *p<0.05, **p<0.01, VAS: Visual analogue scale

**Table 2a.** Binary comparisons (post-hoc evaluations)

| VAS score | Group 1-2 | Group 1-3 | Group 2-3 |
|---|---|---|---|
| Difference 1-2 | 0.010* | 0.096 | 0.339 |
| Difference 3-4 | 0.019* | 0.017* | 0.845 |

Mann-Whitney U test, *p<0.05, VAS: Visual analogue scale

**Table 3.** Evaluations according to RASS scores

| RASS score | Group 1 Min/max (median) | Group 1 Mean ± SD | Group 2 Min/max (median) | Group 2 Mean ± SD | Group 3 Min/max (median) | Group 3 Mean ± SD | [a]p |
|---|---|---|---|---|---|---|---|
| [1]1st minute | -2/2 (0.00) | -0.10±0.78 | -1/2 (0.00) | 0.28±0.78 | -1/2 (0.00) | 0.33±0.73 | 0.036* |
| [2]20th minute | -1/1 (0.00) | 0.03±0.69 | 0/1 (0.00) | 0.03±0.16 | 0/2 (0.00) | 0.33±0.57 | 0.007** |
| [3]40th minute | -2/1 (0.00) | -0.08±0.42 | 0/1 (0.00) | 0.05±0.22 | 0/1 (0.00) | 0.13±0.33 | 0.035* |
| [4]24th hour | -1/1 (0.00) | 0.00±0.23 | 0/0 (0,00) | 0.00±0.00 | 0/0 (0.00) | 0.00±0.00 | 1.000 |
| [b]p | 0.323 | | 0,041* | | 0.001** | | |
| Differences | Min/max (median) | [c]p | Min/max (median) | [c]p | Min/max (median) | [c]p | [a]p |
| 1-2 | -3/1 (0.00) | 0.134 | -2/1 (0.00) | 0.041* | -2/1 (0.00) | 1.000 | 0.024* |
| 1-3 | -2/2 (0.00) | 0.830 | -2/1 (0.00) | 0.090 | -2/2 (0.00) | 0.059 | 0.314 |
| 1-4 | -2/2 (0.00) | 0.400 | -2/1 (0.00) | 0.033* | -2/2 (0.00) | 0.009** | 0.031* |
| 2-3 | -2/1 (0.00) | 0.285 | -1/1 (0.00) | 0.564 | -2/1 (0.00) | 0.005** | 0.058 |
| 2-4 | -2/1 (0,00) | 0,796 | -1/0 (0,00) | 0,317 | -2/1 (0,00) | 0,002** | 0,008** |
| 3-4 | 0/1 (0,00) | 0,083 | -1/0 (0,00) | 0,157 | -1/1 (0,00) | 0,025* | 0,007** |

[a]Kruskal-Wallis test, [b]Friedman test, [c]Wilcoxon Signed Ranks test, *p<0.05, **p<0.01

**Table 3a.** Binary comparisons (post-hoc evaluations)

| RASS score | Group 1-2 | Group 1-3 | Group 2-3 |
|---|---|---|---|
| 1st minute | 0.041* | 0.017* | 0.868 |
| 20th minute | 0.606 | 0.019* | 0.002** |
| 40th minute | 0.105 | 0.020* | 0.238 |
| Difference 1-2 | 0.009** | 0.251 | 0.100 |
| Difference 1-4 | 0.036* | 0.014* | 0.868 |
| Difference 2-4 | 0.805 | 0.023* | 0.002** |
| Difference 3-4 | 0.026* | 0.005** | 0.238 |

Mann-Whitney U Test, *p<0.05, **p<0.01

## Discussion

In our study, we aimed to prepare the patients both physically and mentally for the surgery by minimizing the agitation and anxiety experienced by the patients 60 minutes before the operation, and to prevent the feeling of pain caused by agitation and anxiety in the postoperative period. The drugs we chose for this purpose were Alprazolam from the benzodiazepine group, which could be easily administered in hospital wards, and Tramadol, an opioid derivative.

It is known that peroral administration of 1 mg of Alprazolam 1 hour before induction of anesthesia reduces anxiety and agitation without significant side effects[13]. Tramadol, on the other hand, has been used frequently in both postoperative and preemptive analgesia in recent years. In many studies, anxiety and agitation measurements were performed during the preoperative visit (14-17). Vickers et al. (18) used anxiety measurement to determine the timing of the preoperative visit in a study they conducted. They measured the patients' anxiety one week before, one day before, and just before the operation, and reported that they could not find a significant difference between these measurements. Lichtor et al. (19) conducted a study to determine whether the anxiety level measured in the afternoon of the day before the operation reflected the anxiety level just before the operation. They reported that there was 70% correlation between the anxiety levels measured in both periods. Badner et al. (14) also reported that they showed a 73% correlation between the anxiety levels measured in the afternoon before the operation and just before the operation.

Detection of lower analgesic needs and pain scores during the periods when the clinical active period of antinociceptive therapy was over in patients who underwent preemptive treatment was considered as evidence of preemptive analgesia (20). Wang et al. (21) showed that the pain scores in the first 24 hours after the operation in patients who were given 100 mg of Tramadol before the operation were significantly lower than the group that did not receive Tramadol in their study performed in patients who would undergo total abdominal hysterectomy. In our study, we found that pain scores were lower in the early postoperative period (1st minute) in the patient group given 100

mg Tramadol, similar to this study. But these values were not statistically and clinically significant. Comparing the preemptive efficacy of Tramadol, Pozos-Guillen et al. (22) administered oral Tramadol 1 hour before mandibular third molar tooth extraction to a group, administered oral Tramadol after the procedure in another group and administered saline in control group. It was found that the efficacy of Tramadol given preemptively was 85%. Olmez et al. (23), compared 8 mg Lornoxicam, 100 mg Tramadol and saline infusion in 62 patients who underwent transrectal prostate biopsy. The drugs were administered half an hour before the operation. Tramadol was found to be more effective in the VAS comparison made after the operation. In the literature research of Møiniche et al. (24), 9 studies using opioids as preemptive analgesics were evaluated. In 7 of these studies, no postoperative difference was found between the treatment group and the control group in patients given preoperative opioids. In our study, similar to these studies, we did not find a statistically significant difference in terms of postoperative VAS values in Group 1 and Group 2 patients who received preoperative Tramadol compared to Group 3 patients who did not receive preoperative Tramadol. However, in our study, VAS changes were found to be statistically significant in all groups. We observed a significant decrease in VAS values beginning from the 1st minute to the 24th hour postoperatively in Group 1 and 2 patients. Based on this, we think that Tramadol given preemptively will be effective on postoperative analgesia, although we cannot find a statistical difference. Bösenberg and Ratcliffe (25) found a decrease in pain in the first 2 hours postoperatively when Tramadol was given with a dose of 1-2 μg kg-1 before surgery in patients undergoing inguinal surgery. They did not detect a significant difference in pain scores in the first 30-60 minutes. On the other hand, although there was no difference between the treatment and the control group in terms of VAS scores at the end of the postoperative 1st hour, the total analgesic requirement was less. In our study, similar to this study, we did not find a statistically significant difference between the groups in terms of pain scores. However, VAS values were below 4 beginning from the first minute in all our study groups. This might be due to the Remifentanil we administered intraoperatively. In addition, we thought that the limitation of the patients we included in the groups may have caused this. However, such a result may have arisen because VAS is a subjective assessment. Therefore, we think that clinical, prospective, randomized studies with larger patient groups should be conducted.

It has been reported that high preoperative anxiety and agitation in adult patients increase postoperative pain and cause a significant increase in the need for analgesic and sedative drugs. Pasnau et al. (26) found in their studies that the level of postoperative anxiety and agitation was associated with the level of preoperative anxiety. The rate of medical complications is also higher in patients with high postoperative anxiety (27). In addition, inadequate pain management may increase agitation. In our study, similar to these studies, we found higher agitation scores in the patient group who did not receive Alprazolam and Tramadol preoperatively. De Witte et al. (28) administered oral Alprazolam preoperatively to 45 female patients who were going to undergo laparoscopic gynecological surgery and they evaluated the anxiety, sedation level and VAS score postoperatively. As a result of the study, it was found that the VAS score and sedation and anxiety level of the Alprazolam group were significantly lower than the placebo group. In our study, similar to this study, the RASS value measurements made beginning from the 1st minute to the 24th hour postoperatively in the patients who were given Alprazolam + 100 mg Tramadol in the preoperative period were statistically significantly lower than the decrease in the RASS values of the patients who were given preoperative Alprazolam + 50 mg of Tramadol and those who were not given Alprazolam + Tramadol preoperatively. We found that the combination of Alprazolam given in the preoperative period with 100 mg of Tramadol was more effective on postoperative anxiety than the combination of Alprazolam with 50 mg of Tramadol. Based on these findings, we think that administration of alprazolam in the preoperative period reduces the agitation experienced by the patients in the postoperative period.

We did not measure anxiety in the preoperative period in our study. We accepted that the patients had anxiety in the preoperative period and that the patients experienced agitation due to this anxiety. We decided to measure this existing agitation in the postoperative period. We used RASS to measure agitation in the postoperative period. RASS is a method frequently used in the evaluation of sedation level and agitation, especially in intensive care units.

Contrary to our hypothesis that agitation increased the perception of pain in patients, according to the results of our study, although the agitation scores were lower in Group 1, we did not find the VAS results as we expected. We cannot fully explain the reason for this.

### Study Limitations

The limitations of our study were that the level of anxiety and agitation of the patients was not determined by the "psychiatry" clinic in the preoperative period, the same tests were not repeated postoperatively, patient satisfaction was not questioned in the postoperative period, and the evaluation of the VAS was a subjective evaluation.

## Conclusion

We found that the RASS values of the patients in the group given preoperative 100 mg Tramadol and Alprozam together were significantly lower than the other groups. In conclusion, we found that combining 100 mg of Tramadol preoperatively with Alprazolam, an anxiolytic, effectively reduced anxiety in the postoperative period. Conducting more comprehensive, multi-center studies on this subject will enable a better understanding of the effects of preoperative anxiety on pain and anxiety in the postoperative period in patients undergoing breast cancer surgery.

### Ethics

**Ethics Committee Approval:** The study was conducted with 120 ASA I-III class women in the 20-80 age group who underwent

elective breast surgery between 2012 and 2014 in Cerrahpaşa Medical Faculty Monobloc Operating Room after obtaining the approval of the Ethics Committee of İstanbul University-Cerrahpaşa Cerrahpaşa Faculty of Medicine. It was conducted clinically, randomized and prospectively.

**Informed Consent:** Before the patients participated in the study, the study was explained to the patients in detail and their written consent was obtained.

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

**Authorship Contributions**

Concept: B.A., G.M.K., Design: B.A., G.M.K., Data Collection or Processing: B.A., G.M.K., Analysis or Interpretation: B.A., G.M.K., Literature Search: B.A., G.M.K., Writing: B.A., G.M.K.

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

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## References


1. Zdenkowski N, Tesson S, Lombard J, Lovell M, Hayes S, Francis PA, Dhillon HM, Boyle FM. Supportive care of women with breast cancer: key concerns and practical solutions. Med J Aust 2016;205:471-5.
2. Villar RR, Fernández SP, Garea CC, Pillado MTS, Barreiro VB, Martín CG. Quality of life and anxiety in women with breast cancer before and after treatment. Rev Lat Am Enfermagem 2017;25:e2958.
3. Liesto S, Sipilä R, Aho T, Harno H, Hietanen M, Kalso E. Psychological resilience associates with pain experience in women treated for breast cancer. Scand J Pain 2020;20:545-53.
4. Kissin I. Preemptive analgesia. Anesthesiology 2000;93:1138-43.
5. Węgorowski P, Stanisławek A, Domżał-Drzewicka R, Sysiak J, Rząca M, Milanowska J, et al. The effect of pre-emptive analgesia on the level of postoperative pain in women undergoing surgery for breast neoplasm. Contemp Oncol (Pozn) 2016;20:158-64.
6. Doleman B, Leonardi-Bee J, Heinink TP, Bhattacharjee D, Lund JN, Williams JP. Pre-emptive and preventive opioids for postoperative pain in adults undergoing all types of surgery. Cochrane Database Syst Rev 2018;12:CD012624.
7. Kelly DJ, Ahmad M, Brull SJ. Preemptive analgesia I: physiological pathways and pharmacological modalities. Can J Anaesth 2001;48:1000-10.
8. Bravo L, Mico JA, Berrocoso E. Discovery and development of tramadol for the treatment of pain. Expert Opin Drug Discov 2017;12:1281-91.
9. Yarramalle SP, Munta K, Rao SM, Venkategowda PM, Sunka S, Dudam SK. Comparision of Analgesic Efficacy of Tramadol Infusion Versus Tramadol Plus Ondansetron Infusion In Medical Intensive Care Unit. Indian J Crit Care Med 2018;22:353-6.
10. Tsaousi GG, Chatzistravou A, Papazisis G, Grosomanidis V, Kouvelas D, Pourzitaki C. Analgesic Efficacy and Safety of Local Infiltration of Tramadol in Pediatric Tonsillectomy Pain: A Systematic Review and Meta-Analysis. Pain Pract 2020;20:550-63.
11. Joseph TT, Krishna HM, Kamath S. Premedication with gabapentin, alprazolam or a placebo for abdominal hysterectomy: Effect on pre-operative anxiety, post-operative pain and morphine consumption. Indian J Anaesth 2014;58:693-9.
12. Avanaz A, Yaprak M, Doğru V, Mesci A, Akbaş M, Kısaoğlu C, et al. Effect of Alprazolam as a Preoperative Adjuvant Analgesic on Postoperative Pain in Laparoscopic Donor Nephrectomy Patients. Transplant Proc 2019;51:1044-8.
13. Yücel A. Postoperatif Analjezi. Istanbul. 2004:7-68,145-157.
14. Badner NH, Nielson WR, Munk S, Kwiatkowska C, Gelb AW. Preoperative anxiety: detection and contributing factors. Can J Anaesth 199;37:444-7.
15. Gönüllü M, Turan ED, Erdem LK. Anestezi uygulanacak hastalarda anksiyete düzeyinin araştırılması. Türk Anest ve Rean Cem 1986;14:110-3.
16. Chew ST, Tan T, Tan SS, Ip-Yam PC. A survey of patients' knowledge of anaesthesia and perioperative care. Singapore Med J 1998;39:399-402.
17. Moerman N, Van Dam FSAM, Muller MJ. The Amsterdam preoperative anxiety and information scala. Anasth Analg 1996;82:445-51.
18. Vickers MD, O'Flaherty D, Szekely SM, Read M, Yoshizumi J. Tramadol: pain relief by an opioid without depression of respiration. Anaesthesia 1992;47:291-6.
19. Lichtor JL, Johanson CE, Mhoon D, Faure EA, Hassan SZ, Roizen MF. Preoperative anxiety: does anxiety level the afternoon before surgery predict anxiety level just before surgery? Anesthesiology 1987;67:595-9.
20. Baykara N. Santral sensitizasyon ve preemptif analjezi. Sendrom 2000:12;69-75.
21. Wang F, Shen X, Xu S, Liu Y. Preoperative tramadol combined with postoperative small-dose tramadol infusion after total abdominal hysterectomy: a double-blind, randomized, controlled trial. Pharmacol Rep 2009;61:1198-205.
22. Pozos-Guillen A, Martinez-Rider R, Aguirre-Banuelos P, Perez-Urizar J. Pre-emptive analgesic effect of tramadol after mandibular third molar extraction: a pilot study. J Oral Maxillofac Surg 2007;65:1315-20.
23. Olmez G, Kaya S, Aflay U, Sahin H. Comparison of lornoxicam versus tramadol analgesia for transrectal prostate biopsy: a randomized prospective study. Int Urol Nephrol 2008;40:341-4.
24. Møiniche S, Kehlet H, Dahl JB. A qualitative and quantitative systematic review of preemptive analgesia for postoperative pain relief: the role of timing of analgesia. Anesthesiology 2002;96:725-41.
25. Bösenberg AT, Ratcliffe S. The respiratory effects of tramadol in children under halothane an anaesthesia. Anaesthesia 1998;53:960-4.
26. Pasnau RO, Fawzy FI, Skotzko CE et al. Surgeryandsurgicalsubspecialties, The American Psychiatric Press

Textbook of Consultation-LiaisonPsychiatry. JR Rundell, MG Wise (Ed), Washington DC., AmericanPsychiatricPressInc

27. Surman OS Thesurgicalpatient, Massachusetts General HospitalHandbook of General HospitalPsychiatry. TP Hackett, NH Cassem (Ed), 2. Baský, Littleton, PSG Publishing,1987,s.69-83

28. De Witte JL, Alegret C, Sessler DI, Cammu G. Preoperative alprazolam reduces anxiety in ambulatory surgery patients: a comparison with oral midazolam. Anesth Analg 2002;95:1601-6.

Original Article

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# Physical Symptom Severity of Women in the Early Postpartum Period

## Erken Postpartum Dönemdeki Kadınların Fiziksel Semptom Şiddeti

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## ABSTRACT

**Objective:** This study was carried out to determine the severity of physical symptoms of women on the first postpartum day and postpartum fourth-sixth weeks.

**Methods:** This descriptive and prospective study was conducted between the dates July 2017 and January 2018 in the obstetrics department of an education and research hospital in Ankara. The study was conducted with a total of 140 women volunteering to participate in the research. The data were collected by face-to-face with women on the first day of postpartum period and by phone on the fourth-sixth weeks. The data were collected with using "Descriptive Prosperities Data Collection Form" and "Postpartum Physical Symptom Severity Scale".

**Results:** The most common physical symptoms of women participating in the study were pain in the site of cesarean section or perineum (88.6-47.2%), insufficient sleep quality or insomnia (87.1-64.3%), back pain (49.2-45.0%) and constipation (38.6-33.6%) on first postpartum day and on the fourth-sixth weeks. The least common physical symptoms of women were urinary incontinence (3.5-4.2%), feeling cold (5.7-7.8%), and feeling cold in hands and/or feet (6.4-7.1%). The physical symptoms experienced by women who gave birth by cesarean section were more severe on postpartum first day and those who fed their baby with formula in addition to breast milk were more severe on the postpartum fourth-sixth weeks (p>0.05).

## ÖZ

**Amaç:** Bu araştırma, doğum yapan kadınların postpartum birinci günde ve dördüncü-altıncı haftalar arasında fiziksel semptom şiddetini belirlemek amacıyla yapılmıştır.

**Yöntemler:** Tanımlayıcı ve prospektif tipteki bu çalışma Temmuz 2017-Ocak 2018 tarihleri arasında, Ankara'da bir eğitim araştırma hastanesinin kadın doğum servisinde yürütülmüştür. Çalışma araştırmaya katılmaya gönüllü toplam 140 kadın ile yürütülmüştür. Veriler, kadınlarla postpartum birinci günde yüz yüze ve dördüncü-altıncı haftalar arasında telefon görüşmesi yapılarak toplanmıştır. Veriler "Tanımlayıcı Özellikler Veri Toplama Formu" ve "Postpartum Fiziksel Semptom Şiddet Ölçeği" kullanılarak toplanmıştır.

**Bulgular:** Araştırmaya katılan kadınların postpartum birinci günde ve dördüncü-altıncı haftalar arasında en fazla yaşadıkları fiziksel semptomların sezaryen bölgesi veya perinede ağrı (%88,6-47,2), yetersiz uyku kalitesi veya uykusuzluk (%87,1-64,3), sırt ağrısı (%49,2-45,0) ve kabızlık (%38,6-33,6) olduğu belirlenmiştir. Kadınların en az yaşadıkları fiziksel semptomların ise idrar kaçırma (%3,5-4,2), normalden daha fazla üşüme (%5,7-7,8) ve ellerde ve/veya ayaklarda üşüme (%6,4-7,1) olduğu belirlenmiştir. Sezaryen ile doğum yapan kadınların postpartum birinci günde, bebeğine anne sütü dışında formül mama da verenlerin ise postpartum dördüncü-altıncı haftalar arasında yaşadıkları fiziksel semptomların daha şiddetli olduğu saptanmıştır (p>0,05).

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**Conclusion:** It was found that women who had a cesarean delivery and fed their baby with formula in addition to breast milk experienced more severe physical symptoms. Therefore, nurses should provide counseling to support normal delivery and to support exclusive breastfeeding in the first six months.

**Keywords:** Postpartum period, physical symptom, birth

**Sonuç:** Hemşireler, sezaryen ile doğum yapan ve bebeğini anne sütü dışında formül mama ile de besleyen annelerin fiziksel semptomları daha şiddetli yaşayabileceğini dikkate alarak, normal doğumu ve ilk altı ay yalnızca anne sütü ile beslemeyi destekleyici şekilde danışmanlık vermelidir.

**Anahtar Sözcükler:** Postpartum dönem, fiziksel semptom, doğum

## Introduction

Childbirth is an important experience for women's health (1). The postpartum period is the beginning of a period in which vital changes are experienced for women (2). In this period, in which psychological and sociological changes are experienced as well as physiological changes, woman and her family can encounter many problems that may adversely affect the health of mother and newborn (2,3).

Some of the changes that occur in the postpartum period are urogenital changes, preparation of the breasts for lactation, the beginning of the role of motherhood, hormonal changes and, accordingly, sudden changes in mood. These changes are more intense especially in the early postpartum period (3-6). Bleeding, pain, fever, fatigue, insomnia, vaginal discharge, constipation and urinary tract infections are among the problems due to the changes experienced in the early postpartum period (5,6). In addition, breast problems and related breastfeeding problems can be seen (6,7). In the late postpartum period, symptoms such as incontinence, sexual dysfunction and perineal pain may occur due to birth-related traumas (8-10). These symptoms adversely affect maternal health, maternal adaptation to the postpartum period and quality of life (5,10,11). For these reasons, the postpartum period is critical for mothers and newborns (1-6,8).

It is stated that physical well-being in the postpartum period is related to psychological well-being and adaptation to motherhood. In addition, it is thought that effective management of the physical symptoms of the mother positively affects the maintenance of infant care and breastfeeding (3,5,12). It is of great importance to determine the problems experienced by women in the postpartum period and to what extent these problems affect the role of motherhood (5).

This study was planned to determine the physical symptoms and their severity experienced by women between the first day and the fourth-sixth weeks of the postpartum period, to facilitate women's adaptation to this period and to contribute to the effective management of the process by the nurses.

## Methods

### Type and Sample of the Study

This prospective descriptive study was conducted between July 2017 and January 2018 in the obstetrics clinic of a training and research hospital in Ankara. The universe of the research consisted of women who gave birth and hospitalized in the postpartum service between the dates of the study. Sample selection was not made in the study, and all women who met the inclusion criteria and volunteered to participate in the study were tried to be reached. Women over the age of 18, who could speak Turkish and who gave birth at term (38-42 weeks) were included in the study. Women who had a systemic disease, whose birth was at risk and who did not volunteer to participate in the study were excluded from the study.

Between the dates of the research, 3 of the 160 women who gave birth and were admitted to the postnatal service were not included in the study because they gave birth with forceps, 5 were not included because they could not communicate in Turkish, 4 were not included because they gave birth preterm, 4 were not included because they did not volunteer to participate in the study, and 4 were not included because they could not be reached by phone between the 4$^{th}$ and 6$^{th}$ weeks. The research was completed with 140 postpartum women (87.5%).

### Ethical Aspect of Research

Zekai Tahir Burak Women's Health Training and Research Hospital Clinical Research Ethics Committee Ethics committee permission (decision no: 87/2017, date: 06.06.2017) was obtained to conduct the research. After the participants were informed about the purpose and implementation of the research, their written consent was obtained. The study was conducted in accordance with the principles of the Declaration of Helsinki.

### Data Collection Tools

"Descriptive Characteristics Data Collection Form I-II" and "Postpartum Physical Symptom Severity Scale" were used as data collection tools.

### Descriptive Characteristics Data Collection Form I-II

The forms were prepared by the researchers in line with the literature review (3,8,13). Descriptive characteristics data collection form I consisted of 10 questions in total to determine the sociodemographic and obstetric characteristics of the participants; such as age, employment, income status, number of pregnancies, and the presence of postnatal social support and characteristics of feding the baby in the first 24 hours after birth. Descriptive characteristics data collection form II consisted of a total of 4 questions to determine the social support and feeding characteristics of the participants between the fourth and sixth weeks after birth.

### Postpartum Physical Symptom Severity Scale

The scale was developed by Chien et al. (4) in 2009 to determine the incidence and persistence of postpartum physical symptoms. The scale is a Likert type scale scored between 0 (absent) and 1 (mild), 2 (moderate) and 3 (high), and it consists of a total of 18 items. The total score that can be obtained from the scale varies between 0-54. A high score indicates a high postpartum physical symptom severity, and a low score indicates a low postpartum physical symptom severity. While the scale evaluates all the physical symptoms that may be encountered in the postpartum period, it is suitable for an easy and quick assessment without increasing the burden of research participants, health workers and researchers. The validity and reliability study of the scale in Turkey was conducted by Arkan et al. (3) in 2015, and the Cronbach alpha value was found to be 0.79.

### Data Collecting

Before the study, a preliminary study was made with 10 women to evaluate the applicability and comprehensibility of the data collection form. Accordingly, in order to make the data collection form easier to understand, a few word corrections were made and the form was given its final shape. Pre-treatment women were not included in the study.

Before the application, women who were hospitalized in the postpartum clinic and met the inclusion criteria were informed about the purpose and method of the study. Participation in the study was based on volunteerism. Data were collected in two phases, within the first 24 hours in the postpartum clinic and after birth between four and six weeks. First, the data were collected by the researchers by face-to-face interview method, using the descriptive characteristics data collection form I and the postpartum physical symptom severity scale within the first 24 hours in the postpartum clinic. During the interview, all the questions of the women were answered and it lasted an average of 10-15 minutes. In order to re-evaluate between the four-sixth weeks, an explanation was made to the participants, their permission was obtained, and their contact numbers were recorded to reach them by phone. In the second stage, the descriptive characteristics data collection form II and the postpartum physical symptom severity scale were applied again by contacting the participants by phone between the postpartum fourth and sixth weeks. During the telephone interview, all questions of the women were answered and the interview lasted 5-10 minutes on average.

### Statistical Analysis

The SPSS for Windows Version 22.00 (IBM Corporation, Armonk, New York, USA) package program was used to evaluate the data. Number, percentage, and mean ± standard deviation were calculated for descriptive features. The normal distribution of continuous variables was evaluated with the single-sample Kolmogorov-Smirnov test. The Mann-Whitney U test and the Kruskal Wallis test were used to compare the mean physical symptom severity scores experienced between the first day and the fourth-sixth weeks postpartum according to some characteristics of the participants. A $p<0.05$ value was accepted for statistical significance.

## Results

It was determined that the mean age of the participants was 29.72±5.78 and 48.6% of them graduated from high education. Of the women 70% stated that they were not working and 54.3% of them stated that their income was equal to their expense. In addition, it was determined that 75.8% of the women had planned pregnancy and 45% had their first pregnancy. Of the women 61.4% underwent cesarean section and 38.6% had vaginal delivery (Table 1).

It was determined that 64.3% of women on postpartum first day and 62.1% of women between four and six weeks after birth fed their babies only with breast milk. The rate of women who stated that they gave formula to their babies along with breast milk was found to be 35.7% on the first postpartum day and 37.8% between the fourth and sixth weeks. Women's reasons for using formula on the first postpartum day and between four and six weeks were not enough milk (13.6-27.8%), the doctor's

**Table 1.** Socio-demographic and obstetric characteristics of women (n=140)

| Age | n | % |
|---|---|---|
| 18-34 | 110 | 78.6 |
| 35 or above | 30 | 21.4 |
| Age (mean ± SD) | 29.72±5.78 | |
| **Educational status** | | |
| Elementary school or below | 17 | 12.1 |
| Secondary school | 55 | 39.3 |
| High school | 68 | 48.6 |
| **Working status** | | |
| Working | 42 | 30.0 |
| Not working | 98 | 70.0 |
| **Income status** | | |
| Income does not meet expenses | 11 | 7.9 |
| Income only meets expenses | 76 | 54.3 |
| Income easily meets expenses | 53 | 37.9 |
| **Pregnancy planning status** | | |
| Planned | 106 | 75.8 |
| Not planned | 34 | 24.2 |
| **Number of pregnancies** | | |
| Primigravida | 63 | 45.0 |
| Multigravida | 77 | 55.0 |
| **Delivery type** | | |
| Vaginal delivery | 54 | 38.6 |
| Cesarean section | 86 | 61.4 |

SD: Standard deviation

**Table 2.** Characteristics of women regarding feeding their babies and receiving social support on the first postpartum day and postpartum fourth-sixth weeks (n=140)

| | Postpartum 1st day | | Postpartum 4th-6th weeks | |
|---|---|---|---|---|
| | **n** | **%** | **n** | **%** |
| **Feeding with breast milk or formula** | | | | |
| Only breast milk | 90 | 64.3 | 87 | 62.1 |
| Breast milk and formula | 50 | 35.7 | 53 | 37.8 |
| **Reasons for using formula other than breast milk** | **(n=50) *** | | **(n=53) *** | |
| Not enough breast milk | 19 | 13.6 | 39 | 27.8 |
| The baby is not sucking | 9 | 6.4 | 2 | 1.4 |
| The baby stays in the neonatal intensive care unit | 10 | 7.1 | 6 | 4.3 |
| Doctor's recommendation | 13 | 9.3 | 23 | 16.4 |
| Low birth weight of the baby | 3 | 2.1 | 2 | 1.4 |
| The baby is at risk of jaundice | 1 | 0.7 | 5 | 3.6 |
| **The presence of a relative who helps other than the spouse immediately after the birth** | | | | |
| Yes | 118 | 84.3 | 96 | 68.6 |
| No | 22 | 15.7 | 44 | 31.4 |
| **The level of kinship of the person who will help other than the spouse** | **(n=118)** | | **(n=96)** | |
| Mother | 85 | 72.0 | 71 | 74.0 |
| Mother-in-law | 18 | 15.2 | 17 | 17.7 |
| Other (sister, aunt, grandmother) | 15 | 12.8 | 8 | 8.3 |

*n was folded because more than one option was marked

recommendation (9.3-16.4%), and the baby staying in the neonatal intensive care unit (7.1-4.3%). It was determined that 84.3% of the women on the postpartum first day and 68.6% between the fourth and sixth weeks had someone other than their spouse to help, and that this person was often (72-74%) their mother (Table 2).

It was determined that the postpartum physical symptom severity scale mean score of the women participating in the study on the first postpartum day was 7.85±4.45 [minimum (min): 0, maximum (max): 21], and 6.21±5.16 (min: 0, max: 24) between the fourth and sixth weeks. The most common physical symptoms experienced by women on the first day and the fourth-sixth weeks after delivery were pain in the site of cesarean section and perineum (88.6-47.2%), poor sleep quality and insomnia (87.1-64.3%), back pain (49.2-45.0%), and constipation ( 38.6-33.6%). The least common physical symptoms they experienced were urinary incontinence (3.5-4.2%), feeling cold (5.7-7.8%), and chilling in hands and/or feet (6.4-7.1%). The symptoms which showed most decrease in the four-sixth weeks compared to postpartum first day were pain in the site of cesarean section and perineum (-41.4%), constipation (-26.5%), inadequate sleep quality/insomnia (-22.8), and joint pain (-15%). Vaginal infection (8.6%), excessive vaginal discharge (7.2%), urinary tract infection (3.7%) and hemorrhoids (3.6%) were found to be the symptoms that increased the most between the postpartum first day and postpartum four-sixth weeks (Table 3, Figure 1).

In the study, no statistically significant relationship was found between the postpartum physical symptom severity scale mean scores of women between the postpartum first day and the fourth-sixth weeks in terms of age, education status, employment status, pregnancy planning status, number of pregnancies, and the presence of someone other than the spouse to support them ($p>0.05$). While the mean postpartum physical symptom severity scale score of women who gave birth by cesarean section on the first postpartum day was statistically significantly higher ($z=-2.573$, $p=0.010$) compared to women who delivered vaginally, there was no difference between the types of delivery in terms of the mean scores of the postpartum physical symptom severity scale on the postpartum fourth-sixth weeks ($p>0.05$). While the mean postpartum physical symptom severity scale score on the postpartum fourth-sixth weeks was statistically significantly higher ($z=-3.334$, $p=0.001$) in those who gave formula to their babies other than breast milk compared to those who gave only breast milk, there was no difference in terms of the mean scores of the scale on the first postpartum day between the mothers who gave formula to their babies other than breast milk and those who gave only breast milk ($p>0.05$) (Table 4).

**Table 3.** Physical symptom severity of women on first postpartum day and on postpartum fourth-sixth weeks (n=140)

| | Physical symptom severity on postpartum first day | | | | Physical symptom severity on postpartum fourth-sixth weeks | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Symptoms | **Severity of symptom %** | Mild % | Moderate % | Severe % | **Severity of symptom %** | Mild % | Moderate % | Severe % | Change % |
| Pain in the site of cesarean section or perineum | **88.6** | 27.9 | 45.7 | 15.0 | **47.2** | 30 | 13.6 | 3.6 | -41.4 |
| Poor sleep quality or insomnia | **87.1** | 25 | 41.4 | 20.7 | **64.3** | 25.7 | 28.6 | 10 | -22.8 |
| Constipation | **38.6** | 19.3 | 9.3 | 10.0 | **33.6** | 12.1 | 12.9 | 8.6 | -26.5 |
| Back pain | **49.2** | 27.1 | 15 | 7.1 | **45.0** | 25 | 11.4 | 8.6 | -4.2 |
| Headache | **26.4** | 16.4 | 7.1 | 2.9 | **28.7** | 17.9 | 7.9 | 2.9 | 2.3 |
| Hemorrhoids | **22.1** | 12.1 | 5 | 5 | **25.7** | 10 | 10 | 5.7 | 3.6 |
| Joint pain | **27.1** | 14.3 | 5.7 | 7.1 | **12.1** | 12.9 | 3.6 | 2.1 | -15.0 |
| Numbness in hands | **19.2** | 12.1 | 5.7 | 1.4 | **12.1** | 7.1 | 4.3 | 0.7 | -7.1 |
| Excessive vaginal discharge | **15.0** | 11.4 | 3.6 | - | **22.2** | 12.9 | 5.0 | 4.3 | 7.2 |
| Vaginal infection | **7.1** | 5 | 1.4 | 0.7 | **15.7** | 10.0 | 2.1 | 3.6 | 8.6 |
| Numbness in feet | **11.4** | 7.1 | 4.3 | - | **6.4** | 3.6 | 2.1 | 0.7 | -5.0 |
| Excessive vaginal bleeding | **23.5** | 17.1 | 6.4 | - | **10.7** | 10.0 | - | 0.7 | -12.8 |
| Urinary tract infection | **8.5** | 5 | 1.4 | 2.1 | **12.2** | 7.9 | 3.6 | 0.7 | 3.7 |
| Dizziness | **21.4** | 18.6 | 2.1 | 0.7 | **18.5** | 16.4 | 2.1 | - | -2.9 |
| Varicose veins on legs | **14.3** | 9.3 | 3.6 | 1.4 | **8.6** | 5.7 | 2.9 | - | -5.7 |
| Urinary incontinence | **3.5** | 2.1 | 1.4 | - | **4.2** | 2.1 | 2.1 | - | 0.7 |
| Feeling cold | **5.7** | 5 | 0.7 | - | **7.8** | 5.0 | 1.4 | 1.4 | 2.1 |
| Cold hands and/or feet | **6.4** | 5 | 1.4 | - | **7.1** | 3.6 | 2.1 | 1.4 | 0.7 |
| Mean of total score of Postpartum Physical Symptom Severity Scale | 7.85±4.45 (min: 0, max: 21) | | | | (6.21±5.16) (min: 0, max: 24) | | | | |

min: Minimum, max: Maximum

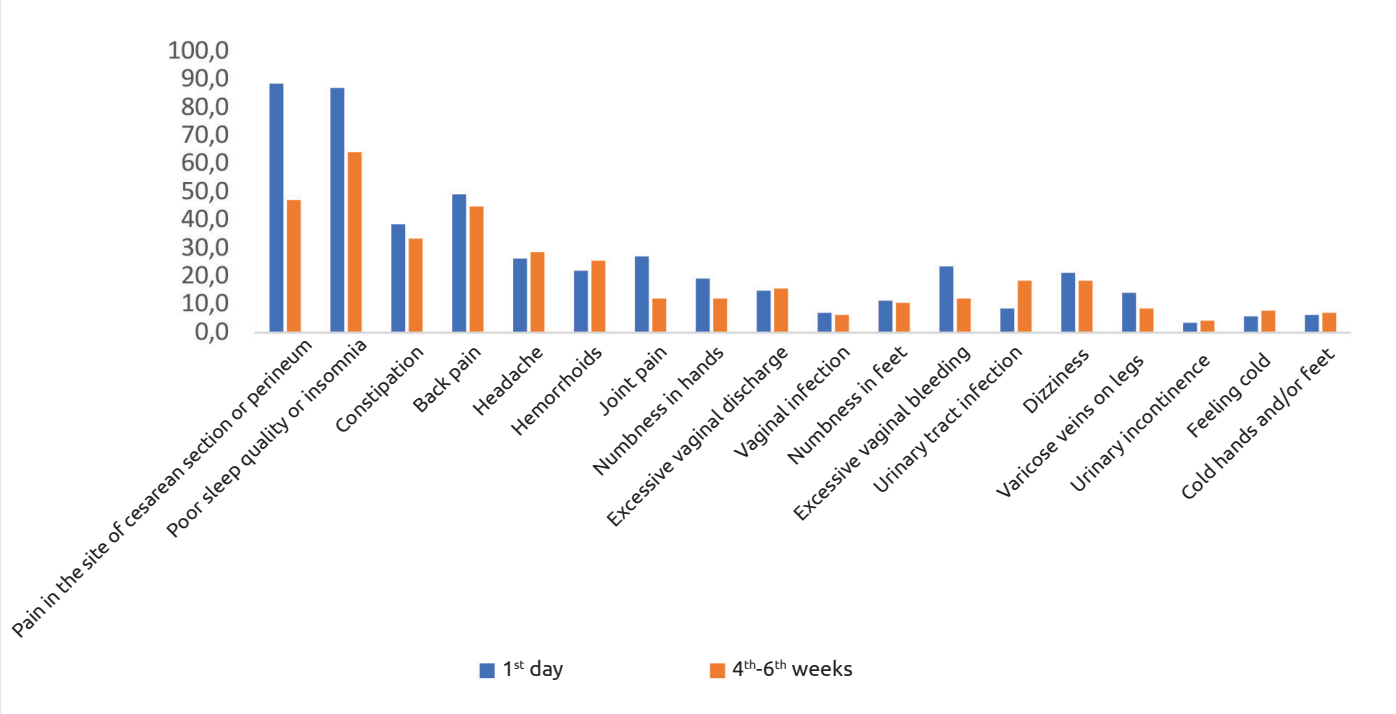


**Figure 1.** Physical symptom severity of women on first postpartum day and postpartum fourth-sixth weeks (n=140)

**Table 4.** According to some characteristics of women, mean physical symptom severity scale score between postpartum first day and four-sixth weeks (n=140)

| | Postpartum physical symptom severity scale mean score (1st day) | Postpartum physical symptom severity scale mean score (between 4 and 6 weeks) |
|---|---|---|
| **Age** | | |
| 18-34 | 7.63±4.45 | 6.20±5.24 |
| 35 or above | 8.66±4.44 | 6.23±4.91 |
| z | -1.233 | -0.400 |
| p[a] | 0.218 | 0.689 |
| **Educational status** | | |
| Elementary school or below | 8.41±5.26 | 8.05±6.11 |
| Secondary school | 7.67±4.79 | 5.72±5.03 |
| High school | 7.86±3.98 | 6.14±4.98 |
| z | 0.733 | 1.783 |
| p[b] | 0.693 | 0.410 |
| **Working status** | | |
| Working | 7.61±4.49 | 5.97±5.10 |
| Not working | 7.90±4.44 | 6.24±5.18 |
| z | -0.419 | -0.235 |
| p[a] | 0.675 | 0.814 |
| **Pregnancy planning status** | | |
| Planned | 7.91±4.20 | 6.16±5.16 |
| Not planned | 7.67±5.22 | 6.35±5.21 |
| z | -0.931 | -0.264 |
| p[a] | 0.352 | 0.792 |
| **Number of pregnancies** | | |
| Primigravida | 7.33±3.72 | 6.57±5.30 |
| Multigravida | 8.28±4.95 | 5.92±5.05 |
| z | -0.670 | -0.810 |
| p[a] | 0.503 | 0.418 |
| **Delivery type** | | |
| Vaginal delivery | 6.51±3.60 | 5.62±4.66 |
| Cesarean section | 8.69±4.74 | 6.58±5.44 |
| z | -2.573 | -0.879 |
| p[a] | 0.010 | 0.379 |
| **Feeding with breast milk or formula** | | |
| Yes | 7.88±4.47 | 7.84±5.42 |
| No | 7.84±4.46 | 5.21±4.75 |
| z | -0.009 | -3.334 |
| p[a] | 0.993 | 0.001 |
| **The presence of a relative who helps** | | |
| Yes | 7.91±4.25 | 6.42±5.35 |
| No | 7.54±5.48 | 5.75±4.74 |
| z | -0.977 | -0.652 |
| p[a] | 0.329 | 0.515 |

[a]Mann-Whitney U test, [b]Kruskal-Wallis test

## Discussion

The postpartum period is a transitional period in which important changes are experienced by women both physiologically and psychologically (3). In this period, women may experience some problems due to the changes in their bodies as well as adapting to motherhood (13,14). These problems are frequently encountered as pain, sleep problems, urinary incontinence, sexual dysfunction and depression (9,15-17).

In this study, which was conducted to determine the severity of physical symptoms experienced by women in the postpartum period, the most common physical symptoms experienced by women in the first postpartum day and in the postpartum fourth-sixth weeks were pain in the site of cesarean section or perineum, poor sleep quality or insomnia, back pain and constipation. Cooklin et al. (13) showed that the most common physical symptoms experienced by women in the first week after delivery were pain in the site of cesarean section, perineal pain, back pain and constipation; and in the sixth week they were back pain, cesarean delivery pain and constipation. Aksu et al. (16) found that the most common physical disorders experienced by postpartum women (n=400) in the sixth week and sixth month were fatigue, sleep problems, dysuria, and low back pain. Cooklin et al. (18) identified the problems that caused the most physical burden to women in the eighth postpartum week as cesarean/perineal pain, back pain, constipation, hemorrhoids, urinary and intestinal incontinence. Since the healing process of women still continues between the fourth and sixth weeks, pain in the site of cesarean section or perineum continues and is the most common physical symptom. At the same time, it is thought that mothers experience sleep problems, fatigue and low back pain symptoms intensely due to reasons such as carrying baby care and housework together and having to wake up at night to feed their babies. Keeping the mother's social support systems strong during this process will help her pass this process more comfortably and smoothly.

In our study, it was determined that almost all of the women on the first postpartum day and more than half of them between the fourth and sixth weeks of the postpartum period had a relative to help other than their spouse, and this person was mostly their mother. In the study conducted by Elmas and Aluş Tokat (19), more than half of the women stated that they received support from their family members in the first postpartum four weeks, and nearly half of the women in the study conducted by Erçel and Kahyaoğlu Süt (20) stated that they received support from their family members in the postpartum period. The existence of support systems of a significant part of women in the postpartum period is considered positive in terms of having a healthier process.

In our study, it was observed that the severity of postpartum physical symptoms decreased between the fourth and sixth weeks compared to the first week, as a natural consequence of the postpartum recovery process. In two different studies evaluating physical health problems in the early postpartum period, Cooklin et al. (13,18) showed that the percentage of women who stated that they experienced at least one physical symptom decreased in the eighth week compared to the first week. Our study results also showed that the physical symptoms experienced by women were observed at different frequencies on the first postpartum day and on the postpartum fourth-sixth weeks. For example; some physical symptoms such as pain in the site of cesarean section or perineum, constipation, poor sleep quality or insomnia showed the greatest reduction; some symptoms such as dizziness, back pain, numbness in the feet decreased at a lower rate and were permanent; and it was determined that there was an increase in the severity of some symptoms such as vaginal infection, vaginal discharge and urinary tract infection. In a study examining postpartum physical symptoms in primiparous women, the symptoms that showed the most decrease between the first week and the fourth week were complaints of perineal pain ($1^{st}$-$4^{th}$ weeks: 74-20%), cesarean delivery pain ($1^{st}$-$4^{th}$ weeks: 95-61%) and constipation ($1^{st}$-$4^{th}$ week: 49-30%), Urinary incontinence (weeks 1-4: 19-8%) and intestinal incontinence (weeks 1-4: 4-1%) were found to be the least common among the symptoms evaluated (13). Chien et al. (4) showed that the physical symptoms that showed the most decrease between the first month and the first year in the postpartum period were pain in the site of cesarean section or perineal pain, poor sleep quality or insomnia and constipation, and that the most increasing symptoms were chilling in the hands and feet. Song et al. (15) determined that the most common physical symptoms experienced by women in the postpartum second day and fourth-sixth weeks were fatigue, edema, nipple problems, and constipation. Studies have shown that the symptoms of back pain experienced in the first days of the postpartum period decrease at a very low rate in the fourth-sixth months or, on the contrary, increase and become permanent (13,15).

It was found that postpartum physical symptom severity scale mean scores of women who gave birth by cesarean section on the first postpartum day were higher than women who delivered vaginally. In a study in Austria in which the physical health symptoms of primiparous mothers were evaluated in the first postpartum eight weeks, it was determined that 94% of the women experienced pain in the site of cesarean section and 74% had perineal pain in the evaluation performed in the first postpartum week (13). In addition, studies indicate that pain associated with childbirth was more permanent, especially in those who gave birth by cesarean section (8,13). In the study conducted by Çapık et al. (1), it was determined that postpartum physical comfort of postpartum women who delivered vaginally was higher than women who gave birth by cesarean section. Egelioğlu Çetişli et al. (21) found that the severity of physical symptoms experienced by primiparous mothers who gave birth by cesarean section between the fourth and sixth weeks of postpartum period was higher than the mothers who had vaginal birth, while in our study, no difference was found between the types of delivery in terms of the mean scores of physical symptoms experienced by women between the fourth and sixth weeks of postpartum period. In the study conducted

by Işık et al. (22), it was found that the pain scores of mothers who had vaginal birth were lower on the postpartum 24th hour than those who gave birth by cesarean section. Webb et al. (23) determined that the functional limitations experienced in the early postpartum period were related to the mode of delivery and that those who had a cesarean section experienced the most severe pain during movement (such as sitting and standing), while those who had vaginal delivery did not experience these limitations. It was thought that the reason for the postpartum physical symptom scores of those who gave birth by cesarean section on the first day of the postpartum period higher than the women who had vaginal birth was due to the severe abdominal pain associated with cesarean section, and the symptoms such as limitation of movement, constipation and insomnia due to this pain. It is thought that the severity of physical symptoms is less due to the faster recovery in normal delivery. It is important for nurses to encourage normal birth by providing education and counseling to women about delivery methods of pregnancy, to reduce cesarean section rates and improve maternal health.

In the study, it was determined that the postpartum physical symptom severity of women who gave only breast milk to their babies between the fourth and sixth weeks of postpartum period was lower than those who gave formula to their babies other than breast milk. Egelioğlu Çetişli et al. (21), found no difference in terms of postpartum physical symptom severity scale scores according to primiparous mothers' feeding status other than breast milk on the postpartum fourth-sixth weeks. In the study conducted by Elmas and Aluş Tokat. (19), it was determined that at the end of the postpartum fourth week, those who fed their babies with formula in addition to breast milk found that their total sleep was more adequate than those who gave only breast milk, and the fatigue they felt was less. These data seem to be different from our research results, but Hughes et al. (24) determined in their study that environmental factors such as noise, mode of delivery and feeding of the newborn did not affect the total sleep duration, and basically, breastfeeding supported maternal sleep. In our study, it was observed that women's inadequate sleep quality/insomnia problems decreased on the postpartum fourth-sixth weeks. This may be due to the fact that mothers fall asleep more easily and feel rested due to the effect of prolactin hormone secreted during breastfeeding, even if they have to wake up more at night to feed their babies (19). Considering that the severity of physical symptoms is less in women who only breastfeed their babies on the fourth-sixth weeks after birth, the importance of exclusively breastfeeding for the first six months should be emphasized during the education and counseling services provided beginning from the prenatal period.

## Conclusion

Determining the physical symptoms experienced by women in the postpartum period and their severity is important for nurses to plan postpartum care and to diagnose problems that may occur later on. According to the results obtained from our study, women in the postpartum period often experienced various physical symptoms such as pain in the site of cesarean section or perineum, poor sleep quality or insomnia, back pain and constipation. In addition, it was determined that the severity of physical symptoms on the first postpartum day was higher in women who gave formula to their babies in addition to breast milk, and it was determined that the severity of physical symptoms on the postpartum fourth-sixth weeks was higher in women who gave birth by cesarean section. These results reveal the importance of normal delivery and exclusive breastfeeding for the first six months. Nursing care, which is planned to reduce and eliminate physical symptoms in the postpartum period, is an important attempt to protect and increase the physical and psychological health of women. In the literature, it is seen that the studies on this subject are quite limited and different physical symptoms are evaluated at different time intervals in the studies (13,21). It is considered that studies with larger samples and long-term follow-up on physical symptoms experienced in the postpartum period will be useful in terms of obtaining strong evidence.

### Ethics

**Ethics Committee Approval:** Zekai Tahir Burak Women's Health Training and Research Hospital Clinical Research Ethics Committee Ethics committee permission (decision no: 87/2017, date: 06.06.2017) was obtained to conduct the research.

**Informed Consent:** After the participants were informed about the purpose and implementation of the research, their written consent was obtained.

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

### Authorship Contributions

Concept: M.U., Design: M.U., G.A., İ.Y., Data Collection or Processing: M.U., G.A., İ.Y., Analysis or Interpretation: M.U., G.A., İ.Y., K.E.K., Literature Search: M.U., G.A., İ.Y., Writing: M.U., G.A., İ.Y.

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

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## References

1. Çapık A, Özkan H, Apay SE. Determination of Affecting Factors and Postnatal Comfort Levels of Postpartum Women. DEUHFED 2014;7:186-92.
2. Yıldız H, Küçükşahin N. Kırsal bölgede annelerin doğum sonu yaşadıkları sorunlar ve bakım gereksinimleri. Türkiye Aile Hekimliği Dergisi 2011;15:159-66.
3. Arkan G, Egelioğlu Çetişli N. Valıdıty And Relıabılıty Study Of Postpartum Physıcal Symptom Severıty Scale. JASCD 2017;4:18-34.
4. Chien LY, Tai CJ, Hwang FM, Huang CM. Postpartum physical symptoms and depressive symptomatology at 1 month and 1 year after delivery: a longitudinal questionnaire survey. Int J Nurs Stud 2009;46:1201-8.

5. Bağcı S, Altuntuğ K. Problems experienced by mothers in postpartum period and their associations with quality of life. International Journal of Human Sciences 2016;13:3266-79.
6. Yonemoto N, Dowswell T, Nagai S, Mori R. Schedules for home visits in the early postpartum period. Cochrane Database Syst Rev 2013;:CD009326.
7. Xiao X, Ngai FW, Zhu SN, Loke AY. The experiences of early postpartum Shenzhen mothers and theirneedforhomevisit services: a qualitative exploratory study. BMC pregnancy and child birth 2020;20:5.
8. Chang SR, Chen KH, Ho HN, Lai YH, Lin MI, Lee CN, et al. Depressive symptoms, pain, and sexual dysfunction over the first year following vaginal or cesarean delivery: a prospective longitudinal study. Int J Nurs Stud 2015;52:1433-44.
9. Kılıç M. Prevalence and risk factors of sexual dysfunction in healthy women in Turkey. Afr Health Sci 2019;19:2623-33.
10. Karakuş A, Yanıkkerem E. Postpartum dönemde inkontinans ve yaşam kalitesi: son 10 yıllık çalışmalar. CBU SBED 2015;2:54-9.
11. Beydağ KD. Adaptation to motherhood in the postpartum period and the nurse's role. TAF Preventine Medicine Bulletin 2007;6:479-84.
12. Aksakallı M, Çapık A, Ejder Apay S, Pasinlioğlu T, Bayram S. Determination of Support Needs and Support Levels Among Postpartum Women. J Psy Nurs 2012;3:129-35.
13. Cooklin AR, Amir LH, Jarman J, Cullinane M, Donath SM; CASTLE Study Team. Maternal Physical Health Symptoms in the First 8 Weeks Postpartum Among Primiparous Australian Women. Birth 2015;42:254-60.
14. Yesilcinar I, Yavan T, Karasahin KE, Yenen MC. The identification of the relationship between the perceived social support, fatigue levels and maternal attachment during the postpartum period. J Matern Fetal Neonatal Med 2017;30:1213-20.
15. Song JE, Chae HJ, Kim CH. Changes in perceived health status, physical symptoms, and Sleep satisfaction of postpartum women over time. Nurs Health Sci. 2014;16:335-42.
16. Aksu S, Varol FG, Hotun Sahin N. Long-term postpartum health problems in Turkish women: prevalence and associations with self-rated health. Contemp Nurse 2017;53:167-81.
17. Wan H, Hu S, Thobaben M, Hou Y, Yin T. Continuous primary nursing care increases satisfaction with nursing care and reduces postpartum problems for hospitalized pregnant women. Contemp Nurse 2011;37:149-59.
18. Cooklin AR, Amir LH, Nguyen CD, Buck ML, Cullinane M, Fisher JRW, et al. Physical health, breastfeeding problems and maternal mood in the early postpartum: a prospective cohort study. Arch Womens Ment Health 2018 ;21:365-74.
19. Elmas S, Aluş Tokat M. The Effects of Newborn Feeding Methods on the Sleep and Fatigue of the Mother. DEUHFED 2016;9:45-51.
20. Erçel Ö, Kahyaoğlu Süt H. Sleep Quality and Quality of Life in Postpartum Woman. JTSM 2020;1:23-30.
21. Egelioğlu Çetişli N, Işık S, Kahveci M, Hacılar A. Postpartum Physical Symptom Severity and Breastfeeding Behaviour of Primipar Mother According to Their Birth Type HEAD 2020;17:98-103.
22. Işık G, Egelioğlu Çetişli N, Başkaya VA. Postpartum Pain, Fatigue Levels and Breastfeeding Self-Efficacy According to Type of Birth. DEUHFED 2018;11:224-32.
23. Webb DA, Bloch JR, Coyne JC, Chung EK, Bennett IM, Culhane JF. Postpartum physical symptoms in new mothers: their relationship to functional limitations and emotional well-being. Birth 2008;35:179-87.
24. Hughes O, Mohamad MM, Doyle P, Burke G. The significance of breastfeeding on sleep patterns during the first 48 hours postpartum for first time mothers. J Obstet Gynaecol 2018;38:316-20.

Original Article

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# Nomophobia and Related Factors in Students of a Faculty of Humanities and Social Sciences

## Bir İnsani ve Sosyal Bilimler Fakültesi Öğrencilerinde Nomofobi ve İlişkili Faktörlerin İncelenmesi

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## ABSTRACT

**Objective:** Nomophobia is defined as the involuntary fear experienced by the individual when he/she cannot access his mobile device or cannot communicate on the mobile device. This study aimed to examine nomophobia and related factors in the first- and fourth-year students in the Department of Turkish Language and Literature and Western Languages and Literatures at the Faculty of Humanities and Social Sciences of Firat University.

**Methods:** In this cross-sectional study, a questionnaire survey including questions about sociodemographic features and smartphone use and nomophobia questionnaire (NMP-Q) was performed.

**Results:** Data were collected from 325 participants (69.2% female), with an average age of 21.06±3.54 years. The NMP-Q score was 73.21±26.60 points. No significant difference was found between the genders according to the NMP-Q score ($p>0.05$). Those carrying chargers, spending time with a smartphone before bedtime, and checking their smartphones as soon as they wake up had a higher NMP-Q score ($p<0.01$). NMP-Q score increased with the increase in the duration of using smartphones, daily usage time, daily frequency of checking smartphones, and daily mobile internet usage time ($p<0.001$).

**Conclusion:** It may be helpful to delay the age of starting smartphone use as much as possible to reduce the level of nomophobia in university students since those who started using smartphones at an earlier age are more prone to nomophobia.

**Keywords:** Nomophobia, university, students, mobile phone

## ÖZ

**Amaç:** Nomofobi, birey mobil cihazına erişemediğinde veya mobil cihaz üzerinde iletişim kuramadığında, bireyin yaşadığı istemsiz korku olarak tanımlanmaktadır. Bu araştırmada Fırat Üniversitesi İnsani ve Sosyal Bilimler Fakültesi Türk Dili ve Edebiyatı ile Batı Dilleri ve Edebiyatları Bölümleri'ndeki birinci ve dördüncü sınıftaki öğrencilerde nomofobi ve ilişkili faktörlerin incelenmesi amaçlanmıştır.

**Yöntemler:** Kesitsel tipte bir araştırmadır. Sosyo-demografik özellikler ve akıllı telefon kullanımı ile ilgili sorular ve nomofobi ölçeğinin yer aldığı bir anket formu uygulanmıştır.

**Bulgular:** Üç yüz yirmi beş öğrenciye ulaşılmıştır. Öğrencilerin %69,2'si kadın olup, tüm öğrencilerin yaş ortalamaları 21,06±3,54'tür. Öğrencilerin, Nomofobi ölçeği puanı 73,21±26,60 olarak saptanmıştır. Nomofobi ölçeği puanlarına göre cinsiyetler arasında istatistiksel olarak anlamlı bir fark bulunmamıştır ($p>0,05$). Yanında şarj aleti taşıyanların, yatmadan önce akıllı telefonla zaman geçirenlerin, uyanır uyanmaz akıllı telefonunu kontrol edenlerin daha yüksek nomofobi ölçeği puanına sahip olduğu bulunmuştur ($p<0,01$). Akıllı telefonu kullanma yılı, günlük kullanma süresi, günlük kontrol sıklığı, günlük mobil internet kullanım süresi arttıkça nomofobi ölçeği puanı artmaktadır ($p<0,001$).

**Sonuç:** Daha erken yaşta akıllı telefon kullanmaya başlayanlar nomofobiye daha yatkın olduğundan, üniversite öğrencilerinde görülen nomofobi düzeyini düşürmek için akıllı telefon kullanmaya başlama yaşını olabildiğince geciktirmeye çalışmak faydalı olabilir.

**Anahtar Sözcükler:** Nomofobi, üniversite, öğrenciler, mobil telefon

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## Introduction

Nomophobia is a disorder of the contemporary digital and virtual society and is the result of the development of new technologies that enable virtual communication (1,2). Developments in technology cause changes in culture. Culture can also affect a person's health-related behavior, as it is one of the factors that drive a person's behavior. To protect the health of individuals and to treat them while they are sick, it is necessary to know their behavior and the factors associated with their behavior (3). Therefore, nomophobia is a public health problem (4,5).

Smartphones have become an important part of people's lives today owing to the developments in communication and information technologies. Nowadays, the use of smartphones is increasing in developed and developing countries (6). The number of smartphone users worldwide has now exceeded three billion. China, India, and the USA have the highest number of smartphone users and are likely to exceed 100 million users (7). As of 2018, there were 41.9 million smartphone users in Turkey. This number is expected to increase to 52.8 million by 2021 and 56.4 million by 2023 (8). According to the We Are Social Statistics of Turkey Electronic Device Use in 2019, 98% of adults in Turkey were mobile phone users and 77% of these people prefer smartphones (9).

Smartphones are mainly used to access information, join social networks, increase social interactions, plan and organize jobs, access e-mails, shop online, and play games (10). Contrary to all these functions and benefits of smartphones, excessive use of smartphones can have negative consequences (11,12). Especially, while young individuals benefit from the opportunities provided by smartphones, they become addicted within a short time and even experience phobia in case of deprivation (13). Nomophobia is the involuntary fear derived from the English word nomophobia ("no mobile phone" and phobia) and refers to the experience when a person cannot access or communicate on their mobile device (1,14,15). Bragazzi et al. stated that nomophobia is a specific phobia and suggested its inclusion in the Diagnostic and Statistical Manual of Mental Disorders (5$^{th}$ Edition). They emphasized that nomophobia may be the forerunner of a more serious psychiatric disorder due to the tendency of psychiatric disorders to cluster together frequently (2,16).

Typical features of nomophobic behaviors include continuously checking whether there are messages or calls, worrying and feeling anxious when the mobile phone is out of range or having restricted use, leaving their smartphone open for 24 h, and going to the bed with a smartphone (2). Young people are more prone to using and adapting emerging technology and therefore more prone to nomophobia (5,17,18). A study conducted on university students in Turkey found that 42.6% of the students had nomophobia. The same study found that gender and the duration of smartphone ownership had affected young adults' nomophobic behaviors, whereas age had no effect (19). In Turkey, another study conducted among university students revealed that the level of nomophobia was higher in women and those with younger age, but no relationship was found between smartphone use time and nomophobia level (20). Despite this information about nomophobia, evidence on this subject is limited. A systematic review about nomophobia published in 2020 emphasized that nomophobia was in the early stages of research since studies on nomophobia were mostly recent, quantitative, and cross-sectional and performed in a limited population (youth and university students). For this reason, most of the studies on nomophobia are in the discovery phase (5).

Because of the small number of studies and information about nomophobia, high prevalence among the young population, and nomophobia being an important psychiatric and public health problem, this study aimed to examine the nomophobia levels and factors related to nomophobia in students of a Faculty of Humanities and Social Sciences.

## Methods

This cross-sectional study focused on 2,111 students at the Faculty of Humanities and Social Sciences, University of Fırat, in the 2018-2019 academic year. The incidence of nomophobia was set as 42.6% (19), so the minimum number of people to be included in the study was 319 according to the following formula: $n=Npqt^2/d^2(N-1) + pqt^2$ (21), with the following values: N (universe size) =2,111, p (probability of occurrence of the event under investigation) =0.426, q (probability of occurrence of the event under investigation not seen) =0.574, t (theoretical value from the t table at a certain degree of freedom and detected error level) =1.96, and d (± deviation to be made according to the frequency of occurrence of the event) =0.05.

The Faculty of Humanities and Social Sciences consisted of six departments. Each department was accepted as a cluster, and two departments from six departments were selected by drawing lots. Selected departments were Turkish Language and Literature, and Western Languages and Literatures. The first- and fourth-year students in selected departments were included in this study for comparison between the freshmen and seniors. There were 109 first-year students and 51 fourth-year students in the Department of Western Languages and Literature. Moreover, there were 84 first-year students and 91 fourth-year students in the Turkish Language and Literature Department. In total, there were 335 first- and fourth-year students in both departments. The target sample was 335 students, but 325 students were enrolled.

The study was performed after it was approved by Fırat University Ethics Committee, and data collection was started in September 2018. The research ethics permission was obtained from Fırat University Non-interventional Research Ethics Committee (date: 21/06/2018, no: 263000).

Data were collected using a researcher-developed questionnaire based on the results of the reviewed relevant literature. The questionnaire was tested through a pilot survey including 18 students, and necessary modifications were made based on the results. The survey was implemented under direct observation after the necessary explanations were made and informed consent was obtained. The survey form consists of two parts: the first section includes questions about demographic information

form and smartphone use, and the second section includes the nomophobia questionnaire (NMP-Q).

**Nomophobia Questionnaire:** The scale was developed by Yıldırım and Correia (15) and adapted to Turkish by Yıldırım et al. (19), which consists of 20 items. It consists of a total of four subdimensions: "not being able to access information (4 items)," "losing connectedness (5 items)," "not being able to communicate (6 items)," and "giving up convenience (5 items)." Cronbach's alpha values of the original scale and the Turkish version of the scale were 0.94 and 0.92, respectively. Cronbach's alpha values of the subdimensions were 0.82, 0.81, 0.93, and 0.87 on the original scale and 0.94, 0.91, 0.90, and 0.74 on the Turkish version of the scale. The confirmatory factor analysis results of the Turkish version of the scale were as follows: $\chi 2$ (164) =469.90, normed $\chi 2$ =2.86, comparative fit index =0.92, and root mean square error of approximation =0.08. The Turkish NMP-Q was a valid and reliable measure of nomophobia. It is a 7-point Likert-type scale. Total scores are calculated by summing up responses to each item, resulting in a nomophobia score ranging from 20 to 140, with higher scores corresponding to a more severe nomophobia. The nomophobia scale does not have a specific cut-off point.

### Statistical Analysis

SPSS 21.0 package program (IBM Corp., Armonk, NY, USA) was used in data analysis and error checks, and tables and statistical analyses were made through this program. Depending on the nature of the variables in the statistical analysis, the following analyses were run: percentage, average, t-test, one-way analysis of variance, Tukey HSD, Pearson correlation analysis, and multiple linear regression analysis. Averages were calculated with standard deviation (mean ± standard deviation), and $p<0.05$ was accepted as the level of statistical significance.

## Results

In this study, 69.2% (n=225 people) of the included students were female students, and the average age of all students was 21.06±3.54 [minimum (min) =17, maximum (max) =42] years. The socioeconomic level of 88.3% of the students (n=287) was moderate, and 52.3% of students (n=170) belonged to Turkish Language and Literature Department, and 56.6% of the students (n=184) were on the first class. Students' average duration of using smartphones, average daily smartphone usage time, average daily mobile internet usage time, and average age of starting using a smartphone were 4.78±2.37 years, 5.65±3.86 hours, 4.43±3.77 hours, and 16.27±4.04 years, respectively. The frequency of accessing social media via smartphone was as follows: 5.2% (n=17), never; 11.4% (n=37), rarely; 40.6% (n=132), sometimes; 29.9% (n=97) often; and 12.9% (n=42), always.

Table 1 presents the scores on the NMP-Q and its subdimensions. The students' NMP-Q score was 73.21±26.60 (min =20, max =140). The scores on the subdimensions were as follows: not being able to access information, 16.04±7.34 (min = 4, max = 28); losing connectedness, 17.28 ± 8.33 (min =5, max =35); not being able to communicate, 26.19±11.11 (min =6, max =42); and giving up convenience, 13.98±8.53 (min =5, max =35).

According to Table 2, the NMP-Q score did not differ significantly according to gender, socioeconomic level, and class ($p>0.05$). The NMP-Q score was significantly higher in the group aged ≤13 years than in the other age groups. Those who see themselves as smartphone addicts, carry a charger with them, spend time with a smartphone before bedtime, leave their smartphones open at night, and check their smartphone as soon as they wake up had a higher NMP-Q score ($p<0.05$).

As shown in Table 3, the most frequent reason for smartphone use was to follow developments in the environment and agenda. In this study, 84.9% of the participants (n=276) thought that an expensive smartphone is not a prestigious tool. NMP-Q scores were significantly higher in students who answered *yes* to the following statements about smartphone use: "It allows me to follow the developments on the agenda," "It gives me access to social media (Facebook, Twitter, etc.)," "Thanks to its functions, it allows me to play games easily," and "An expensive smartphone increases my prestige around me" ($p<0.05$).

Correlation coefficients between continuous variables are presented in Table 4. The NMP-Q score correlated negatively with age ($r =-0.13$, $p<0.01$). Table 4 also indicates that the NMP-Q score correlated positively with the smartphone use duration (r=0.21), daily smartphone usage time (r=0.29), daily frequency of checking smartphone (r=0.27), and daily mobile internet usage time (r=0.34).

The results of the multiple linear regression analysis using NMP-Q score as the dependent variable are shown in Table 5. Variables such as age, duration of using a smartphone, daily smartphone usage time, daily frequency of checking smartphone, and daily mobile internet usage time contributed significantly to the model and explained 16% of the change in the NMP-Q

**Table 1.** Students' scores on NMP-Q and its subdimensions

| NMP-Q and its subdimensions | M ± SD | Min-max |
|---|---|---|
| Not being able to access information | 16.04±7.34 | 4-28 |
| Losing connectedness | 17.28±8.33 | 5-35 |
| Not being able to communicate | 26.19±11.11 | 6-42 |
| Giving up convenience | 13.98±8.53 | 5-35 |
| NMP-Q | 73.21±26.60 | 20-140 |

SD: Standard deviation, Min: Minimum, Max: Maximum, NMP-Q: Nomophobia questionnaire

**Table 2.** Some features of the students and NMP-Q scores according to these features

| Features | n | % | NMP-Q score M ± SD | Test statistics |
|---|---|---|---|---|
| **Gender** | | | | |
| Male | 100 | 30.8 | 71.19±25.80 | t= -0.913 |
| Female | 225 | 69.2 | 74.11±26.96 | p=0.362 |
| **Socioeconomic level** | | | | |
| Low | 21 | 6.5 | 70.47±27.53 | F=0.338 |
| Middle | 287 | 88.3 | 73.64±25.93 | p=0.713 |
| High | 17 | 5.2 | 69.23±36.43 | |
| **Class** | | | | |
| Grade 1 | 184 | 56.6 | 73.19±28.74 | t= -0.017 |
| Grade 4 | 141 | 43.4 | 73.24±23.62 | p=0.986 |
| **Age to start using a smartphone** | | | | |
| ≤13 | 69 | 21.2 | 84.46±27.98*§ | F=9.253 |
| 14-17 | 164 | 50.5 | 71.91±26.03* | **p<0.001** |
| ≥18 | 92 | 28.3 | 67.08±24.16§ | |
| **See yourself as a smartphone addict** | | | | |
| Yes | 115 | 35.4 | 87.68±25.22 | t=7.920 |
| No | 210 | 64.6 | 65.28±23.91 | **p<0.001** |
| **Have a charger with you** | | | | |
| Yes | 105 | 32.3 | 79.11±25.52 | t=2.792 |
| No | 220 | 67.7 | 70.39±26.70 | **p=0.006** |
| **Spending time with your smartphone before bedtime** | | | | |
| Yes | 276 | 84.9 | 76.30±25.69 | t=5.173 |
| No | 49 | 15.1 | 55.77±25.06 | **p<0.001** |
| **Turn off your smartphone at night** | | | | |
| Yes | 54 | 16.6 | 65.05±23.43 | t=-2.487 |
| No | 271 | 83.4 | 74.83±26.93 | **p=0.013** |
| **Checking your phone as soon as you wake up** | | | | |
| Yes | 226 | 69.5 | 79.10±25.80 | t=6.395 |
| No | 99 | 30.5 | 59.75±23.41 | **p<0.001** |
| **Total** | 325 | 100.0 | | |

*,§: Groups that cause the difference detected with the Tukey HSD test, SD: Standard deviation, NMP-Q: Nomophobia questionnaire

score. Daily mobile internet usage time contributed the most to the change in the NMP-Q score (B=2.07, p<0.01).

## Discussion

The NMP-Q score of the students was calculated as 73.21±26.60 (Table 1). Similarly, in a study conducted by Aşık (22) on vocational college students in Turkey, the NMP-Q score was 72.09. Additionally, the NMP-Q score was 79.71 in the study conducted by Gezgin (23) on university students in Turkey. In addition, the NMP-Q score was 74.65±18.80 in a study conducted on adolescents in Iran (24). Furthermore, it was 67.31±25.70 in a study conducted on adolescents in Spain (25) and 82.39±18.63 in a study conducted on nursing students in Spain (26). In national and international studies on nomophobia, university students have similar levels of nomophobia. This finding is compatible with those of the present study.

In the present study, although the NMP-Q score was higher in female students than in male students, they did not differ significantly (Table 2). Likewise, no significant relationship has been found between gender and nomophobia in many studies (13,27-32). Contrary to our findings, some studies have revealed that the level of nomophobia was significantly higher in women than in men (19,20,26,33-36). With the difference in the findings, further studies are needed to investigate the effect of gender on individuals' susceptibility to nomophobia.

No difference was found between the NMP-Q scores of the students according to their socioeconomic levels (Table 2).

**Table 3.** Students' purposes of using a smartphone and NMP-Q scores according to the purposes of using the smartphone

| Smartphone usage purposes | n | % | NMP-Q score M ± SD | Test statistics |
|---|---|---|---|---|
| **Following the developments on the agenda** | | | | |
| Yes | 311 | 95.7 | 73.91±26.55 | t=2.263 |
| No | 14 | 4.3 | 57.57±23.39 | **p=0.024** |
| **Communicating with family and friends** | | | | |
| Yes | 309 | 95.1 | 73.44±26.58 | t=0.707 |
| No | 16 | 4.9 | 68.62±27.45 | p=0.480 |
| **Using its functions (taking videos, taking photos, alarm clock, MP3 player, etc.)** | | | | |
| Yes | 309 | 95.1 | 73.33±26.48 | t=0.350 |
| No | 16 | 4.9 | 70.93±29.63 | p=0.726 |
| **Access to the internet** | | | | |
| Yes | 301 | 92.6 | 73.83±26.51 | t=1.503 |
| No | 24 | 7.4 | 65.37±26.98 | p=0.134 |
| **Access to social media** | | | | |
| Yes | 286 | 88.0 | 75.67±26.34 | t=4.668 |
| No | 39 | 12.0 | 55.12±21.18 | **p<0.001** |
| **Playing games** | | | | |
| Yes | 177 | 54.5 | 77.62±26.24 | t=3.322 |
| No | 148 | 45.5 | 67.93±26.15 | **p=0.001** |
| **Thought that an expensive phone increases my prestige** | | | | |
| Yes | 49 | 15.1 | 92.08±28.16 | t=5.638 |
| No | 276 | 84.9 | 69.86±24.91 | **p<0.001** |
| **Total** | 325 | 100.0 | | |

SD: Standard deviation, NMP-Q: Nomophobia questionnaire

This finding is supported by a study conducted on high school students in Turkey, in which the NMP-Q score did not change according to the socioeconomic level (36). The widespread use of smartphones, in both developing and developed countries (6), may explain why nomophobia did not differ according to the socioeconomic level.

The NMP-Q score was higher in those who carry a charger with them, spend time with a smartphone before bedtime, leave their smartphone on at night, and use their smartphone as soon as they wake up (Table 2). Similar results were reported in other studies conducted in Turkey (36-38). These results suggest that individuals with nomophobia have features such as having a charger with them, spending time with a smartphone before bedtime, leaving their smartphone open at night, and using the smartphone as soon as they wake up.

NMP-Q scores were significantly higher in those who use their smartphone to follow the agenda, access social media, and play games (Table 3). In studies conducted on high school students and vocational college students in Turkey, the NMP-Q score was significantly higher in students who use their smartphones to connect to social media in parallel with our finding (36,37). The increasing use of social media has made these platforms a part of life, leading to anxiety in situations when social media is not accessible. Therefore, excessive use of social media is considered a nomophobic behavior (39).

As the ages of the students increased, the NMP-Q score decreased (Table 4). Some studies can support this finding. For example, in a study of university students and public employees in Turkey, Erdem et al. reported a negative relationship between age and NMP-Q score (34). In addition, Gurbuz et al. (29) examined 17-29-year-olds and Gezgin et al. (20) evaluated students of the Faculty of Education in Turkey and showed that the NMP-Q score decreased with increasing age. This negative relationship is also supported by multiple linear regression analysis, which shows that age is a negative predictor of the nomophobia scale score (Table 5). By contrast, other studies in university students have found no significant relationship between age and NMP-Q scores (19,26-28,30,33,40). The contradictory findings related to age in all these studies may be due to the limited age range of university students analyzed and the age ranges of these samples

**Table 4.** Pearson correlation coefficients among continuous variables

| Variables | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| **1. NMP-Q score** | 1 | | | | | |
| **2. Age** | -0.13** | | | | | |
| **3. Duration of using a smartphone** | 0.21*** | 0.10* | | | | |
| **4. Daily smartphone usage time** | 0.29*** | -0.17** | 0.23*** | | | |
| **5. Daily frequency of checking smartphones** | 0.27*** | -0.08 | 0.11* | 0.48*** | | |
| **6. Daily mobile internet usage time** | 0.34*** | -0.14** | 0.27*** | 0.87*** | 0.49*** | 1 |

The numbers in the variables row represent the same number of variables in the variables column. *p<0.05, **p<0.01, ***p<0.001.
NMP-Q: Nomophobia questionnaire

**Table 5.** Multiple linear regression analysis predicting the NMP-Q score

| Variables | B | SH B | p |
|---|---|---|---|
| **Age** | -0.82 | 0.39 | **0.039** |
| **Duration of using a smartphone** | 1.61 | 0.60 | **0.008** |
| **Daily smartphone usage time** | -0.56 | 0.72 | 0.439 |
| **Daily frequency of checking smartphones** | 0.08 | 0.03 | **0.017** |
| **Daily mobile internet usage time** | 2.07 | 0.75 | **0.006** |

Model $R^2$ =0.16, p<0.001, NMP-Q: Nomophobia questionnaire

were insufficient to distinguish nomophobia among age groups (30).

The present study shows that as the duration of smartphone use increased, the NMP-Q score increased (Table 4). The same result was found in the studies carried out in Turkey by Yıldırım et al. (19), Gezgin et al. (20), and Sırakaya (37). Furthermore, the duration of smartphone use is a positive predictor of the nomophobia scale score (Table 5) (41). However, some studies have not found a significant relationship between the duration of smartphone use and NMP-Q score (23,28,42,43). In the present study, the NMP-Q score increased as the students' daily smartphone use time increased (Table 4). This finding is consistent with the literature (28,36). As the daily smartphone usage time increases, the NMP-Q score also increased. The NMP-Q score increased with increasing daily frequency of checking smartphone (Table 4). Similarly, several studies have found that as the daily frequency of smartphone checks increases, the NMP-Q score significantly increases (37,38,42,43). In addition, the multivariate analysis showed that the daily frequency of smartphone checks is a positive predictor of the nomophobia scale score (Table 5). Individuals who have high mobile internet usage during the day had higher NMP-Q scores (Table 4). Likewise, other studies have found a significant relationship between daily mobile internet usage time and NMP-Q score (37,42,43). In addition to its positive contribution to the change in the nomophobia scale score, the duration of daily mobile internet usage made the most contribution in the model (Table 5). Accordingly, daily mobile internet usage appears to be the most important predictor of nomophobia (23).

### Study Limitations

This study has some limitations. For example, the small sample size prevents the generalization of the results of this study. Therefore, more comprehensive and multicenter studies are needed regarding the factors that affect the levels of nomophobia and the behavior of individuals with nomophobia. Since the nomophobia scale used in the study did not have a cut-off point, the frequency of nomophobia among students and the levels of nomophobia of students could not be determined.

## Conclusion

This study identified behaviors of individuals with nomophobia, such as seeing oneself as a smartphone addict, always carrying a charger, spending time with a smartphone before going to sleep, not turning off the smartphone while sleeping, using the smartphone upon waking up, using the smartphone to follow current developments, using it to access social media, using a smartphone for gaming, and believing that an expensive phone will increase a person's prestige. The level of nomophobia increases as the duration of smartphone use, daily smartphone usage time, daily frequency of checking the smartphone, and daily mobile internet usage increases and as age decreases. Although age is a negative predictor of nomophobia, duration of smartphone use, daily frequency of checking smartphone, and daily mobile internet usage time are positive predictors of nomophobia. Daily mobile internet usage time contributes most to the change in the nomophobia score. Since those who started using smartphones at an earlier age are more prone to nomophobia, it may be beneficial to try to delay the age of start using smartphones as much as possible to reduce the level of nomophobia as seen in university students. These issues should be considered to raise awareness about behavioral addiction types such as nomophobia in health education given to the public within the scope of preventive medicine to prevent nomophobia. Society should be conscious about the rational and correct use of technology. Healthcare providers, parents, and teachers can play a key role in

these matters. For this reason, our work on university students, who will be the parents and teachers of the future, is valuable. Future studies of the relationship among nomophobia, quality of life, health behavior, and physical activity may help in further clarifying the nature of nomophobia.

### Ethics

**Ethics Committee Approval:** The study was performed after it was approved by Fırat University Ethics Committee, and data collection was started in September 2018. The research ethics permission was obtained from Fırat University Non-Interventional Research Ethics Committee (date: 21/06/2018, no: 263000).

**Informed Consent:** Obtained.

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

### Authorship Contributions

Concept: E.P., F.N.K., A.F.O., S.E.D., Design: E.P., F.N.K., A.F.O., S.E.D., Data Collection or Processing: E.P., F.N.K., Analysis or Interpretation: E.P., F.N.K., Literature Search: E.P., F.N.K., Writing: E.P., F.N.K., A.F.O., S.E.D.

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## References

1. King AL, Valença AM, Nardi AE. Nomophobia: the mobile phone in panic disorder with agoraphobia: reducing phobias or worsening of dependence? Cogn Behav Neurol 2010;23:52-4.
2. Bragazzi NL, Del Puente G. A proposal for including nomophobia in the new DSM-V. Psychol Res Behav Manag 2014;7:155-60.
3. Fişek NH. Halk Sağlığı'na Giriş. 1st ed. Ankara: Çağ Matbaası; 1983.
4. Basu S, Garg S, Singh MM, Kohli C. Addiction-like Behavior Associated with Mobile Phone Usage among Medical Students in Delhi. Indian J Psychol Med 2018;40:446-51.
5. Rodríguez-García AM, Moreno-Guerrero AJ, López Belmonte J. Nomophobia: An Individual's Growing Fear of Being without a Smartphone-A Systematic Literature Review. Int J Environ Res Public Health 2020;17:580.
6. Lian L, You X, Huang J, Yang R. Who overuses smartphones? Roles of virtues and parenting style in smartphone addiction among Chinese college students. Comput Human Behav 2016;65:92-9.
7. O'Dea S. Number of smartphone users worldwide from 2016 to 2021 2020 [updated 10.06.2020. Available from: https://www.statista.com/statistics/330695/number-of-smartphone-users-worldwide/.
8. O'Dea S. Forecast of the smartphone user penetration rate in Turkey from 2018 to 2024 2020 [updated 10.06.2020. Available from: https://www.statista.com/statistics/568281/predicted-smartphone-user-penetration-rate-in-turkey/.
9. We Are Social. Türkiye elektronik cihaz kullanım istatistikleri 2019 [updated 10.06.2020. Available from: https://wearesocial.com/global-digital-report-2019.
10. Park N, Kim Y-C, Shon HY, Shim H. Factors influencing smartphone use and dependency in South Korea. Comput Human Behav 2013;29:1763-70.
11. Soni R, Upadhyay R, Jain M. Prevalence of smart phone addiction, sleep quality and associated behaviour problems in adolescents. International Journal of Research in Medical Sciences 2017;5:515.
12. Pearson C, Hussain Z. Smartphone addiction and associated psychological factors. Addicta 2016;3:193-207.
13. Erdem H, Kalkın G, Türen U, Deniz M. Üniversite öğrencilerinde mobil telefon yoksunluğu korkusunun (nomofobi) akademik başarıya etkisi. Süleyman Demirel Üniversitesi İktisadi ve İdari Bilimler Fakültesi Dergisi 2016;21:923-36.
14. King ALS, Valença AM, Silva ACO, Baczynski T, Carvalho MR, Nardi AE. Nomophobia: Dependency on virtual environments or social phobia? Comput Human Behav 2013;29:140–4.
15. Yıldırım C, Correia AP. Exploring the dimensions of nomophobia: Development and validation of a self-reported questionnaire. Comput Human Behav 2015;49:130-7.
16. Kamibeppu K, Sugiura H. Impact of the mobile phone on junior high-school students' friendships in the Tokyo metropolitan area. Cyberpsychol Behav 2005;8:121-30.
17. Darvishi M, Noori M, Nazer MR, Sheikholeslami S, Karimi E. Investigating Different Dimensions of Nomophobia among Medical Students: A Cross-Sectional Study. Open Access Maced J Med Sci 2019;7:573-8.
18. Musa R, Janiffa S, Rahman S. Who's at risk for smartphone nomophobia and pathology; the young or matured urban millennials? Advanced Science Letters 2017;23:7486-9.
19. Yıldırım C, Şumuer E, Adnan M, Yıldırım S. A growing fear: Prevalence of nomophobia among Turkish college students. Information Development 2016;32:1322-31.
20. Gezgin DM, Şumuer E, Arslan O, Yıldırım S. Nomophobia prevalence among pre-service teachers: A case of Trakya University. Trakya Üniversitesi Eğitim Fakültesi Dergisi 2017;7.
21. Sümbüloğlu K, Sümbüloğlu V. Biyoistatistik. 8th ed. Ankara: Hatiboğlu Yayınevi; 1988.
22. Aşık NA. Aidiyet duygusu ve nomofobi ilişkisi: Turizm öğrencileri üzerinde bir araştırma. Turar Turizm Araştırma Dergisi 2018;7:24-42.
23. Gezgin DM. Exploring the influence of the patterns of mobile internet use on university students' nomophobia levels. European Journal of Education Studies 2017;3:29-53.
24. Lin CY, Griffiths MD, Pakpour AH. Psychometric evaluation of Persian Nomophobia Questionnaire: Differential item functioning and measurement invariance across gender. J Behav Addict 2018;7:100-8.
25. González-Cabrera J, León-Mejía A, Pérez-Sancho C, Calvete E. Adaptation of the Nomophobia Questionnaire (NMP-Q) to Spanish in a sample of adolescents. Actas Esp Psiquiatr 2017;45:137-44.

26. Aguilera-Manrique G, Márquez-Hernández VV, Alcaraz-Córdoba T, Granados-Gámez G, Gutiérrez-Puertas V, Gutiérrez-Puertas L. The relationship between nomophobia and the distraction associated with smartphone use among nursing students in their clinical practicum. PLoS One 2018;13:e0202953.
27. Öz H, Tortop HS. Üniversite okuyan genç yetişkinlerin mobil telefon yoksunluğu korkusu (nomofobi) ile kişilik tipleri arasındaki ilişkinin incelenmesi. Yeni Medya Elektronik Dergisi 2018;2:146-59.
28. Adnan M, Gezgin DM. Modern çağın yeni fobisi: Üniversite öğrencileri arasında nomofobi prevalansı. Ankara Üniversitesi Eğitim Bilimleri Fakültesi Dergisi 2016;49:141-58.
29. Gurbuz IB, Ozkan G. What is Your Level of Nomophobia? An Investigation of Prevalence and Level of Nomophobia Among Young People in Turkey. Community Ment Health J 2020;56:814-22.
30. Apak E, Yaman ÖM. Üniversite öğrencilerinde nomofobi yaygınlığı ve nomofobi ile sosyal fobi arasındaki ilişki: Bingöl Üniversitesi örneklemi. Addicta: The Turkish Journal on Addictions 2019;6:611-29.
31. Yavuz M, Altan B, Bayrak B, Gündüz M, Bolat N. The relationships between nomophobia, alexithymia and metacognitive problems in an adolescent population. Turk J Pediatr 2019;61:345-51.
32. Uysal Ş, Özen H, Madenoğlu C. Social Phobia in Higher Education: The Influence of Nomophobia on Social Phobia. The Global e-Learning Journal 2016;5:1-8.
33. Cain J, Malcom DR. An Assessment of Pharmacy Students' Psychological Attachment to Smartphones at Two Colleges of Pharmacy. Am J Pharm Educ 2019;83:7136.
34. Türen U, Erdem H, Kalkın G. No Mobile Phone Phobia (Nomophobia) Prevalence: Samples of Undergraduate Students and Public Employees from Turkey. International Journal of Informatics Technologies 2017;10:1-12.
35. Arpaci I, Baloğlu M, Özteke Kozan Hİ, Kesici Ş. Individual Differences in the Relationship Between Attachment and Nomophobia Among College Students: The Mediating Role of Mindfulness. J Med Internet Res 2017;19:e404.
36. Eren B, Kılıç ZN, Günal SE, Kırcalı MF, Öznacar BB, Topuzoğlu A. Lise öğrencilerinde nomofobinin ve ilişkili etkenlerin değerlendirilmesi. Anadolu Psikiyatri Derg 2020;21:133-40.
37. Sırakaya M. Ön lisans öğrencilerinin nomofobi düzeylerinin akıllı telefon kullanım durumlarına göre incelenmesi. Mersin Üniversitesi Eğitim Fakültesi Dergisi 2018;14:714-27.
38. Kaplan-Akıllı G, Gezgin DM. Üniversite öğrencilerinin nomofobi düzeyleri ile farklı davranış örüntülerinin arasındaki ilişkilerin incelenmesi. Mehmet Akif Ersoy Üniversitesi Eğitim Fakültesi Dergisi 2016;40:51-69.
39. Durak HY. What would you do without your smartphone? Adolescents' social media usage, locus of control, and loneliness as a predictor of nomophobia. Addicta: The Turkish Journal on Addictions. 2018;5:543-57.
40. Sethia S, Melwani V, Melwani S, Priya A, Gupta M, Khan A. A study to assess the degree of nomophobia among the undergraduate students of a medical college in Bhopal. Int J Community Med and Public Health 2018;5:2442-5.
41. Gonçalves S, Dias P, Correia A-P. Nomophobia and lifestyle: smartphone use and its relationship to psychopathologies. Computers in Human Behavior Reports 2020;2:100025.
42. Gezgin D, Şahin YL, Yıldırım S. Sosyal ağ kullanıcıları arasında nomofobi yaygınlığının çeşitli faktörler açısından incelenmesi. Eğitim Teknolojisi Kuram ve Uygulama 2017;7:1-15.
43. Gezgin DM, Hamutoğlu NB, Sezen-Gültekin G, Ayas T. The relationship between nomophobia and loneliness among Turkish adolescents. International Journal of Research in Education and Science 2018;4:358-74.

Original Article

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# Nurses' Narratives of Remarkable Patient Health Care Events: Analysis of Seventeen Health Stories from Turkey and Palestine Using the Narrative Approach

## Hemşirelerin Dikkat Çeken Hasta Sağlık Olayları Hikayeleri: Türkiye ve Filistin'den On Yedi Sağlık Olayının Öyküleme Yaklaşımı ile Analizi

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## ABSTRACT

**Objective:** Nurses spend most of their time with patients. Stories are the formation of experiences that add meaning to life, raise awareness, and guide people. This study aimed to examine the aforementioned concepts from the nurses' narratives.

**Methods:** The researchers undertook an elaborate review of quantitative and qualitative studies. Seven doctoral students in nursing and 10 nurses from different departments in Palestinian hospitals were interviewed about qualitative care. In this study, 17 health stories from Turkey and Palestine were analyzed. Demographic data of all 17 participants were synthesized using a descriptive statistical format. The 17 stories generated 31,657 words for analysis.

**Results:** Seven themes were identified as figural across clinical specialties, including patient's final moments are difficult, cases involving children, violence and troublesome patients, unforgettable events, intricacies, interrogative, individual and teamwork.

**Conclusion:** Nurses' work environments are challenging. Sometimes, they experience unforgettable events that leave permanent marks in their memories. These events create physical distress, which affects how they provide care to patients. If the challenges are solved, then the nurses' quality of life and satisfaction will improve, enabling them to offer optimum care to patients.

**Keywords:** Narrative, nursing, health care, experience

## ÖZ

**Amaç:** Hemşireler zamanlarının çoğunu hastalarla geçirir. Hikayeler, hayata anlam katan, farkındalığı artıran ve insanlara rehberlik eden deneyimlerin oluşumudur. Bu araştırma, hemşirelerin hikayelerinden elde edilen kavramların incelenmesi amacıyla yapılmıştır.

**Yöntemler:** Araştırmacılar nicel ve nitel çalışmaları ayrıntılı bir şekilde incelemişlerdir. Türkiye'den hemşirelikte yedi doktora öğrencisi ile görüşülmüş ve Filistin hastanelerinde farklı bölümlerde çalışan on hemşire ile görüşülmüştür. Bu çalışmada Türkiye ve Filistin'den 17 sağlık öyküsü analiz edilmiştir. On yedi katılımcının tümü için demografik, tanımlayıcı bir istatistik biçimi kullanılarak bir araya getirilmiştir. On yedi hikaye analiz için 31, 657 kelime üretilerek değerlendirilmiştir.

**Bulgular:** Klinik uzmanlık alanlarında yedi tema figüratif olarak tanımlandı: Hastanın zor olan son anları, çocukları içeren olgular, şiddet ve sorunlu hastalar, unutulmaz olaylar, karmaşıklıklar, sorgulayıcı, bireysel ve takım çalışmasıdır.

**Sonuç:** Hemşirelerin çalışma ortamları zorlayıcıdır ve bazen anılarında kalıcı izler bırakan unutulmaz olaylarla karşılaşırlar. Bu olaylar, hemşirelerin hastalara nasıl bakım sağladığını etkileyen fiziksel stres yaratır. Zorluklar çözülürse, hemşirelerin yaşam kalitesi ve memnuniyeti artacak böylece hastalara optimum bakım sunmalarını sağlayacaktır.

**Anahtar Sözcükler:** Öykü, hemşire, sağlık hizmeti, tecrübe

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## Introduction

Nurses spend most of their time with patients. Work experiences gather various stories that contain a range of emotions, such as happiness, sadness, and anger. These stories are important from the perspective of the fundamentals of nursing. Stories are the formation of experiences that add meaning to life, raise awareness, and guide people. Professional nurses also use memories to guide new colleagues (1,2).

Nurses express their emotions through stories. An in-depth analysis of the stories experienced in literature reveals the patient-nurse relationship. Awareness of the feelings, burnout, human love, resentments, and empathy experienced by the nurse becomes hidden in the stories. By analyzing the stories, nurses' feelings, understanding of the patient, and importance of mutual communication can be understood and enhanced, which improved not only the nurses' quality of life and satisfaction but also their services (3).

This narrative investigation aimed to inspect the experience of nurses in practice in several hospitals in Palestine and compare them with those of doctorate nursing students in Turkey. Many quantitative studies have been performed on various quantitative aspects such as job satisfaction and perceived stress (4-7). However, only a few studies have focused on key areas from the perspectives of nurses. In this study, the actuality of practice, as detailed by nurses' expression is explored.

### Background

The researchers undertook an elaborate review of quantitative and qualitative studies. However, a comprehensive synopsis is beyond the scope of this paper. Since the information used in this article was nurses' exact descriptions, the literature review for this paper was limited to qualitative studies and theoretical studies from the perspectives of nurses.

Some studies have examined nurses' attitudes toward unforgettable events, such as those leading to deaths in Turkey and Palestine. Cevik and Kav (8) examined the attitudes of nurses toward taking care of patients in their last days through a cross-sectional study in Turkey and found that 82% of the nurses interviewed were not comfortable talking about death and had a less positive attitude toward the care of patients who were dying. The researchers argued that the lack of education and experience were the causes of this attitude. They proposed that nurses should be provided with more chances to talk about their experiences and personal feelings about death. They also recommended that more educational programs be tailored so that nurses can comprehend their attitudes toward death, overcome fear, enhance communication, and bolster their coping strategies (8).

A similar study also investigated the attitudes of nursing students toward providing palliative care in Palestine. Abu-El-Noor and Abu-El-Noor (9) conducted a cross-sectional study involving graduating nursing students at the Gaza University (n=141). The findings demonstrated that nursing students had a negative attitude toward taking care of the sick and their families at the terminal phase. They suggested that theoretical education should emphasize palliative care to refine the quality of care at the terminal stage (9).

The rationale for the high nurse turnover, leading to a shortage of nurses, has also been explored. Gök and Kocaman (10) conducted a descriptive study among nurses (n=134) to investigate the phenomenon and found that negative public opinion and adverse working conditions were the main reasons that nurses left the profession, opting to take other careers such as teaching. They suggested improving the nurses' working conditions and addressing the problem in a multidimensional approach (10).

Several studies have highlighted the challenges that nurses undergo in Palestine. Manenti et al. (11) noted that attacks against health care providers and patients were a rising challenge. They detailed an instance where a hospital was attacked, and the attackers searched for individual patients. The increased violence in the area has also led to anxiety, depression, and psychological distress among nurses and the patient population (11).

In summary, the literature suggests that nursing students in Turkey and Palestine harbor negative attitudes toward providing palliative care to a patient, and the lack of experience and education could be one of the reasons. Since some of the study participants are highly educated nurses (PhD students), the findings may help account for the role of education and experience in nurse's perspectives. Moreover, nurses in Turkey and Palestine encounter several challenges, such as negative public opinion, increased violence toward health care providers, depression, and psychological distresses. Thus, this study aimed to examine these concepts from the nurses' narratives. If the challenges are solved, nurses' quality of life and satisfaction will improve, enabling them to offer optimum care to patients.

## Methods

This narrative study was based on the rational perspectives of Miller and Salkind (12), Sönmez and Alacapınar (13).The researchers undertook an elaborate review of quantitative and qualitative studies. A purposive sample of Seven doctoral students in nursing were interviewed in the qualitative scientific research course for the second semester of the year (2018-2019) at Ankara Yıldırım Beyazıt University in Turkey in 4 months. By contrast, 10 nurses from different departments working in Palestinian hospitals were interviewed in 5 months. The 17 stories generated 31,657 words for analysis.

Nurses were approached using a network sampling method and invited to give their narratives. The inclusion criteria were as follows: (a) should have worked in a hospital for a minimum of 5 years (the period needed to be competent and knowledgeable on a particular subject), (b) willing to narrate their experiences to the researcher for an hour, (c) and is a licensed and registered nurse. This inclusion criterion was adapted from Gunther and Thomas (14). After explaining the purpose of the study and obtaining written permission, a 45-60 min period was allotted for each participant to narrate their experience.

The narrative was a personal, in-depth, non-directive type. The researcher asked the participants to "elaborate on an unforgettable instance that you gave nursing care to a patient." The researcher only interrupted to seek clarification during the narration. Consistent with the guidelines on narrative studies, no list of questions or prespecified agenda were utilized (15). Some of the stories were audiotaped and then transcribed verbatim. Participants' identities and whereabouts were altered to maintain confidentiality. The researchers engaged in bracketing of stories to evaluate formed ideas concerning potential research findings.

The sample from Palestine was distributed in a range of clinical areas: gynecology (Gyn, n=3), medical-surgical [(MS), n=1], pediatrics [(PD), n=2], oncology [(ONC), n=1], intensive care [(ICU), n=1], and emergency department [(ED), n=2]. Demographic information was obtained from each participant. The sample from Turkey was also distributed in a range of clinical areas: Gyn, (n=1); MS, (n=1); PD, (n=1); ONC, (n=1); ICU, (n=2); and ED, (n=1), but all of them were PhD students. Demographic information was obtained from each participant (mean age, 42; range, 23-60 years). Moreover, 59 percent of the participants were of Arabic (Palestinian) origin, and others were from Ankara Yıldırım Beyazıt University and were PhD nursing students and (Turkish). The educational levels for both samples were as follows: 10%, diploma; 34%, bachelor of science in nursing; 15%, master of science in nursing; and 41%, PhD students.

The data analysis comprised the identification of the figural (predominant) themes, which came out clearly from the narratives. The researchers signed agreements of confidentiality before working on the transcripts. About half of the printed versions were read between the researchers and categorized into appropriate themes during the data analysis period. The examined data mainly came from the interview transcriptions. The researchers obtained additional data from a reflexive journal and personal notes. During data analysis, themes were derived at both latent and manifest levels (13,14). As noted by Squire (14), when carrying out a narrative study, data analysis can take an inductive or deductive thematic analysis. For this study, both approaches were utilized. Deductively, the researcher, observing the directions provided in theory-based thematic analysis, analyzed the meaning making of nurses' experiences premised on predetermined themes (14). Themes were based on Schachter-Singer's (1962) two-factor theory, which argues that emotion is based on two factors: cognitive label and psychological arousal. Inductively, the study also allowed for the emergence of new themes (16).

The researchers performed all interviews and completed all transcription works before data analysis to prevent the imposition of meaning from one interview to the next. The data analysis process started with the creation of a profile for every nurse to present each of them in context. The demographic data of all 17 participants were put together using a descriptive statistical format. The 17 stories generated 31,657 words for analysis. As noted, additional data came from the researcher's notes and reflexive journals.

**Findings**

The majority of the participants did not have a problem with responding to the question, "elaborate on an unforgettable instance that you gave nursing care to a patient". Moreover, the themes were similar across the two populations. Their responses were instant, thorough, and intense. Only one of the nurses was unable to concentrate on a particular unforgettable patients and events, instead of detailing a "typical" day or the technical aspects of the job. A table of themes and subthemes is presented in the appendix. Seven themes were identified as figural across clinical specialties: 1) Patient's final moments are difficult, 2) cases involving children, 3) violence and troublesome patients, 4) unforgettable events, 5) intricacies, 6) interrogative, 7) individual and teamwork.

**Patient's Final Moments are Difficult**

A significant number of unforgettable events took place when the patient was dying, and these experiences were reported by nurses from Turkey and Palestine. In some instances, the nurses felt helpless since they could not do anything to save the patient's life. Science had been tested to its limit. For example, one of the nurses noted, "We were using the latest devices and giving the heaviest drugs, whatever the technology of our country requires." The family also has the most profound connection and wants to be informed about their patient's condition at each moment. However, the nurse is not always at the bedside since the time of death is usually unpredictable, and the family cannot be present at all times. One of the respondents working in the intensive care unit noted the following about the final moments, "What is difficult is to inform the family about a patient who will be dying soon. This is probably the most difficult moment for us health professionals. If you work in intensive care, you cannot escape at least once a day."

Although the nurses are almost always available at the end time, feelings of loneliness abide. For instance, a critical care nurse noted, "My primary objective was letting him know that he was not dying alone," which illustrates the lonely feeling of the patient at that moment. The feeling of sadness in this phase is stronger when the nurse has a long-term attachment to the patient.

**Cases Involving Children**

Cases that involved children were also among the most heartfelt of all 17 scenarios. Children were presented as innocent, and their suffering attracted the attention of everyone, not just the nurses. For example, one of the nurses narrated about a child who had been diagnosed with cerebral palsy, and the mother was to give an oral aspiration. However, she appeared psychologically tired and dramatically pushed the catheter down the child's mouth. The nurse noted that cases of psychologically tired mothers and caregivers were common, especially those involving children.

Cases involving children, especially at birth, were also among the unforgettable moments. These instances are usually characterized by higher death rates, and death was noted as one of the key themes. For example, one of the nurses at the neonatal department said, "Sometimes things go wrong. The hardest part

of this is that the beings who are so hasty to come to the world leave so quickly." The nurse and caregivers are usually involved in a deep emotional connection with the child. One of the nurses detailed how parents would touch the child affectionately each time they came to visit. When the child died, the nurse was sent to a deep emotional turmoil wondering what she would tell the parents when they came to visit.

**Violence and Troublesome Patients**

Cases of violence in the health care setting were narrated by several nurses, particularly from Palestine hospitals. Some of them involved patients who wanted to wreak havoc and did not need treatment. One of the nurses at the ED said of the frequency with which they experience these cases, "We often encounter this situation and have no difficulty in understanding the true intentions of these patients." The nurses had to be cunning enough to deal with these types of patients.

Moreover, violence in the form of attacks on the hospital personnel was rampant. This was a significant case with Palestinian nurses. One of them narrated how their hospital was attacked by the Israeli army in broad daylight. She said, "They had clothes that resembled those of the army. All operations stopped for four hours as they searched the hospital for a certain patient whom they did not found." One of the pediatric nurses also noted, "One day, we were surrounded by the Israeli army. We did not have any help. We thought we were going to die. I have heard several of such cases in the Palestine border before." One of the nurses narrated how their hospital was attacked by an armed militia. These instances left most of the nurses feeling unsafe. Moreover, no action was taken to beef up security following such incidents. Noteworthy, there were no reported cases of violence by nurses in Turkey.

Some nurses from both countries especially those who worked in ICU, MS units, and OB-Gyn departments showed that if their colleagues or doctors fail to respect them or their insights, the outcome of which is the death of the patients, and they consider this as a type of abuse and violence toward them. Moreover, the respondents mentioned the need for better collaboration among healthcare professionals so that the views of each are integrated into decision making especially in ICU and MS units.

**Unforgettable Events**

As the respondents gave narratives of exceptional occurrences, they extensively made use of the phases "frequently remarkable" or "I will always remember." These narratives were given in explicit detail. They are mostly similar to a change-of-shift report, generating evaluative information from various systems. Many participants started their tales by explaining an ordinary daily operation. As one emergency nurse stated, "Many things happen daily; it's a routine, but one stands out in mind." A nurse from the oncology department stated, "Each day you come across many patients; they all look similar, and few things remain in your memory." The patient's first sight appeared to foretell the future: "I was in my normal routine in the ED and came across this man shouting and some people restraining him against the bed, attempting to have him intubated. I was like, "It will be a terrible and hard day." Another nurse noted, "I mean, imminent disaster was all over his face. It was….one of those instances that I could feel everything was not correct."

Sensational occurrences were uttermost cases of the unprecedented disgust of burns, maimed bodies, and inexplicable wounds. One nurse (ED nurse) noted, "Well, in the emergency department some of the most terrible incidences stick to your memory." A nurse said that a particular client was "separated from one region down to the knee because of a very severe car accident."

Despite heroic efforts by the nurses, many of the stories ended with the patient's death. The losses had a strong emotional effect on the nurses, especially when the nurse appeared helpless at preventing the client's looming demise. However, as an oncology nurse noted, "I'm not shedding tears all the time," and these experiences were reported by nurses from Turkey and Palestine.

**Intricacies**

Save for a few hilarious vignettes, occurrences detailed by the nurses proved to be tragic and catastrophic, finding them unrehearsed, and giving them a chance to contemplate vagueness, "You could not find the solution…I always wonder what happened." For instance, one nurse said about sudden death by cardiac arrest, "He did not smoke. He did not abuse drugs. He was a physically fit young lad whom I knew many things were going on for him. Why did this impediment occur to him? We will never find out anyway."

One of the means of surviving is attempting to comprehend what transpired and the reason behind it. Retroactive mirroring on providing care to patients appeared to be centered at creating sense from unfathomable incidents. The nurses appeared to be trying to deal with the uncertain outcomes of care and their distress by deriving "lessons" that, to some extent, influenced their practice. An ED nurse reflected, "Neither of our clinical expertise could rescue her. The things I gleaned from the situation were the vitality of acting promptly and the essence of cooperation from all team members." Even the mysterious recoveries inspired the search for meaning, "I mean, she began gaining a little bit of kidney function back, which was sort of wonderful" (MS nurse).

**Interrogative**

Despite knowing "what and why," nurses often imagined if they could have taken another action to divert the result. One nurse remembered a client who passed out suddenly while she was taking her lunch break, "You let go of the traumatizing event, and you wonder. "What different action could I have undertaken?" …liable, liable! You know, what did I do?" Moreover, the participants from Turkey and Palestine often wondered about their inaction and action, as one nurse said, "I mean, if I had tipped the ER doctor and said, "You, I almost have a code, could you rush and intubate my patient?" that gentleman might have been well and alive."

**Individual and Teamwork**

The loneliness of a nurse providing care was explicit in several of the narratives, as the nurses detailed their experiences of working

single-handedly contrary to the odds. An ED attendant revealed why she shifted from the ICU, "Quite often, I felt like we were alone. In the ICU where I worked daily, many of the caregivers had a burnout, and they did not discern it. They did not want to be helped. They were reluctant to rise and assist other people and provide care for the sick since they were just tired with it all." Nurses from both countries revealed that, sometimes, "The nurse is needed to take an uncomfortable procedure that the nurse thinks and may cause more bad than good to a patient with very poor outcomes for survival, and all of this raises tension, confusion, and conscientiousness during personal work and isolation."

Some nurses from both countries, particularly those who worked in close departments, had a belief that their colleagues shared a friendship that made work enjoyable and held them from quitting the career. Indeed, one of the ED nurses stated, "…but to have the entire team at that instance, it aided in pulling each other through the crisis period. To make things moving for that client." Nurses who formed friendships with colleagues gained from assistance.

## Discussion

This narrative study aimed at understanding the experiences of nurses during extraordinary and unforgettable events. The stories were described in complete detail. Albeit the majority of stories ending in death, some were miraculous recoveries. The participants experienced the boundaries of science.

The retrospective descriptions involved questioning what could have been done better or hopelessness in finding out what transpired. The participants experienced the boundaries of science and delved into the sphere of experiential questioning, for which there are no definite responses. The theme of individual and teamwork spouses isolation or distress, a feeling often encountered by the nurses and their association (or lack thereof) with physicians, coworkers, and patients during exceptional events. The participants also detailed lessons they learned from the events and how they influenced their practice. These residues of moral distress can impede a nurse's ability to provide care.

Death is an unavoidable event, which brings with it some of the strongest feelings. Most of the nurses experienced intense feelings of sadness and helplessness during the patient's death. Rodgers et al. (17) investigated the effect of bathing and honoring practice on nurses and families at the time of patient's death and found that they had a positive influence and eased the grieving process. Thus, bathing, dressing, and honoring practices need to be introduced to reduce the feelings that come with death for both nurses and family, in addition to the need for a more systematic debriefing for both of them (17). Zheng et al. (18) investigated the effect of systematic debriefing on nurses, and the results of this systematic review could provide evidence for nurses' coping approaches when dealing with patient death, and the recommendations could be employed by nurses to deal with the losses of patients and in cases of complicated conditions.

The findings are also in line with the results of several studies. Cevik and Kav (8) noted that a lack of education might be the critical reason for nurses' negative perspectives on caring for patients at their end times. In this study, although the events surrounding the end of life were traumatizing at times, nurses did not harbor negative attitudes toward care provision. They did their best and examined methods that could have handled the situation better even after the patient was dead. Since some of the participants were PhD students and had more than 5 years of experience in the nursing profession, the researcher concludes that education level and experience are vital in forming positive attitudes toward extraordinary events in nursing (8). Moreover, Leana et al. (19) found that being empathetic as a nurse led to positive outcomes of treatment. Kelo et al. (20) argued that more training and administrative procedures for nurses are needed to enhance the quality of empowerment education they provide to children and families. Thus, nurses with a lower level of knowledge should be exposed to experiences and training that enhance positive attitudes and empathy at the time of death.

Besides, the finding that nurses in both Turkey and Palestine, especially in the ICU and ED, often experience burnouts, stress, and sadness are consistent with other findings in the literature. Manenti et al. (11) noted that Palestinian nurses faced physical distress, depression, and sadness.

Manenti et al. (11) detailed the increasing cases of violence in health care institutions, which were also found from the narratives from Palestine. Cheung et al. (21) found that patients, their relatives, and colleagues were the foremost perpetrators of workplace violence. However, in this study, most of the violence came from the armed militia. The victims suffer irreversible physical and psychological harm. Thus, apart from amending policy so that there is zero tolerance for workplace violence in healthcare settings, hospitals located in war zones need to be properly guarded so that instances of violence are minimized (21).

Instances necessitating coordination of nurses and family were also found in the narratives from Palestine and Turkey. An example was the case whereby the mother needed to perform an oral aspiration on a child. These instances were associated with feelings of helplessness and the psychological tiredness of the families. Hamano et al. (22) noted that proper coordination of care between the nurse and family and among care providers leads to an improved quality of life of the patient, which can create positive feelings in the provider. Proper coordination of care is also vital for patients with multiple illnesses such as diabetes and cancer since it ensures that each provider performs their role, and in turn, no one experiences burnout (23,24). Thus, the coordination of care needs to be enhanced in various hospitals to create positive experiences for nurses and provide friendly hospital or family-centered care for bereaved patients.

Cases involving children were some of the most emotional experiences of nurses. Studies have suggested that considering the nurses' conceptions of the child's challenges is critical in fostering a positive relationship between the nurse and family, as it ultimately influences the treatment outcome (25). For children

who are nearing the end of life, spiritual education is effective in easing their mental distress (26). Thus, nurses should be trained by chaplains, Imams, and other spiritual leaders on how to communicate spiritual meanings of illness and concepts of the afterlife to children so that they can be more relaxed in times of suffering, which may reduce nurses' feelings of helplessness. Several studies have also detailed the importance of safeguarding of supervision of children. For example, Little et al. (27) found that safeguarding of supervision leads to more reflective practices for nurses, which then led to better practice. Thus, proper clinical supervision should be provided to ensure that not only the child's needs are met, but also benefit the nurses through improved practice (27).

However, the study did not find significant differences between the nurses in Palestine and Turkey. The only slight difference was the high number of violence presented by Palestine participants. It was contrary to the expectation given the increased cases of violence in Palestine that have put stress on social amenities, led to population increase in some areas, and increased the number of casualties compared with Turkey, where the situation is relatively calm. Thus, the researcher suggests conducting a more detailed comparative study to establish the differences in nurses' perspectives in the two countries.

## Conclusion

Nurses are always in contact with the patients and are sometimes the determining factor between life and death. Their work environments are challenging, and sometimes, they encounter unforgettable events that leave permanent marks in their memories. These events create physical distress, which affects how nurses provide care to patients. Nurses also face other challenges, such as burnout and violence in the workplace. Sometimes, their colleagues or doctors fail to respect them or their insights, which may lead to the death of the patients. Thus, there is a need for better collaboration among healthcare professionals so that the views of each are integrated into the decision making. Moreover, there is a need for policy change to attract more nurses to the field, especially in the ICU, which will reduce stress and enhance the standard care provided to the patients at their final moments. Cases of violence are common, especially among Palestinian nurses. Therefore, hospitals in war-torn areas should be provided enough security to avoid any interruptions and ensure the safety of the health personnel. There is also a need to provide more education and opportunities for the nurses so that they can form positive attitudes toward care provision for patients at their end of life and in extraordinary events.

### Ethics

**Ethics Committee Approval:** The study was approved by the Al-Quds University Ethics Committee (approval number: 30/01/2020, 100/REC/2020).

**Informed Consent:** Informed consent was obtained.

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

### Authorship Contributions

Surgical and Medical Practices: A.G.B., Ö.G.İ., Concept: A.G.B., C.K., T.O., Design: A.G.B., Ö.G.İ., C.K., T.O., Data Collection or Processing: A.G.B., Ö.G.İ., Analysis or Interpretation: A.G.B., C.K., T.O., Literature Search: A.G.B., Ö.G.İ., Writing: A.G.B., Ö.G.İ., C.K., T.O.

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## References

1. Birimoğlu C, Ayaz S. Nursing Students' Perceptions of Caring Behaviors. Hacettepe Üniversitesi Hemşirelik Fakültesi Dergisi 2015;2:40-8.
2. Smith MC, Turkel MC, Robinson-Wolf Z. Caring in Nursing Classics: An Essential Resource. United States of America Springer: Publishing Company; 2013:8-42.
3. Donaldson-Andersen J. The nurse's role in supporting patients and family in sharing personal accounts of traumatic events: a personal experience. J Trauma Nurs 2017;24:134-40.
4. Gabrani A, Hoxha A, Gabrani J, Petrela E, Zaimi E, Avdullari E. Perceived organizational commitment and job satisfaction among nurses in Albanian public hospitals: A cross-sectional study. International Journal of Healthcare Management 2016; 9:110-8.
5. Helbing E, Teems M, Moultrie D. An investigation of job satisfaction among nurses in the emergency department. ABNF Journal 2017;28:1-62.
6. Iyer RD. Moderating effect of gender on the relationship between role stres and job satisfaction among nurses in Mumbai. Journal of Management & Public Policy 2017;9:41-52.
7. Iyer RD, Deshmukh M. Moderating effect of work places pirituality on role stres or and job satisfaction among Indian nurses. Journal of Management & Public Policy 2018;9:15-30.
8. Cevik B, Kav S. Attitudes and experiences of nurses to ward deathand caring fordying patients in Turkey. Cancer Nurs 2013;36:E58-65.
9. Abu-El-Noor NI, Abu-El-Noor MK. Attitude of Palestinian nursing students toward caring for dying patients: A call for change in health education policy. Journal of Holistic Nursing 2015;34:193-9.
10. Gök AU, Kocaman G. Reasons for leaving nursing: a study among Turkish nurses. Contemp Nurse 2011;39:65-74.
11. Manenti A, Goyet CV, Reinicke C, MacDonald J, Donald J. Report of a fieldassessment of healthconditions in theoccupiedPalestinianterritory. World Health Organization. 2016. Retrievedfrom https://apps.who.int/gb/Statements/Report_Palestinian_territory/Report_Palestinian_territory-fr.pdf
12. Miller DC, Salkind NJ. Narrative Research. InHandbook of Research Design & Social Measurement (6th ed). 2002.

13. Sönmez V, Alacapınar FG. Örneklendirilmiş Bilimsel Araştırma Yöntemleri. 5. Baskı Anı Yayıncılık. 2017.
14. Gunther M, Thomas SP. Nurses' narratives of unforgettable patient care events. J Nurs Scholarsh 2006;38:370-6.
15. Squire C. Approachesto Narrative Research. ESRC National Centrefor Research Methods Review Paper. 2008. Retrieved from http://eprints.ncrm.ac.uk/419/1/ Methods Review Paper NCRM-009.pdf
16. Dror OE. Deconstructing the "two factors": The historical origins of the Schachter–Singer Theory of Emotions. SageJournals, 2017;9:7-16.
17. Rodgers D, Calmes B, Grotts J. Nursing Care at the Time of Death: A Bathing and Honoring Practice. Oncol Nurs Forum 2016;43:363-71.
18. Zheng R, Lee SF, Bloomer MJ. How nurses cope with patient death: A systematic review and qualitative meta-synthesis. JCN 2018;27:e39-49.
19. Leana C, Meuris J, Lamberton C. Morethan a feeling: The role of empathetic care in promoting safety in health care. ILR Review 2018;71:394-425.
20. Kelo M, Martikainen M, Eriksson E. Patient education of children and their families: Nurses' experiences. Pediatric Nursing 2013;39:71-9.
21. Cheung T, Lee PH, Yip PSF. The association between workplace violence and physicians' and nurses' job satisfaction in Macau. PLoS One 2018;13:e0207577.
22. Hamano J, Morita T, Fukui S, Kizawa Y, Tunetou S, Shima Y, et al. Trust in Physicians, Continuity and Coordination of Care, and Quality of Death in Patients with Advanced Cancer. J Palliat Med 2017;20:1252-9.
23. Girault A, Ferrua M, Lalloué B, Sicotte C, Fourcade A, Yatim F, et al. Internet-based Technologies to improve cancer care coordination: Current use and attitudes among cancer patients. European Journal of Cancer 2015;51:551-7.
24. Goebel J, Valinski S, Hershey DS. Improving coordination of care among health care professionals and patients with Diabetes and cancer. Clinical Journal of Oncology Nursing 2016;20.
25. Isma GE, Bramhagen AC, Ahlstrom G, Östman M, Dykes AK. Swedish child health care nurses' conceptions of over weight in children: a qualitative study. BMC Family Practice 2012;13:57.
26. Ferrell B, Wittenberg E, Battista V, Walker G. Nurses' Experiences of Spiritual Communication with Seriously III Children. J Palliat Med 2016;19:1166-70.
27. Little M, Baker T, Jinks AM. A qualitative evaluation of community nurses' experiences of child safeguarding supervision. Child Abuse Review 2018;27:150-7.

**Appendix 1.** Themes and subthemes

| Themes | Subthemes |
|---|---|
| Patients' final moments | Death, despair, loneliness, science limitations, and intense emotions |
| Cases involving children | Birth, innocence, psychological tiredness, and drama |
| Violence and troublesome patients | Desperation, insecurity, helplessness, and havoc |
| Unforgettable events | Terrible incidence, losses, helplessness are frequently remarkable |
| Intricacies | Tragic and catastrophic and distress |
| Interrogative | Guilt, need, and weakness, a sense of responsibility |
| Individual and teamwork | Shared a friendship, crisis, helping |

Original Article

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# Examination of Fatigue, Well-Being and Life Habits in Children with Cancer Diagnosis

## Kanser Tanısı Almış Çocuklarda Yorgunluk, İyilik Hali ve Yaşam Alışkanlıklarının İncelenmesi

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## ABSTRACT

**Objective:** In this study, it was planned to examine fatigue, well-being and life habits in children with cancer.

**Methods:** This cross-sectional analytical study was conducted between September 2019-January 2020. "24-Hour Child Fatigue Scale", "Child Well-being Assessment" and Child Life Habit Questionnaire (LIFE-H for Children 1.0)" were administered to 20 children with cancer aged 5-15 years. Pearson's correlation coefficient was used to determine the statistical relationship between life habits, fatigue and well-being. Statistical significance level was accepted as p<0.05.

**Results:** There were significant relationships between fatigue and personal care, shelter and mobility parameters of life habits (r=-0.66, r=0.54, r=0.45, p<0.01, respectively) and there were significant relationships between fatigue and negative emotions (r=0.46), overall life satisfaction (r=-0.52), general happiness (r=-0.49) and positive emotions (r=-0.44 *) parameters of well-being assessment. Life habits scale was found to be related with nutrition, physical fitness and communication parameters of Child Life Habit Questionnaire were found to be most related with the meaning and purpose parameter of the well-being assessment (p<0.01). There were significant relationships between positive emotions and recreation (r=0.45, p=0.04); optimism and communication (r=-0.44, p=0.04); personal care (r=-0.49, p=0, 02), social life (r=-0.46, p=0.04) and autonomy; and mobility and negative emotions (r=-0.45, p=0.04).

## ÖZ

**Amaç:** Bu çalışmada kanser tanısı almış çocuklarda yorgunluk, iyilik hali ve yaşam alışkanlıklarının incelenmesi amaçlandı.

**Yöntemler:** Kesitsel analitik tipteki bu çalışma, Eylül 2019-Ocak 2020 tarihleri arasında gerçekleştirildi. Yaş aralığı 5-15 yıl olan kanser tanısı almış 20 çocuğa "24 Saatlik Çocuk Yorgunluk Ölçeği", "Çocuklarda İyilik Hali Değerlendirmesi" ve Çocuk Yaşam Alışkanlığı Anketi (LİFE-H for Children 1.0)" uygulandı. Yaşam alışkanlıkları, yorgunluk ve iyilik hali arasında istatistiksel olarak ilişkiyi belirlemek için Pearson korelasyon katsayısı kullanıldı. İstatistiksel anlamlılık düzeyi p<0,05 olarak kabul edildi.

**Bulgular:** Yorgunluk ile yaşam alışkanlıkları parametrelerinden kişisel bakım, barınma ve mobilite arasında (sırasıyla; r=-0,66, r=0,54, r=0,45; p<0,01) ve iyilik hali değerlendirmesinin negatif duygular (r=0,46), genel yaşam doyumu (r=-0,52), genel mutluluk (r=-0,49) ve pozitif duygular (r=-0,44) arasında anlamlı ilişki saptandı. Çocuk Yaşam Alışkanlığı Anketindeki beslenme, fiziksel uygunluk ve iletişim parametreleri ile en fazla iyilik halinin anlam ve amaç parametresi arasında ilişkili bulundu (p<0,01). Rekreasyon ile pozitif duygular (r=0,45, p=0,04), iletişim ile iyimserlik (r=-0,44, p=0,04), kişisel bakım (r=-0,49, p=0,02) ve toplumsal yaşam (r=-0,46, p=0,04) ile otonomi arasında, mobilite ile negatif duygular (r=-0,45, p=0,04) arasında anlamlı ilişki görüldü.

**Sonuç:** Bu çalışmada tespit edilen ilişkiler dikkate alınarak kanser tanılı çocukların değerlendirmesi ve tedavi yaklaşımları

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**Conclusion:** Considering the relationships determined in this study, the evaluation of the children with cancer and treatment approaches can be shaped. The fact that fatigue affects all aspects of children's life reveals the importance of dealing with fatigue. It is recommended to focus on the meaning and purpose and regain autonomy for children in order to rearrange the life habits of the children and ensure their well-being.

**Keywords:** Cancer, child, fatigue, life habits, wellbeing

şekillendirilebilir. Yorgunluğun, çocukların yaşamının bütün boyutlarını etkilemesi yorgunlukla başa çıkmanın önemini ortaya koymaktadır. Çocukların yaşam alışkanlıklarının yeniden düzenlenebilmesi ve iyilik halinin sağlanması için anlam ve amaç üzerine odaklanmak ve çocuklara otonomi kazandırmak önerilmektedir.

**Anahtar Sözcükler:** Kanser, çocuk, yorgunluk, yaşam alışkanlıkları, iyilik hali

## Introduction

Diagnosis of cancer in childhood is rarer than in adults. Between 2001 and 2010, diagnosis of childhood cancer was 13% more common than in the 1980s, and its incidence in the 0-14 age group was 140 per million (1,2). Today, 70% of children diagnosed as having cancer recover, but 30% die due to recurrence of the disease and lack of response to treatment (3-5). Although it was important how the treatment process would progress in diseases such as cancer in the past, psychosocial issues have started to attract more attention with the prolongation of life expectancy (6,7). Therefore, the effects of cancer treatment on physical and psychosocial well-being and quality of life have become increasingly important (8).

Cancer and chemotherapy generally leads to symptoms such as joint and muscle pain, fatigue, edema, growth retardation, fatigue, anxiety, depression, sleep disorder, increased cytokine production, cachexia, decreased physical function, anemia, anger, frustration, isolation from daily life, and introversion in children (9). Fatigue is a frequent finding in 70-100% of children and young patients with cancer (9-11). It can occur at the time of diagnosis and becomes increasingly common as the disease progresses (12,13). Cancer-related fatigue results from the complex effect of physical, mental, emotional, environmental and pathological factors (12,14). Fatigue, which is a subjective and multidimensional experience, negatively affects the lives of patients with cancer. Therefore, it is very important to evaluate fatigue in cancer from the patient's perspective (15,16).

Studies on well-being have increased in recent years (17,18). Thomas used an expression for well-being as "it is abstract, difficult to define and even harder to measure" (19). Well-being is a subjective expression and includes much more than the concept of happiness (20). It is reported that well-being consists of three interrelated components: Satisfaction with life, positive and negative emotions (21). Studies on the well-being of children with cancer have increased in recent years (22,23).

Life habits are defined as "the daily activities and social roles necessary to ensure the survival and self-development of a person throughout life" (24). In the latest version of the International Classification of Functioning, Disability and Health (ICF), "Disability and Health" is defined as participation of a person in relation to his/her life and nine activities that have an impact on participation are listed as follows: Learning and application of knowledge, general tasks and needs, communication, mobility, personal care, home life, interpersonal interaction and relationships, major living spaces and communal, social and civic life. The World Health Organization emphasizes the necessity of benefiting from this activity list when evaluating life habits (25). Although there are reports in the literature on life habits, they do not cover all parts that a child participates in life or all aspects of these parts (26-29).

The stability of the well-being of individuals depends on a dynamic balance (30,31), and this balance includes parameters such as physical well-being, large amount of physical resources, absence of fatigue, emotional control, social functionality, and activities (32,33). Fatigue can change physical condition, psychological and spiritual self, cognitive functioning, expectations and quality of life (34). Curt found in his study that fatigue affected every aspect of daily life and stated that these were related to the physical, emotional, psychological and social consequences of fatigue (15). Children may not be aware of changes in fatigue, physical endurance, and activities of daily life, but children over the age of 13 may notice a lack of energy (35). It is known that many components change simultaneously in the lives of children with cancer. However, there is no study in the literature examining the relationship between fatigue, well-being and life habits in children.

The aim of this study is to evaluate the fatigue, well-being and life habits that are thought to affect the treatment process in children diagnosed as having cancer and to examine the relationship between them.

## Method

### Type of Research

This research was a cross-sectional analytical type study.

### Population-Sample of the Research

In this study, which was carried out between September 2019 and January 2020, all children between the ages of 5-15 who were hospitalized in the pediatric department of Hacettepe University Oncology Hospital, were diagnosed as having cancer, were not in the terminal phase, and in whom treatment was started were included. Twenty children, 11 girls and 9 boys, who completed the questionnaires in time, formed the sample of the study.

**Data Collection Tools**

Research data were collected using the "Child and Parent Information Form, 24-Hour Child Fatigue Scale, Child Well-Being Assessment and Child Life Habit Questionnaire".

**Child and Parent Introduction Form:** This form was created by researchers to determine the introductory characteristics of children and parents. In the form, five questions were about children's age, gender, education level; and five questions were about parents' age, education level, occupation, income status and family type. According to the information obtained by the parents, the children who got a passing grade in their classes were considered to be successful at a "moderate level" in terms of school success; children with grades above the class average were considered to be successful at "good level".

**The 24-Hour Child Fatigue Scale:** It was developed in 2001 by Hinds et al. (36) and revised in 2007 to shorten it. The Turkish validity and reliability of the scale was performed by Gerçeker and Yılmaz (37) in 2010. This scale, which is the 24-hour form of the child fatigue scale, includes 10 items questioning whether the child has been tired in the last 24 hours. It includes 5 different options for each item as "not at all, a little, some, quite a bit, and a lot" and each item is scored between 1-5. A minimum of 10 and a maximum of 50 points are obtained from the scale. As the scores obtained from the scale increase, the child's fatigue level increases (37).

**The Child Well-being Assessment:** It consists of 21 questions included in the New Economics Foundation publication, Guide for Measuring Children's Well-being, and each question is answered by the child (38,39). Translation of the scale was carried out in accordance with the Beaton translation protocol (40). The questions were grouped under four main headings as "well-being dimension, general life satisfaction, general happiness, positive and negative emotions". The well-being dimension consists of sub-parameters such as "positive emotions, negative emotions, life satisfaction, vitality, optimism, resilience, autonomy, meaningful and purposeful activities, relationships". Low scores in optimism, autonomy, meaningful and purposeful activities, and relationships have positive meaning. High scores in the resilience parameter have negative meaning. These parameters are answered as "agree" or "disagree". In general life satisfaction, the child indicates where his/her life is on a ladder with steps between 0-10. In general happiness, the child chooses one of the facial expressions, these are scored between 1-5 and a high score indicates that the child is happy. The positive and negative emotions part includes 5 different options for each question as "never, one day, a few days, most days, and every day" and is scored between 1-5. A high score for positive emotions and a low score for negative emotions indicate a positive state of well-being. The scoring of most parameters is different from each other. The parameters with a total score of 5 are positive emotions 1, negative emotions 1 and vitality parameters. The parameter with a total score of 3 is life satisfaction parameter. The parameter with a total score of 2 are optimism, resilience, autonomy, meaningful and purposeful activities, and relationships. The total score of the positive emotions parameter is 25, and the total score of the negative emotions parameter is 20 (38).

**Child Life Habit Questionnaire:** This questionnaire was developed by Noreau et al. (41) in 2002. It is a form consisting of 12 groups under the main headings of "nutrition, physical fitness, personal care, communication, accommodation, mobility, responsibilities, interpersonal relations, social life, education, work, recreation" and containing a total of 64 questions with a total score of 10. For each life habit, it is required to answer two questions: Level of success and type of assistance. In this form, which is a special scoring method, a high score has a positive value in terms of the child's participation in the activity (41). The translation of the questionnaire was done in accordance with the Beaton principle (40). Considering that the children did not have any working activities, the "work" parameter of the life habit form was not included in the study.

**Data Collection Method**

The data were collected by the researcher between September 2019 and January 2020, using the face-to-face interview technique with children in whom treatment was started at Hacettepe University Oncology Hospital and who were hospitalized. Child and Parent introduction forms were filled by the researcher with the help of the parents through face-to-face interview technique.

**Ethical Aspect of Research**

The children participating in the study and their parents were informed about the purpose of the study and a signed informed consent form was obtained from the parents. The study was approved by the Hacettepe University Non-interventional Clinical Research Ethics Committee (GO/677).

**Evaluation of Data**

The SPSS 17.00 program was used for statistical analysis of the data. Variables determined by measurement were expressed as mean ± standard deviation. Percentage (%) was calculated for variables determined by counting. The normal distribution of the variables was examined with the Kolmorov-Smirnov test. "Pearson correlation coefficient" was used to examine the relationship between life habits, fatigue and well-being, all of which had normal distribution Statistical significance level was accepted as $p<0.05$. The coefficient strength of the correlation and the level of relationship were as follows: 0.00-0.25 very weak, 0.26-0.49 weak, 0.50-0.69 moderate, 0.70-0.89 high, 0.90-1.0 very high (42).

## Results

The mean age of the children participating in the study was 11.25±3.04 years (minimum 5; maximum 15 years), and the mean age of their parents was 40.20±7.31 years. It was determined that 55% of the children were girls, 60% were attending secondary school, 65% had good school success, and 80% knew the diagnosis of the disease. It was determined that 45% of the parents were primary school graduates, 15% were

self-employed, 70% received minimum wage, and 85% had nuclear family type (Table 1).

The mean score of the participants in the 24-Hour Child Fatigue Scale (29.40±9.42) was found to be moderate (Table 2).

In the Child Well-being Assessment of the children participating in the study, their general life satisfaction (7.40±2.45) was found to be above the average, and their general happiness (3.85±1.03) was at a moderate level. In the title of Positive and Negative Emotions; the scores of negative emotions 1 (3.05±0.60) and negative emotions 2 (12.40±2.56) parameters were more than moderate level, the scores of positive emotions 1 (3.70±0.57) and positive emotions 2 (14.40±3.83) parameters were found to be less than moderate level (Table 3).

In the Life Habits Form, the score of personal care parameter (4.85±2.84) was below the average. The scores of mobility parameter (5.14±3.43), social life parameter (5.66±4.69), recreation parameter (5.40±2.19), and accommodation parameter (5.35±2.74), which included the individual's domestic activities, were found to be at moderate level (Table 4).

There was no significant relationship between the descriptive characteristics of the children and their fatigue and well-being ($p>0.05$). However, a moderate correlation was found between the age and education level of the children and the nutrition, communication and responsibility steps of their life habits and between the school success of the children and the personal care and communication parameters of their life habits ($p<0.05$) (Table 5).

**Table 1.** Introductory characteristics of children and their parents (n=20)

| | | n | % |
|---|---|---|---|
| Mean age of the children | 11.25±3.04 (minimum 5; maximum 15) | | |
| Gender of children | Girl | 11 | 55.0 |
| | Boy | 9 | 45.0 |
| Education level of children | Primary school | 7 | 35.0 |
| | Middle school | 12 | 60.0 |
| | Not started school | 1 | 5.0 |
| School success of children | Not started school | 1 | 5.0 |
| | Moderate | 6 | 30.0 |
| | Good | 13 | 65.0 |
| Awareness of children about their disease | Know | 16 | 80.0 |
| | Do not know | 4 | 20.0 |
| Education level of parents | Illiterate | 1 | 5.0 |
| | Primary school | 9 | 45.0 |
| | Middle school | 1 | 5.0 |
| | High school or its equivalent | 5 | 25.0 |
| | Faculty | 4 | 20.0 |
| Occupation of parents | Housewife | 9 | 45.0 |
| | Officer | 5 | 25.0 |
| | Self-employment | 3 | 15.0 |
| | Retired | 2 | 10.0 |
| | Other | 1 | 5.0 |
| Income of parents | Below minimum wage | 3 | 15.0 |
| | Minimum wage | 14 | 70.0 |
| | Above minimum wage | 3 | 15.0 |
| Family type | Nuclear | 17 | 85.0 |
| | Large | 2 | 10.0 |
| | Broken | 1 | 5.0 |

**Table 2.** Mean scores of the 24-hour child fatigue scale

| | Minimum | Maximum | Mean | Standard deviation |
|---|---|---|---|---|
| Fatigue | 11.00 | 46.00 | 29.40 | 9.42 |

**Table 3.** Mean scores of the child well-being assessment

| | | Minimum | Maximum | Mean | Standard deviation |
|---|---|---|---|---|---|
| Well-being status | Positive emotions 1 | 3.00 | 5.00 | 3.70 | 0.57 |
| | Negative emotions 1 | 2.00 | 4.00 | 3.05 | 0.60 |
| | Life satisfaction | 1.00 | 3.00 | 2.30 | 0.73 |
| | Vigor | 1.00 | 5.00 | 3.30 | 0.97 |
| | Optimism | 1.00 | 2.00 | 1.20 | 0.41 |
| | Robustness | 1.00 | 1.00 | 1.00 | 0.00 |
| | Autonomy | 1.00 | 2.00 | 1.25 | 0.44 |
| | Meaning and purpose | 1.00 | 2.00 | 1.05 | 0.22 |
| | Relationships | 1.00 | 1.00 | 1.00 | 0.00 |
| | General life satisfaction | 3.00 | 10.00 | 7.40 | 2.45 |
| | General happiness | 2.00 | 5.00 | 3.85 | 1.03 |
| | Positive emotions 2 | 8.00 | 25.00 | 14.40 | 3.83 |
| | Negative emotions 2 | 7.00 | 17.00 | 12.40 | 2.56 |

**Table 4.** Mean scores of the child life habit questionnaire

| | | Minimum | Maximum | Mean | Standard deviation |
|---|---|---|---|---|---|
| Life habits | Nutrition | 0.00 | 10.00 | 6.30 | 2.76 |
| | Physical Fitness | 1.48 | 10.00 | 6.81 | 2.19 |
| | Personal care | 1.11 | 10.00 | 4.85 | 2.84 |
| | Communication | 0.28 | 10.00 | 8.62 | 2.48 |
| | Shelter | 1.11 | 10.00 | 5.35 | 2.74 |
| | Mobility | 0.00 | 10.00 | 5.14 | 3.43 |
| | Responsibility | 2.59 | 10.00 | 7.37 | 2.56 |
| | Interpersonal communication | 1.78 | 10.00 | 8.70 | 2.21 |
| | Communal living | 0.00 | 10.00 | 5.66 | 4.69 |
| | Education | 0.00 | 10.00 | 6.00 | 4.46 |
| | Recreation | 2.22 | 9.11 | 5.40 | 2.19 |

There was a moderate negative correlation between fatigue and life habits parameters such as personal care, accommodation and mobility ($p<0.05$). When the well-being of the children was examined, a weak positive correlation was found between positive emotions 1 and recreation parameter, and between optimism and communication parameter ($p<0.05$). Again, a weak negative correlation was found between the autonomy parameter of children and personal care and social life ($p<0.05$). In addition, there was a weak negative correlation between the meaning and purpose parameter of children and nutrition and physical fitness, and a high level of negative correlation between the meaning and purpose parameter and communication ($p<0.05$), while a weak negative correlation was found between the negative emotions 2 parameter and mobility ($p<0.05$). In addition, a weak positive correlation was found between fatigue and negative emotions 1 parameter, a moderate negative correlation was found between fatigue and general life satisfaction parameter, and a weak negative correlation was found between fatigue and general happiness and positive emotions 2 parameters ($p<0.05$). These data showed that children's strongest aspects were in communication, life satisfaction, vitality and optimism parameters (Table 6).

When the relationship between the introductory information of the parents and their living habits was examined, no relationship was found other than the age of the parents. There was a weak relationship between parental age and children's responsibility for their life habits ($r=0.46$, $p=0.04$), and a moderate relationship between parent age and social life ($r=0.56$, $p=0.01$) ($p<0.05$). A weak correlation was found between family income and well-being and positive emotions 1 ($r=-0.49$, $p=0.02$) and negative emotions 1 ($r=046$, $p=0.03$). There was a weak correlation between the number of children of parents and positive emotions 1 ($r=0.44$, $p=0.04$), while the number of children of parents and negative emotions 1-2 ($r=-0.50$, $p=0.02$; $r=-0.48$, $p=0.03$, respectively) parameters were moderately correlated ($p<0.05$).

**Table 4.** Mean scores of the child life habit questionnaire

| | | Minimum | Maximum | Mean | Standard deviation |
|---|---|---|---|---|---|
| Life habits | Nutrition | 0.00 | 10.00 | 6.30 | 2.76 |
| | Physical Fitness | 1.48 | 10.00 | 6.81 | 2.19 |
| | Personal care | 1.11 | 10.00 | 4.85 | 2.84 |
| | Communication | 0.28 | 10.00 | 8.62 | 2.48 |
| | Shelter | 1.11 | 10.00 | 5.35 | 2.74 |
| | Mobility | 0.00 | 10.00 | 5.14 | 3.43 |
| | Responsibility | 2.59 | 10.00 | 7.37 | 2.56 |
| | Interpersonal communication | 1.78 | 10.00 | 8.70 | 2.21 |
| | Communal living | 0.00 | 10.00 | 5.66 | 4.69 |
| | Education | 0.00 | 10.00 | 6.00 | 4.46 |
| | Recreation | 2.22 | 9.11 | 5.40 | 2.19 |

**Table 5.** The relationship between children's life habits and introductory characteristics

| | | | Age | Education level | School success |
|---|---|---|---|---|---|
| Life habits | Nutrition | r | 0.53* | 0.51* | 0.34 |
| | | p | 0.01 | 0.02 | 0.14 |
| | Physical fitness | r | 0.33 | 0.44 | 0.13 |
| | | p | 0.14 | 0.05 | 0.55 |
| | Personal care | r | 0.16 | 0.12 | 0.48* |
| | | p | 0.47 | 0.61 | 0.03 |
| | Communication | r | 0.51* | 0.49* | 0.50* |
| | | p | 0.02 | 0.02 | 0.02 |
| | Shelter | r | 0.19 | 0.28 | 0.29 |
| | | p | 0.40 | 0.23 | 0.21 |
| | Mobility | r | 0.35 | 0.34 | 0.25 |
| | | p | 0.12 | 0.13 | 0.28 |
| | Responsibility | r | 0.47* | 0.55* | 0.41 |
| | | p | 0.03 | 0.01 | 0.07 |
| | Interpersonal communication | r | 0.05 | 0.09 | 0.004 |
| | | p | 0.81 | 0.69 | 0.98 |
| | Communal living | r | 0.38 | 0.32 | 0.28 |
| | | p | 0.09 | 0.15 | 0.22 |
| | Education | r | 0.38 | 0.35 | 0.39 |
| | | p | 0.09 | 0.12 | 0.08 |
| | Recreation | r | 0.32 | 0.40 | 0.37 |
| | | p | 0.16 | 0.07 | 0.10 |

## Discussion

In our study, it was determined that children diagnosed as having cancer had moderate fatigue and fatigue was mostly associated with personal care, mobility and accommodation, while well-being was associated with general life satisfaction and general happiness parameter. Personal care, accommodation, mobility, social life, recreation and responsibility parameters were most affected by the life habits of children. It was observed that the most impairment in well-being was in the areas of resilience, autonomy, positive and negative emotions. It was determined that the most affected life habits were personal care activities and no child could fully perform recreational activities. The physical fitness and communication parameters of life habits were found to be highly correlated with the meaning and purpose parameter, which was the well-being parameter and which questioned whether the activities in one's life were worth living.

**Table 6.** The relationship between children's life habits and fatigue and well-being

| | | Fatigue | Positive emotions1 | Negative emotions1 | Life satisfaction | Vigor | Optimism | Autonomy | Meaning and purpose | General Life satisfaction | General happiness | Positive emotions2 | Negative emotions2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Nutrition | r | -0.31 | 0.40 | 0.00 | 0.20 | 0.17 | 0.01 | -0.33 | -0.53* | 0.23 | 0.27 | -0.01 | -0.25 |
| | p | 0.17 | 0.07 | 0.97 | 0.38 | 0.46 | 0.94 | 0.14 | 0.01 | 0.02 | 0.24 | 0.94 | 0.28 |
| Physical fitness | r | -0.20 | 0.28 | -0.006 | 0.37 | 0.34 | -0.04 | -0.11 | -0.57** | 0.29 | 0.35 | 0.20 | -0.24 |
| | p | 0.38 | 0.23 | 0.98 | 0.10 | 0.13 | 0.85 | 0.61 | 0.009 | 0.21 | 0.12 | 0.38 | 0.30 |
| Personal care | r | -0.66** | 0.25 | -0.40 | 0.02 | -0.04 | 0.07 | -0.49* | -0.24 | 0.14 | 0.28 | 0.22 | -0.30 |
| | p | 0.00 | 0.27 | 0.08 | 0.92 | 0.84 | 0.74 | 0.02 | 0.29 | 0.53 | 0.21 | 0.34 | 0.19 |
| Communication | r | -0.04 | 0.24 | 0.31 | 0.27 | 0.26 | -0.44* | -0.37 | -0.79** | 0.27 | 0.15 | 0.09 | -0.17 |
| | p | 0.85 | 0.30 | 0.18 | 0.23 | 0.25 | 0.04 | 0.10 | 0.00 | 0.24 | 0.51 | 0.67 | 0.45 |
| Shelter | r | -0.54* | 0.23 | -0.18 | 0.12 | 0.18 | 0.20 | -0.27 | -0.26 | 0.21 | 0.37 | 0.20 | -0.19 |
| | p | 0.01 | 0.32 | 0.44 | 0.60 | 0.42 | 0.39 | 0.24 | 0.25 | 0.36 | 0.10 | 0.38 | 0.40 |
| Mobility | r | -0.45* | 0.42 | -0.24 | 0.19 | 0.29 | -0.04 | -0.23 | -0.25 | 0.16 | 0.27 | 0.38 | -0.45* |
| | p | 0.04 | 0.06 | 0.30 | 0.41 | 0.21 | 0.85 | 0.31 | 0.28 | 0.48 | 0.24 | 0.09 | 0.04 |
| Responsibility | r | 0.001 | -0.21 | 0.13 | -0.06 | -0.07 | 0.02 | -0.14 | -0.37 | -0.08 | -0.04 | 0.002 | -0.11 |
| | p | 0.99 | 0.37 | 0.55 | 0.79 | 0.75 | 0.91 | 0.54 | 0.10 | 0.73 | 0.86 | 0.99 | 0.62 |
| Interpersonal communication | r | -0.33 | 0.26 | -0.18 | 0.11 | 0.31 | -0.22 | -0.20 | -0.28 | 0.13 | 0.17 | 0.37 | -0.40 |
| | p | 0.15 | 0.26 | 0.43 | 0.62 | 0.18 | 0.34 | 0.38 | 0.22 | 0.58 | 0.44 | 0.10 | 0.07 |
| Communal living | r | -0.40 | 0.07 | -0.10 | 0.10 | 0.12 | -0.10 | -0.46* | -0.28 | 0.25 | 0.15 | 0.12 | -0.30 |
| | p | 0.07 | 0.74 | 0.66 | 0.64 | 0.61 | 0.66 | 0.04 | 0.22 | 0.27 | 0.50 | 0.59 | 0.19 |
| Education | r | -0.15 | -0.06 | 0.18 | -0.24 | -0.15 | 0.10 | -0.44 | -0.31 | -0.26 | -0.19 | 0.06 | -0.15 |
| | p | 0.51 | 0.80 | 0.43 | 0.30 | 0.52 | 0.64 | 0.05 | 0.17 | 0.26 | 0.40 | 0.77 | 0.50 |
| Recreation | r | -0.28 | 0.45* | -0.27 | 0.15 | 0.31 | 0.004 | -0.05 | -0.34 | 0.22 | 0.35 | 0.29 | -0.37 |
| | p | 0.23 | 0.04 | 0.23 | 0.52 | 0.18 | 0.98 | 0.83 | 0.14 | 0.34 | 0.13 | 0.21 | 0.10 |
| Fatigue | r | 1 | -0.33 | 0.46* | -0.05 | -0.23 | -0.008 | 0.40 | 0.01 | -0.52* | -0.49* | -0.44* | 0.24 |
| | p | | 0.14 | 0.03 | 0.81 | 0.32 | 0.97 | 0.07 | 0.95 | 0.01 | 0.02 | 0.04 | 0.29 |

The concerns about fatigue and other physical symptoms that cancer patients usually complain about are ignored by health professionals (43,44). In the literature, there is no study examining the effect of fatigue on life habits in individuals with chronic fatigue, but in the study of Kobayashi et al. (45) in high school and university students, it was found that fatigue did not affect people's life habits except for their physical condition. Fatigue affects the mental well-being of individuals and triggers psychological distress (46,47). It is difficult to understand the fatigue experienced by these children without questioning their daily life and well-being, to understand the effects of fatigue-related interventions, and to develop coping strategies related to fatigue. Understanding the effects of fatigue in children with chronic health problems is an important step towards improving life habits and well-being. Physical exercises help individuals with chronic diseases to cope with fatigue and improve their well-being (9).

Studies on childhood quality of life are available in the literature (48,49), but studies on well-being are scarce. As a matter of fact, the National Statistics Office opened a discussion on the deficiencies in this regard and emphasized how important well-being was for people (50), but only one study on well-being in children was found in our country (51). In our study, it was found that 100% of the participants agreed with the statement "When something goes wrong in my life, it usually takes a long time to return to normal", which was the question of the robustness dimension of the well-being scale, and their negative emotions were at moderate level. For this reason, the importance of well-being in children should not be ignored.

Although studies on activity participation (52-55) are available in the literature, no study is found considering all aspects of children's life habits. In our study, it was observed that fatigue had an effect on life habits in children with cancer. It has been determined that the most affected one is the personal care parameter and it is thought that occupational therapists should mainly work on this issue. The parameters of recreation and social life are affected by the well-being of the person, and the continuity of these life habits, which include the activities that most affect the psychological well-being of an individual, is of great importance for people. Occupational therapists should adapt and maintain these activities for children with chronic diseases.

A relationship was found between parental age and child's life habits, responsibility and social life parameters. It was learned that the protective approach of parents decreased as they got older and they gave more responsibility to their children. In this regard, if the parents are young, education should be given to give up this protective approach and to give their children as much responsibility as necessary.

There are several studies showing that independence in personal care is associated with an increase in the quality of life in children, and it is emphasized that personal care is one of the most important elements of life (56,57). In order to improve personal care, first of all, fatigue should be eliminated. At the same time, the relationship of personal care with well-being should not be ignored. In order to cope with fatigue, occupational therapists should evaluate fatigue with all aspects of a person's life and explain the nature of fatigue to children and their parents. Cooper stated that when leisure time, self-care and productive activities had aerobic component, fatigue could be overcome not only in physical but also in social and cognitive dimensions (9).

While dealing with children, the strengths of children such as communication, life satisfaction, vitality and optimism should not be ignored. The relationship observed between school success and personal care and communication parameters of life habits showed that school success was not only related to success in lessons, but also related to personal care of children. It is thought that the reason for this may be due to the fact that children are not independent in this regard, they cannot continue their routines and due to the difference in their external appearance (eg, hair loss). It has been observed that children need regulations in a way that they will not be isolated from their peers. In order for people to continue their work and productive activities, daily life activities, and leisure time activities in a routine, these activities must be in a certain balance. Considering the information obtained and the balance of activities, it has been determined that correcting the problems seen in children's daily routines, especially personal care activities, can improve school success, which is among the productive activities. Coping with fatigue will help improve self-care and school success.

Impairment in the autonomy section, which questioned whether the well-being of the child let him/her to make free decisions or not, and impairment in the sheltering parameter of life habits, including responsibility and housework, and the fact that sheltering parameter was related to different parameters showed that occupational therapists should focus on this issue. In addition, a relationship was observed between the age and education level of the children and the nutrition, communication and responsibility parameters of their life habits. It is an important finding that should not be overlooked that as the age of the children increases, their responsibilities increase, while they do not take enough responsibility. In many studies, it has been emphasized that as the child gets older, gaining autonomy becomes one of the important goals in the child's life (58-60). Taking this effect into account is very important for the child's psychological well-being. In various studies, it has been emphasized that children with chronic diseases should gradually take responsibility for their diseases as they get older (61-64). Even if their parents are well-intentioned, children begin to see themselves as incompetent because they do not take responsibility as they get older (65). Children must be given responsibility. Educating families in this regard is of great importance for the development of the child's autonomy ability, fulfilling his/her responsibilities and preserving his/her psychological well-being. Giving children home chores at an early age helps to build lasting mastery, responsibility and self-confidence in emotional control in children (66). Parents should give their children responsibility and help develop their autonomy abilities in cooperation with their children or, if necessary, through adaptive methods (67).

The lack of Turkish validity and reliability of the Child Life Habit Questionnaire and the Child Well-being Assessment emerged as a limitation. It was difficult to apply the questionnaire in children because it was a long questionnaire and we did not have the opportunity to meet beforehand with the children. As a result of our study, it was discovered that if all dimensions of life habits were to be evaluated, pre-recognition was important and evaluations should be done towards noon. The evaluations of those who want to study on children with cancer should be brief. It should be investigated why the resilience dimension of well-being was always answered negatively. The relationship between school success and personal care should be examined in detail.

### Study Limitations

The small number of patients, the fact that the patient population included in the study was recruited from a single institution, and the patients' participation in the study during the acute care period were the limitations of our study. The small number of patients affected the generalization of the study. Considering the possibility that the hospital environment may have affected children, it is recommended that different studies be conducted in the home after chemotherapy.

## Conclusion

As a result, our study revealed important parameters that might hinder the life habits, thus daily activities and social roles of Turkish children with cancer. Our study showed that fatigue was an important finding of cancer and its important effects on living habits and well-being should not be ignored.

### Ethics

**Ethics Committee Approval:** The study was approved by the Hacettepe University Non-Interventional Clinical Research Ethics Committee (GO/677).

**Informed Consent:** The children participating in the study and their parents were informed about the purpose of the study and a signed informed consent form was obtained from the parents.

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

### Authorship Contributions

Concept: S.S., S.Ş., B.S.A., Design: S.S., B.S.A, Data Collection or Processing: S.S., Analysis or Interpretation: S.S., B.S.A., Literature Search: S.S., Writing: S.S.

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## References

1. Steliarova-Foucher E, Colombet M, Ries LAG, Moreno F, Dolya A, Bray F, et al. International incidence of childhood cancer, 2001-10: a population-based registry study. Lancet Oncol 2017;18:719-31.
2. Agost L. Pediatric renal tumors and their possible relation with endogamous populations in central Argentina. Rev Cubana Pediatr 2019;91:1-18.
3. Cooper TM, Sison EAR, Baker SD, Li L, Ahmed A, Trippett T, et al. A phase 1 study of the CXCR4 antagonist plerixafor in combination with high-dose cytarabine and etoposide in children with relapsed or refractory acute leukemias or myelodysplastic syndrome: A pediatric oncology experimental therapeutics ınvestigators' consortium study (POE 10-03). Pediatr Blood Cancer 2017;64:e26414.
4. Pui CH, Carroll WL, Meshinchi S, Arceci RJ. Biology, risk stratification, and therapy of pediatric acute leukemias: an update. J Clin Oncol 2011;29:551-65.
5. Veerman AJ, Kamps WA, van den Berg H, van den Berg E, Bökkerink JP, Bruin MC, et al. Dexamethasone-based therapy for childhood acute lymphoblastic leukaemia: results of the prospective Dutch Childhood Oncology Group (DCOG) protocol ALL-9 (1997-2004). Lancet Oncol 2009;10:957-66.
6. James K, Keegan-Wells D, Hinds PS, Kelly KP, Bond D, Hall B, et al. The care of my child with cancer: parents' perceptions of caregiving demands. J Pediatr Oncol Nurs 2002;19:218-28.
7. Van Dongen-Melman JE, Van Zuuren FJ, Verhulst FC. Experiences of parents of childhood cancer survivors: a qualitative analysis. Patient Educ Couns 1998;34:185-200.
8. Gordijn MS, van Litsenburg RR, Gemke RJ, Huisman J, Bierings MB, Hoogerbrugge PM, et al. Sleep, fatigue, depression, and quality of life in survivors of childhood acute lymphoblastic leukemia. Pediatr Blood Cancer 2013;60:479-85.
9. Cooper J. Occupational therapy in oncology and palliative care. West Sussex, UK: John Wiley & Sons 2013.
10. Fu JB, Asher A. Exercise therapy and fatigue management. InA. Gulati, V. Puttanniah, B. M. Bruel, W. S. Rosenberg, & J. C. Hung (Eds.), Essentials of Interventional Cancer Pain Management. New York, NY, USA: Springer. 2019. p. 395-401.
11. Knowles G, Borthwick D, McNamara S, Miller M, Leggot L. Survey of nurses' assessment of cancer-related fatigue. Eur J Cancer Care (Engl) 2000;9:105-13.
12. Berger AM, Walker SN. An explanatory model of fatigue in women receiving adjuvant breast cancer chemotherapy. Nurs Res 2001;50:42-52.
13. Aapro M, Scotte F, Bouillet T, Currow D, Vigano A. A Practical Approach to Fatigue Management in Colorectal Cancer. Clin Colorectal Cancer 2017;16:275-85.
14. Hammick M, Stone P; Cancer Fatigue Forum. Cancer fatigue and its impact on patients: knowledge within the cancer care team. J Interprof Care 2003;17:183-92.
15. Curt GA. The impact of fatigue on patients with cancer: overview of FATIGUE 1 and 2. Oncologist 2000;5:9-12.
16. Porock D, Juenger JA. Just go with the flow: a qualitative study of fatigue in biotherapy. Eur J Cancer Care (Engl) 2004;13:356-61.
17. Zuurmond M, Nyante G, Baltussen M, Seeley J, Abanga J, Shakespeare T, et al. A support programme for caregivers of children

with disabilities in Ghana: Understanding the impact on the wellbeing of caregivers. Child Care Health Dev 2019;45:45-53.

18. Seligman M. Flourish: A new understanding of happiness, well-being-and how to achieve them. London, UK: Nicholas Brealey Pub 2011.
19. Thomas J. Working paper: current measures and the challenges of measuring children's well-being. April. Household, Labour Market and Social Wellbeing, Office for National Statistics, Cardiff Road, Newport, NP10 8XG 2009
20. Marks N, Shah H. A well-being manifesto for a flourishing society. J Public Ment Health 2004;3:9-15.
21. Diener E, Suh E. Measuring quality of life: Economic, social, and subjective indicators. Socl Indi Res 1997;40:189-216.
22. Neville AR, Moothathamby N, Naganathan M, Huynh E, Moola FJ. "A place to call our own": The impact of camp experiences on the psychosocial wellbeing of children and youth affected by cancer - A narrative review. Complement Ther Clin Pract 2019;36:18-28.
23. Storey L, Fern LA, Martins A, Wells M, Bennister L, Gerrand C, et al. A Critical Review of the Impact of Sarcoma on Psychosocial Wellbeing. Sarcoma 2019;2019:9730867.
24. Desrosiers J, Noreau L, Robichaud L, Fougeyrollas P, Rochette A, Viscogliosi C. Validity of the Assessment of Life Habits in older adults. J Rehabil Med 2004;36:177-82.
25. World Health Organization (WHO). International Classification of Functioning, Disability, and Health: Children & Youth Version:ICF-CY. Geneva, CHE: World Health Organization 2007.
26. Bedell GM, Dumas HM. Social participation of children and youth with acquired brain injuries discharged from inpatient rehabilitation: a follow-up study. Brain Inj 2004;18:65-82.
27. Detmar SB, Hosli EJ, Chorus AM, van Beekum T, Vogels T, Mourad-Baars PE, et al. The development and validation of a handicap questionnaire for children with a chronic illness. Clin Rehabil 2005;19:73-80.
28. King GA, Law M, King S, Hurley P, Hanna S, Kertoy M, et al. Measuring children's participation in recreation and leisure activities: construct validation of the CAPE and PAC. Child Care Health Dev 2007;33:28-39.
29. Law M, Finkelman S, Hurley P, Rosenbaum P, King S, King G, et al. Participation of children with physical disabilities: Relationships with diagnosis, physical function, and demographic variables. Scand J Occup Ther 2004;11:156-62.
30. Headey B, Wearing A. Subjective well-being: A stocks and flows framework. In F. Strack, M. Argyle & N. Schwarz (Eds.), Subjective Well-being: An Interdisciplinary Perspective. Oxford, UK: Pergamon Press 1991. p. 49-73.
31. Headey B, Wearing AJ. Understanding happiness: A theory of subjective well-being. Melbourne, VIC, AU: Longman Cheshire 1992.
32. Herzlich C. Health and illness: A social psychological analysis (Vol. 5). London, UK: Academic Press, 1973.
33. Abraham C, Sheeran P. Cognitive representations and preventative health behaviour: A review. In K. J. Petrie & J. A. Weinman (Eds.), Perceptions of Health & Illnes Third Avenue, NY, USA: Routledge 2013. p. 213-40.
34. Wu HS, McSweeney M. Cancer-related fatigue: "It's so much more than just being tired". Eur J Oncol Nurs 2007;11:117-25.
35. Hokkanen H, Eriksson E, Ahonen O, Salantera S. Adolescents with cancer: experience of life and how it could be made easier. Cancer Nurs 2004;27:325-35.
36. Hinds PS, Hockenberry M, Rai SN, Zhang L, Razzouk BI, McCarthy K, et al. Nocturnal awakenings, sleep environment interruptions, and fatigue in hospitalized children with cancer. Oncol Nurs Forum 2007;34:393-402.
37. Gerçeker GÖ, Yilmaz HB. Reliability and validity of Turkish versions of the child, parent and staff cancer fatigue scales. Asian Pac J Cancer Prev 2012;13:3135-41.
38. Huppert FA, Baylis N, Keverne B. The Science of Well-being. New York, USA: Oxford University Press 2005.
39. Marks N, Shah H, Westall A. The power and potential of well-being indicators: Measuring young people's well-being in Nottingham. London, UK: New Economics Foundation 2004.
40. Beaton D, Bombardier C, Guillemin F, Ferraz MB. Recommendations for the Cross-Cultural Adaptation of the DASH & Quick DASH Outcome Measures. Institute for Work Health 2007;1-45.
41. Noreau L, Fougeyrollas P, Vincent C. The LIFE-H: Assessment of the quality of social participation. Technol Disabil 2002;14:113-8.
42. Köse SK. (2008). Korelasyon ve regresyon analizi. Çevrimiçi) http:// tr. scribd. com/doc/2066772/korelasyon-analizi, 9.
43. Davies B, Whitsett SF, Bruce A, McCarthy P. A typology of fatigue in children with cancer. J Pediatr Oncol Nurs 2002;19:12-21.
44. Hockenberry MJ, Hinds PS, Barrera P, Bryant R, Adams-McNeill J, Hooke C, et al. Three instruments to assess fatigue in children with cancer: the child, parent and staff perspectives. J Pain Symptom Manage 2003;25:319-28.
45. Kobayashi H, Demura S, Goshi F, Minami M, Nagasawa Y, Sato S, et al. [The relationship among subjective symptoms of fatigue, subjective fatigue feeling, and life habits of high school and college students]. Nihon Eiseigaku Zasshi 1999;54:552-62.
46. Garralda ME, Rangel L. Annotation: Chronic Fatigue Syndrome in children and adolescents. J Child Psychol Psychiatry 2002;43:169-76.
47. Van Dam NT, van Vugt MK, Vago DR, Schmalzl L, Saron CD, Olendzki A, et al. Mind the Hype: A Critical Evaluation and Prescriptive Agenda for Research on Mindfulness and Meditation. Perspect Psychol Sci 2018;13:36-61.
48. Engelen V, Koopman HM, Detmar SB, Raat H, van de Wetering MD, Brons P, et al. Health-related quality of life after completion of successful treatment for childhood cancer. Pediatr Blood Cancer 2011;56:646-53.
49. Parsons SK, Fairclough DL, Wang J, Hinds PS. Comparing longitudinal assessments of quality of life by patient and parent in newly diagnosed children with cancer: the value of both raters' perspectives. Qual Life Res 2012;21:915-23.
50. Dodge R, Daly AP, Huyton J, Sanders LD. The challenge of defining wellbeing. International Journal of Wellbeing 2012;2:222-35.
51. Yolcuoğlu İG. Sosyal çalışma ve çocuğun iyilik hali. Toplum ve Sosyal Hizmet 2009;20:85-94.

52. Allender S, Cowburn G, Foster C. Understanding participation in sport and physical activity among children and adults: a review of qualitative studies. Health Educ Res 2006;21:826-35.

53. Berg C, Neufeld P, Harvey J, Downes A, Hayashi RJ. Late effects of childhood cancer, participation, and quality of life of adolescents. OTJR 2009;29:116-24.

54. Horn TS, Horn JL. Family influences on children's sport and physical activity participation, behavior, and psychosocial responses. In G. Tenenbaum & R. C. Eklund (Eds.), Handbook of Sport Psychology. Hoboken, NJ, USA: John Wiley & Sons Inc 2007. p. 685-711.

55. Salmon J, Booth ML, Phongsavan P, Murphy N, Timperio A. Promoting physical activity participation among children and adolescents. Epidemiol Rev 2007;29:144-59.

56. Weissberg-Benchell J, Goodman SS, Antisdel Lomaglio J, Zebracki K. The use of Continuous Subcutaneous Insulin Infusion (CSII): parental and professional perceptions of self-care mastery and autonomy in children and adolescents. J Pediatr Psychol 2007;32:1196-202.

57. Beacham BL, Deatrick JA. Health care autonomy in children with chronic conditions: implications for self-care and family management. Nurs Clin North Am 2013;48:305-17.

58. Allen JP, Hauser ST, Bell KL, O'Connor TG. Longitudinal assessment of autonomy and relatedness in adolescent-family interactions as predictors of adolescent ego development and self-esteem. Child Dev 1994;65:179-94.

59. Collins WA, Gleason T, Sesma A. Jr. Internalization, autonomy, and relationships: Development during adolescence. In J. E. Grusec & L. Kuczynski (Eds.), Parenting and Children's Internalization of Values: A Handbook of Contemporary Theory. Hoboken, NJ, US: John Wiley & Sons Inc 1997. p. 78-99

60. Smetana JG. The development of autonomy during adolescence: A social-cognitive domain theory view. In B. Soenens, M. Vansteenkiste, & S. Van Petegem (Eds.), Autonomy in Adolescent Development: Towards Conceptual Clarity. Hove, UK: Psychology Press 2017. p. 69-89.

61. Andersen RM. Revisiting the behavioral model and access to medical care: does it matter? J Health Soc Behav 1995;36:1-10.

62. Drotar D, Ievers C. Age differences in parent and child responsibilities for management of cystic fibrosis and insulin-dependent diabetes mellitus. J Dev Behav Pediatr 1994;15:265-72.

63. McQuaid EL, Kopel SJ, Klein RB, Fritz GK. Medication adherence in pediatric asthma: reasoning, responsibility, and behavior. J Pediatr Psychol 2003;28:323-33.

64. Annunziato RA, Bucuvalas JC, Yin W, Arnand R, Alonso EM, Mazariegos GV, et al. Self-Management Measurement and Prediction of Clinical Outcomes in Pediatric Transplant. J Pediatr 2018;193:128-33.

65. Pomerantz EM, Eaton MM. Developmental differences in children's conceptions of parental control:"They love me, but they make me feel ıncompetent". Merrill-Palmer Quarterly 2000;46:140-67.

66. Doinita NE, Maria ND. Attachment and parenting styles. Procedia Soc Behav Sci 2015;203:199-204.

67. Wiebe DJ, Berg CA, Korbel C, Palmer DL, Beveridge RM, Upchurch R, et al. Children's appraisals of maternal involvement in coping with diabetes: enhancing our understanding of adherence, metabolic control, and quality of life across adolescence. J Pediatr Psychol 2005;30:167-78.

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# Electrodiagnostic Features of Peroneal Neuropathy Associated with Weight Loss and Leg Posture

## Kilo Kaybı ve Bacak Postürü ile İlişkili Peroneal Nöropatinin Elektrodiagnostik Özellikleri

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## ABSTRACT

**Objective:** Weight loss and leg postures are common conditions associated with peroneal neuropathy at the fibular head (PNFH). This study aimed to find the electrodiagnostic features of PNFH associated with weight loss and those of PNFH associated with leg postures such as crossing legs or squatting.

**Methods:** Patients with clinical and electrodiagnostic characteristics that were compatible with PNFH associated with weight loss and leg postures were included in this retrospective cohort study. The patients were divided into three groups: Patients with PNFH associated only with leg postures, patients with PNFH associated only with weight loss, and patients with PNFH associated with both leg postures and weight loss.

**Results:** Twelve patients with PNFH related to leg postures, five patients with PNFH related to weight loss, and four patients with PNFH related to both leg postures and weight loss were included in the study. Although these three groups had similar electrodiagnostic characteristics, the degree of motor conduction block obtained by recording from the tibialis anterior muscle was higher in patients with PNFH associated only with leg postures than in patients of other groups (p=0.017).

**Conclusion:** The electrodiagnostic features of PNFH associated with weight loss and leg postures are generally similar. PNFH associated with weight loss may not only depend on leg posture; factors such as metabolic changes may also play a role in its pathophysiology.

**Keywords:** Peroneal neuropathy, electrodiagnostic tests, nerve conduction study, leg posture, weight loss

## ÖZ

**Amaç:** Kilo kaybı ve bacak postürleri, fibula başında peroneal nöropati (FBPN) ile ilişkili sık görülen durumlardır. Bu çalışmanın amacı kilo kaybı ve bacak bacak üstüne atma veya çömelme gibi bacak postürleri ile ilişkili FBPN'nin elektrodiagnostik özelliklerinin bulunmasıdır.

**Yöntemler:** Klinik ve elektrodiagnostik özellikleri kilo kaybı ve bacak postürleri ile ilişkili FBPN ile uyumlu olan hastalar bu retrospektif kohort çalışmasına dahil edildi. Hastalar üç gruba ayrıldı: Sadece bacak postürleri ile ilişkili FBPN hastaları, sadece kilo kaybı ile ilişkili FBPN hastaları, hem bacak postürleri hem de kilo kaybı ile ilişkili FBPN hastaları.

**Bulgular:** Bacak postürleri ile ilişkili 12 FBPN hastası, kilo kaybı ile ilişkili beş FBPN hastası ve hem bacak postürleri hem de kilo kaybı ile ilişkili dört FBPN hastası çalışmaya dahil edildi. Bu üç grup benzer elektrodiagnostik özelliklere sahip olmasına rağmen, tibialis anterior kasından kayıt yapılarak elde edilen motor iletim bloğunun şiddeti sadece bacak postürleri ile ilişkili FBPN hastalarında diğer gruplara göre daha yüksekti (p=0,017).

**Sonuç:** Kilo kaybı ve bacak postürleri ile ilişkili FBPN'nin elektrodiagnostik özellikleri genellikle benzerdir. Kilo kaybı ile ilişkili FBPN sadece bacak postürüne bağlı olmayabilir, aynı zamanda metabolik değişiklikler gibi faktörler de patofizyolojisinde rol oynayabilir.

**Anahtar Sözcükler:** Peroneal nöropati, elektrodiagnostik testler, sinir iletim çalışması, bacak postürü, kilo kaybı

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## Introduction

Peroneal neuropathy at the fibular head (PNFH) is the most common entrapment neuropathy of the lower limbs (1,2). Patients typically present with weakness of foot dorsiflexion and paresthesia on the dorsum of the foot or lateral calf (1-3). Nerve conduction studies and needle electromyography (EMG) are important tests in the diagnosis of PNFH; they are also used for differential diagnosis of diseases or conditions such as lumbosacral radiculopathy, lumbosacral plexopathy, or sciatic nerve injury (2,3). In addition, electrodiagnostic findings may provide information for the prognosis of PNFH (2,4). In nerve conduction studies, the peroneal motor conduction block and/or the slowing of the peroneal motor nerve conduction velocity (NCV) across the below fibular head-popliteal fossa segment (BFH-PF) is observed (1,2). In needle EMG, active denervation findings and/or neurogenic motor unit action potentials (MUPs) are observed in muscles innervated by the peroneal nerve (1-3). Conditions such as external compression, direct trauma, diabetes mellitus, and alcoholism can cause PNFH (2,3). Further, conditions such as crossing legs, squatting, or weight loss are associated with PNFH (1-3,5-8). Some studies have reported that PNFH associated with weight loss is due to the reduction of the protective tissue of the peroneal nerve (5,9-11), while others have presented that metabolic factors may affect the development of PNFH (6). With this background, this study aimed to find the electrodiagnostic characteristics of patients who developed PNFH after their legs were in the same position repetitively (such as while crossing them or squatting) and/or after they had experienced weight loss. Furthermore, our objective was to determine if there is a relationship between weight loss and leg postures concerning PNFH.

## Methods

### Subjects

Patients who applied to the EMG laboratory between July 2017 and January 2019 and whose clinical features and electrophysiological findings were compatible with PNFH were included in this retrospective cohort study. To qualify, a patient had to have a history of weight loss or of their legs being held in the same position repetitively, such as when crossing their legs or squatting. If either or both of the following neurological examination findings were present, patients were included in the study: 1) Weakness of foot dorsiflexion and/or eversion and/or 2) sensory abnormality on the peroneal nerve sensory dermatome. Patients with any of the following were excluded from the study: Polyneuropathy; a disease that can cause polyneuropathy, such as diabetes mellitus; a neurodegenerative disease; a family history of neurodegenerative disease; history of major trauma in the lower limbs; and nerve conduction study, needle EMG, or magnetic resonance imaging (MRI) findings compatible with polyneuropathy, lumbosacral plexopathy, lumbosacral radiculopathy, or sciatic neuropathy. The strengths of foot dorsiflexion and eversion were analyzed using the Medical Research Council (MRC) scale (12). The Turkish version of the Leeds assessment of neuropathic symptoms and signs (LANSS) was used to evaluate neuropathic complaints (13). Knee/leg MRI and X-ray film findings of all patients were also recorded. Patients were divided into three groups: Patients with PNFH associated only with leg postures, patients with PNFH associated only with weight loss, and patients with PNFH associated with both leg postures and weight loss.

### Electrodiagnostic Tests

Nerve conduction studies and needle EMG were performed using a Cadwell Sierra Summit EMG unit (Cadwell Laboratories, Kennewick, WA, USA). Electrodiagnostic tests were performed when the skin temperature of the limb was ≥32 °C; otherwise, cold limbs were warmed. Low-high band filters for sensory and motor nerve conduction studies were set at 20 Hz-2 kHz and 20 hz-10 kHz, respectively. In nerve conduction studies, recording and stimulation were performed with surface electrodes. The sweep speed and sensitivity for motor nerve conduction studies were 5 ms/division and 2 mV/division, respectively. For sensory nerve conduction studies, the sweep speed and sensitivity were 1 ms/division and 10 μV/division, respectively. Sensory and motor nerve conduction studies of the posterior tibial, peroneal, superficial peroneal, and sural nerves were performed bilaterally using conventional methods (14,15). Compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) amplitudes were measured from peak to peak. Onset latency was used for the NCV of the sensory nerves. In addition, median and ulnar nerve conduction studies were performed on one upper extremity. The peroneal nerve stimulation points were the ankle, BFH, and popliteal fossa. The peroneal nerve motor conduction study was performed by recording from both the extensor digitorum brevis (EDB) and the tibialis anterior (TA) muscles. Recommended values were used for the reference values of the nerve conduction study (14-16). The lower limits of the peroneal NCV from the EDB and TA muscles were 42 m/s and 43 m/s, respectively (14,16). If the peroneal nerve CMAP amplitude obtained by popliteal fossa stimulation was reduced by more than 50% compared with the CMAP amplitude obtained by below the fibular head stimulation, it was considered as a conduction block. It was considered abnormal if the peroneal motor NCV across the BFH-PF slowed more than 6 m/s or 12% compared with the peroneal NCV across the BFH-ankle segment (14). The peroneal nerve CMAP and the superficial peroneal SNAP amplitudes were considered abnormal if they were below the reference value (peroneal CMAP amplitude-EDB <2.6 mV, peroneal CMAP amplitude-TA <1.7 mV, superficial peroneal SNAP amplitude <5 μV) or 50% of the intact side value (14-16). Axonal involvement was considered if the amplitude of the peroneal nerve CMAP or the superficial peroneal nerve SNAP was abnormal (1,2). Needle EMG was performed visually using a concentric needle electrode (length: 50 mm, diameter: 0.46 mm, Bionen Medical Devices, Florence, Italy). The low-high band filter for needle EMG was set at 10 Hz-10 kHz. The sweep speed was 10 ms/division for the detection of active denervation and analysis of MUPs. Sensitivity was set to 100 μV/division and 200-1000 μV/division at rest and during mild muscle contraction, respectively. The presence of active denervation was carefully

analyzed. Active denervation severity was scored as follows: No positive sharp wave (PSW) or fibrillation potential, 0; single PSW or fibrillation potential in at least two areas, 1; moderate numbers of PSW or fibrillation potentials in three or four areas, 2; many PSW or fibrillation potentials in all areas, 3; and PSW or fibrillation potentials that fill the entire screen in all areas, 4. MUP analysis was performed during mild muscle contraction. At least 20 MUPs were evaluated in each muscle. The duration and amplitude of MUPs were recorded. The interference pattern was also analyzed. If the MUP duration was >15 ms or the MUP amplitude was >4 mV, this MUP was considered neurogenic. The following muscles were studied in all patients: TA, peroneus longus, medial gastrocnemius, vastus lateralis, short head of biceps femoris, and L3, L4, L5, and S1 paraspinal muscles. The gluteus medius and gluteus maximus muscles were also examined in some patients.

### Statistical Analysis

The Shapiro-Wilk test was used to determine the distribution of the data. Pearson's chi-squared test was used to analyze categorical variables. The Kruskal-Wallis test was used in group comparisons. Tamhane's T2 test was used for post-hoc analysis and multiple comparisons. The mean ± standard deviation, median, and minimum-maximum values of numerical data were calculated for descriptive statistics. Spearman's test was used for correlation; p-value <0.05 was considered significant. The Statistical Package for the Social Sciences version 22.0 (SPSS IBM Corp., Armonk, NY, USA) was used to perform the statistical analysis.

## Results

This study included 21 patients with PNFH associated with weight loss or leg postures. Clinical, electrodiagnostic, and MRI findings of the patients were not compatible with lumbosacral radiculopathy or plexopathy. The mean age of the patients was 31.9±15.9 (range; 15-82) years. Moreover, 17 of the 21 (81%) patients were male. The mean height, weight, and body mass index of the patients were 176.4±8.5 cm, 69.0±13.2 kg, and 22.1±3.4 (range; 15.2-27.7) kg/m2, respectively. The mean duration of patient complaints at the time of applying electrodiagnostic tests was 35.1±13.9 (range; 21-60) days. The means of these time intervals were 31.7±13.1 (range; 21-60) days in patients with PNFH associated only with leg postures, 39.0±13.4 (range; 30-60) in patients with PNFH associated only with weight loss, and 40.3±17.9 (range; 21-60) days in patients with PNFH associated with both leg postures and weight loss. The time intervals did not differ significantly among the groups (p=0.349). The clinical features of the patients are shown in Table 1. PNFH was associated only with leg postures in 12 patients (crossing legs in 9, squatting in 3), only with weight loss in 5 patients, and both conditions in 4 patients (weight loss and crossing legs in 4). The mean weight loss per month was 4.6±2.2 (range; 2.5-7.5) kg. Patients with weight loss had exhibited it for at least 3 months. Of the nine patients with weight loss, one had surgery due to obesity. The cause of weight loss in the other four patients was dieting to address obesity. In the remaining four patients, the cause of weight loss was not clear. All patients complained of weakness, and 11 had paresthesia. PNFH developed suddenly in all patients. Neurological examinations

**Table 1.** Clinical features of the patients

| Clinical feature | Number of patients (%) |
|---|---|
| Male | 17 (81.0%) |
| Peroneal neuropathy in the right lower extremity | 15 (71.4%) |
| **Condition** | |
| Leg posture | 12 (57.1%) |
| Weight loss | 5 (23.8%) |
| Both leg posture and weight loss | 4 (19.1%) |
| **Symptoms** | |
| Paresthesia | 11 (52.4%) |
| Weakness | 18 (100%) |
| **Neurological examination** | |
| Sensory loss | |
| Dorsum of the foot | 8 (38.1%) |
| Lateral calf | 1 (4.8%) |
| Dorsum of the foot and lateral calf and deep peroneal nerve dermatome | 8 (38.1%) |
| None | 4 (19.1%) |
| **Weakness** | |
| Dorsiflexion of the foot | 20 (95.2%) |
| Eversion of the foot | 17 (81.0%) |
| None | 0 (0%) |

revealed weakness in all patients, and sensory loss was present in 17 of them. In the follow-up, electrodiagnostic tests were not performed; however, the neurological examination findings of 14 patients were completely normal, and the muscle strength of the seven patients was better than the previous examination findings. Three of the seven patients who could not fully recover had a superficial peroneal nerve SNAP amplitude abnormality. Neurological examinations were repeated at 2-5 months from the time of electrodiagnostic testing.

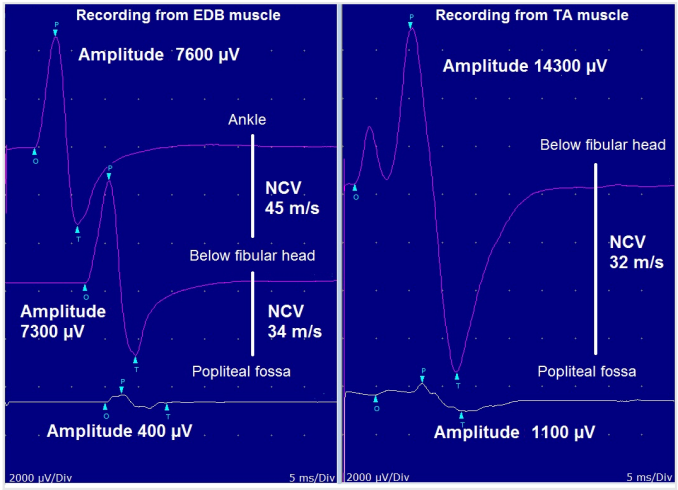


**Figure 1.** Motor conduction block in a patient

Peroneal neuropathy of patient 6 was associated with both weight loss and crossing leg. There was peroneal motor conduction block and slowing of peroneal Nerve conduction velocity across the below fibular head-popliteal fossa segment. BFH-PF: Below fibular head-popliteal fossa segment, EDB: Extensor digitorum brevis, NCV: Nerve conduction velocity, TA: Tibialis anterior

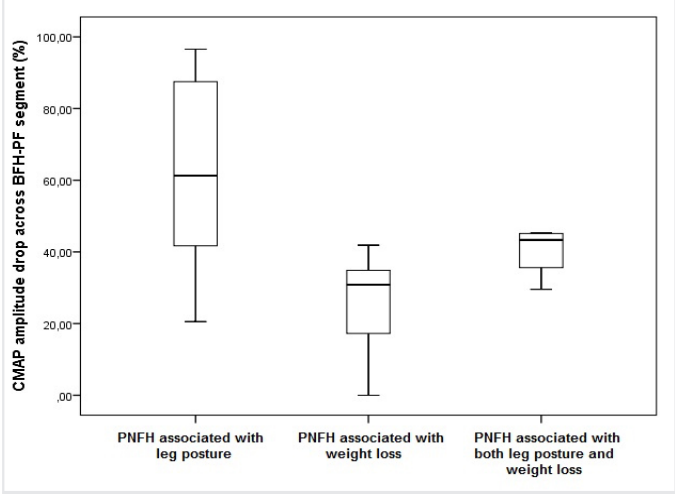


**Figure 2.** Peroneal compound muscle action potential amplitude drop in percentage across the knee segment obtained from the tibialis anterior muscle among the groups

CMAP: Compound muscle action potential, PNFH: Peroneal neuropathy at the fibular head

The electrodiagnostic findings of the patients are shown in Table 2, 3. Abnormal slowing of NCV and an abnormal amplitude drop in percentage obtained from the EDB or TA muscles across BFH-PF were found in 14 and 20 patients, respectively. Examples of the conduction block of patient 6 are shown in Figure 1. The peroneal CMAP amplitude drop in percentage across BFH-PF obtained from TA muscle was higher in patients with PNFH associated only with leg postures than in patients only with weight loss or with both leg postures and weight loss (Tamhane's T2 test, p=0.009, p=0.037). The peroneal CMAP amplitude drop in percentage across BFH-PF obtained from TA muscle between the groups is shown in Figure 2. Table 4 shows the correlation between the MRC scores and the electrodiagnostic findings. While an inverse correlation was present between the severity of the conduction block and the MRC scores of peroneal innervated muscles, no correlation was found between the severity of the active denervation and muscle weakness. Figure 3 shows the correlation of the peroneal CMAP amplitude drop obtained from TA muscle across BFH-PF and the MRC score of the ankle dorsiflexion. The mean LANSS score of the patients was 5.9±3.1 (range; 0-12). The LANSS score was 12 in only one patient and less than 12 in the others.

## Discussion

Many conditions such as trauma, masses, and diabetes mellitus can cause PNFH. In addition, weight loss and leg posture are among the most important risk factors for PNFH (1-3,5-8). At the fibular head, the peroneal nerve becomes superficial and

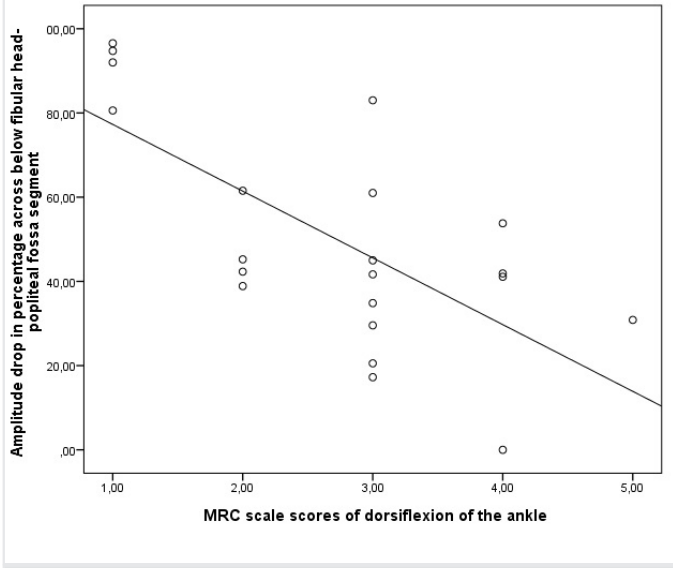


**Figure 3.** Correlation of foot dorsiflexion strength and amplitude drop obtained from the tibialis anterior muscle across the knee segment

Amplitude drop was obtained by recording from the tibialis anterior muscle. An inverse correlation was found between foot dorsiflexion muscle strength and amplitude reduction across the knee segment (p=0.002, r=-0.659). Spearman;s test was used; p-value <0.05 was considered significant. MRC: Medical Research Council scale

**Table 2.** Electrodiagnostic findings among the groups

| Electrodiagnostic parameter | PNFH associated only with leg posture, mean ± SD/median (min-max) | PNFH associated only with weight loss, mean ± SD/median (min-max) | PNFH associated with both leg posture and weight loss, mean ± SD/median (min-max) | p-value |
|---|---|---|---|---|
| Peroneal nerve CMAP amplitude (EDB) (mV) | 6.9±2.1/7.1 (3.0-11.3) | 5.8±1.7/6.1 (3.9-8.2) | 7.9±3.3/8.1 (3.8-11.9) | 0.395 |
| Peroneal nerve CMAP amplitude (TA) (mV) | 8.1±3.9/7.5 (2.6-14.5) | 7.2±2.1/6.6 (5.4-10.7) | 7.9±3.3/8.3 (3.6-11.5) | 0.737 |
| Peroneal NVC across BFH-PF (EDB) (m/s) | 36.0±4.1/37 (29-41) | 36.6±12.1/34 (22-53) | 31.5±4.2/31 (27-37) | 0.353 |
| Peroneal NVC across BFH-PF (TA) (m/s) | 37.8±8.9/38.5 (22-53) | 42.4±14.3/33 (31-59) | 34.3±4.8/35.5 (28-38) | 0.682 |
| Peroneal NCV drop across BFH-PF (EDB) (m/s) | 13.0±4.8/12 (6-20) | 10.8±7.3/11 (3-19) | 16.8±9.3/17.5 (5-27) | 0.457 |
| Peroneal NCV drop in percentage BFH-PF EDB (%) | 26.2±8.6/26 (13-41) | 24.0±17.2/26.8 (5-46) | 32.9±15.1/35.7 (14-47) | 0.519 |
| Peroneal nerve CMAP amplitude drop across BFH-PF EDB (%) | 62.8±36.4/85.9 (0-98) | 40.4±35.3/28.7 (2-84) | 60.3±29.9/60.9 (23-96) | 0.368 |
| Peroneal nerve CMAP amplitude drop across BFH-PF TA (%) | 63.9±25.3/61.3 (21-97) | 24.9±16.6/30.9 (0-42) | 40.4±7.4/43.3 (30-45) | 0.017 |
| Superficial peroneal nerve SNAP amplitude (uV) | 15.9±7.7/15.9 (3-27) | 16.4±9.7/17.7 (6-26) | 13.9±4.7/15.7 (9-18) | 0.794 |

The peroneal compound muscle action potential (CMAP) amplitude drop in percentage across the below fibular head-popliteal fossa segment obtained from the tibialis anterior was higher in patients with peroneal neuropathy at the fibular head (PNFH) associated only with leg posture than in patients with PNFH associated only with weight loss and with both leg posture and weight loss (Tamhane's T2 test, p=0.009, p=0.037). Significance was set at p-value <0.05. Note that peroneal nerve CMAP was not obtained in one patient, and superficial peroneal nerve sensory nerve action potential was not obtained in three patients
BFH-PF: Below fibular head-popliteal fossa segment, CMAP: Compound muscle action potential, EDB: Extensor digitorum brevis, NCV: Nerve conduction velocity, PNFH: Peroneal neuropathy at the fibular head, SNAP: Sensory nerve action potential, TA: Tibialis anterior

more sensitive to compression. According to some authors, the peroneal nerve protective tissue decreases as a result of weight loss, causing the nerve to become more susceptible to trauma (5,9-11). A previous study reported that weight loss is not the only reason for increased susceptibility, arguing that metabolic changes are also associated with PNFH (6). In the present study, nine patients had PNFH associated with weight loss. In four of these patients, peroneal neuropathy was also associated with leg postures. This finding indicates that individuals who have recently lost weight should pay attention to their leg posture or that their legs should not remain immobile for a long time. The remaining five patients had no history of squatting or crossing their legs. This may indicate that metabolic conditions such as electrolyte or lipid abnormalities can trigger PNFH in addition to or instead of protective tissue reduction (6,17,18).

In this study, the degree of the motor conduction block obtained by recording from the TA muscle was higher in PNFH cases related only to leg posture, which suggests that demyelinating features may be more pronounced in these cases than in those associated with weight loss. The degree of conduction block may vary with the time of the nerve conduction study, but the duration of the nerve conduction studies did not differ between the groups in this study. Moreover, the number of patients in this study was low. This study's finding that the degree of conduction block was lower in PNFH associated solely with weight loss should be confirmed by further studies. In this study, patients had completely recovered or were in the recovery phase. This finding shows that the prognosis of PNFH due to weight loss or leg posture is good (5,6,9,10).

Nerve conduction studies have an important place in the diagnosis and differential diagnosis of PNFH (1-3). In addition, electrodiagnostic studies provide information on prognosis (2,4). The reduced superficial peroneal nerve SNAP and peroneal nerve CMAP amplitude may be associated with poor prognosis

**Table 3.** Electrodiagnostic abnormalities in groups

| Electrodiagnostic abnormality | Number of patients with abnormality in electrodiagnostic tests/number of patients examined | | | |
|---|---|---|---|---|
| | PNFH associated only with leg posture | PNFH associated only with weight loss | PNFH associated with both leg posture and weight loss | All patients |
| Nerve Conduction studies | | | | |
| Peroneal nerve distal CMAP amplitude-EDB <2.6 mV-TA <1.7 mV | 3/11-3/12 | 2/5-1/5 | 1/4-1/4 | 6/20-5/21 |
| Peroneal NVC across BFH-PF EDB <42 m/s-TA <43 m/s | 8/11-8/12 | 3/5-3/5 | 4/4-4/4 | 15/20-15/21 |
| Peroneal NCV drop across BFH-PF (EDB) >6 m/s | 10/11 | 3/5 | 3/4 | 16/20 |
| Peroneal NCV drop in percentage across BFH-PF EDB >12% | 10/11 | 3/5 | 4/4 | 17/20 |
| Peroneal nerve CMAP amplitude drop in percentage across BFH-PF EDB >50%-TA >50% | 7/11-8/12 | 2/5-0/5 | 3/4-0/4 | 12/20-8/21 |
| Superficial peroneal nerve SNAP amplitude <5 uV | 3/12 | 0/5 | ¼ | 4/21 |
| Superficial peroneal NCV <39 m/s | 0/10 | 1/5 | 0/3 | 1/18 |
| Reduced peroneal CMAP or superficial peroneal SNAP amplitude (axonal involvement) | 6/12 | 2/5 | ¼ | 9/21 |
| Needle EMG | | | | |
| Active denervation in TA-PL muscles | 12/12-8/12 | 5/5-4/5 | 4/4-2/4 | 21/21-14/21 |
| Neurogenic findings in TA-PL muscles | 1/10-0/10 | 0/5-0/5 | 0/4-0/4 | 1/18-0/18 |

Note that peroneal nerve compound muscle action potential was not obtained in one patient, and superficial peroneal nerve sensory nerve action potential was not obtained in three patients

BFH-PF: Below fibular head-popliteal fossa segment, CMAP: Compound muscle action potential, EDB: Extensor digitorum brevis muscle, EMG: Electromyography, NCV: Nerve conduction velocity, PL: Peroneus longus, PNFH: Peroneal neuropathy at the fibular head, SNAP: Sensory nerve action potential, SNAP: Sensory nerve action potential, TA: Tibialis anterior

**Table 4.** Correlation of electrodiagnostic findings and muscle weakness

| MRC score | | Amplitude drop across BFH-PF in percentage-EDB muscle | Amplitude drop across BFH-PF in percentage-TA muscle | Severity of active denervation in the TA muscle | Severity of active denervation in the PL muscle |
|---|---|---|---|---|---|
| Dorsiflexion of the foot | P | 0.001 | 0.002 | 0.609 | 0.932 |
| | R | -0.679 | -0.628 | 0.119 | 0.020 |
| Eversion of the foot | P | 0.009 | 0.006 | 0.514 | 0.447 |
| | R | -0.565 | -0.579 | 0.151 | -0.176 |

Muscle strength was evaluated using the Medical Research Council scale. Spearman's test was used for correlation. Significance was set at p-value <0.05
EDB: Extensor digitorum brevis, PL: Peroneus longus, TA: Tibialis anterior, BFH-PF: Below fibular head-popliteal fossa segment

(4). In this study, four patients had superficial peroneal nerve BSAP amplitude abnormality, and three of these have not yet fully recovered. When recording from both the TA and EDB muscles, conduction block across BFH-PF was observed in 14 of 21 patients. This finding demonstrated the importance of the conduction block and that recording should be made from both the TA and EDB muscles. When patients are examined according to the conditions associated with PNFH, it can be said that PNFH associated with weight loss and leg posture have similar electrodiagnostic and clinical features. Most of the patients had motor conduction block indicating demyelination; the peroneal nerve CMAP or superficial peroneal nerve SNAP amplitude abnormality indicating axonal damage was present in a few patients. All these findings support the conclusion that demyelinating features are more pronounced in PNFH associated with both weight loss and leg posture.

The presence of active denervation found in all patients indicates that active denervation findings were caused by not only axonal degeneration but also motor conduction block. Active denervation appears to have been caused by the loss of fewer axons in case of severe demyelination (19). We could not find a correlation between the degree of active denervation and muscle strength. As mentioned earlier, the active denervation finding may be related to the conduction block and may poorly reflect axonal damage (2,19,20). An inverse correlation was found between

MRC scores of the muscles and the degree of conduction block. Conduction block and peroneal nerve CMAP/SNAP amplitudes are some of the parameters that can be used in the follow-up of PNFH.

The weakness and needle EMG abnormalities were higher in the TA muscle than in the peroneus longus muscle, and abnormalities of the superficial peroneal nerve BSAP were present in 4 of 21 patients. All these findings show that the deep peroneal nerve is more affected than the superficial peroneal nerve, which can be explained by the topographic distribution of the peroneal nerve fascicle (19). In accordance with previous studies, weakness was more pronounced than sensory complaints (1-3). Moreover, the LANSS score was <12 in all patients, except for one. This finding shows that pain was rarely observed in patients with PNFH related to leg posture or weight loss. In this study, most patients were male, and PNFH was unilateral in all patients. These findings are consistent with the literature (19).

### Study Limitations

This study had some limitations. First, the time of the electrodiagnostic test was not the same for each patient. Although the interval between the time when the electrodiagnostic test was performed and the time when the complaints first started varied only slightly between patients (21-60 days), this can still be considered a limitation. Second, a small number of patients was included. Finally, the study followed a retrospective design.

## Conclusion

This study showed that PNFH associated with weight loss and leg postures generally have similar electrodiagnostic features. The study revealed that every patient with PNFH due to weight loss did not necessarily have a history of repetitive leg postures, such as crossing legs. Moreover, the conduction block in PNFH due to weight loss was less severe than that in PNFH due to leg posture. Therefore, this study shows that leg posture may not be the only factor causing PNFH in patients with PNFH due to weight loss but also other factors such as metabolic changes.

### Ethics

**Ethics Committee Approval:** Ethics committee approval was received from Adana City Training and Research Hospital Ethics Committee (number 45/624)

**Informed Consent:** Retrospective study.

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

### Authorship Contributions

Concept: H.F., Design: H.F., Data Collection or Processing: H.F., İ.Ö., Analysis or Interpretation: H.F., İ.Ö., Literature Search: H.F., İ.Ö., Writing: H.F., İ.Ö.

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

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## References

1. Katirji MB, Wilbourn AJ. Common peroneal mononeuropathy: a clinical and electrophysiologic study of 116 lesions. Neurology 1988;38:1723-8.
2. Masakado Y, Kawakami M, Suzuki K, Abe L, Ota T, Kimura A. Clinical neurophysiology in the diagnosis of peroneal nerve palsy. Keio J Med 2008;57:84-9.
3. Baima J, Krivickas L. Evaluation and treatment of peroneal neuropathy. Curr Rev Musculoskelet Med 2008;1:147-53.
4. Smith T, Trojaborg W. Clinical and electrophysiological recovery from peroneal palsy. Acta Neurol Scand 1986;74:328-35.
5. Sprofkin BE. Peroneal paralysis; a hazard of weight reduction. AMA Arch Intern Med 1958;102:82-7.
6. Sotaniemi KA. Slimmer's paralysis--peroneal neuropathy during weight reduction. J Neurol Neurosurg Psychiatry 1984;47:564-6.
7. Elias WJ, Pouratian N, Oskouian RJ, Schirmer B, Burns T. Peroneal neuropathy following successful bariatric surgery. Case report and review of the literature. J Neurosurg 2006;105:631-5.
8. Cruz Martínez A. Slimmer's paralysis: electrophysiological evidence of compressive lesion. Eur Neurol 1987;26:189-92.
9. Marwah V. Compression of the lateral popliteal (common peroneal) nerve. Lancet 1964;2:1367-9.
10. Nagler SH, Rangell L. Peroneal palsy caused by crossing the legs. J Am Med Assoc 1947;133:755-61.
11. Watemberg N, Amsel S, Sadeh M, Lerman-Sagie T. Common peroneal neuropathy due to surfing. J Child Neurol 2000;15:420-1.
12. Kleyweg RP, van der Meché FG, Schmitz PI. Interobserver agreement in the assessment of muscle strength and functional abilities in Guillain-Barré syndrome. Muscle Nerve 1991;14:1103-9.
13. Yucel A, Senocak M, Kocasoy Orhan E, Cimen A, Ertas M. Results of the Leeds assessment of neuropathic symptoms and signs pain scale in Turkey: a validation study. J Pain 2004;5:427-32.
14. Chen S, Andary M, Buschbacher R, Del Toro D, Smith B, So Y, Zimmermann K, Dillingham TR. Electrodiagnostic reference values for upper and lower limb nerve conduction studies in adult populations. Muscle Nerve 2016;54:371-7.
15. Oh S. Clinical Electromyography: Nerve Conduction Studies. 3rd ed. Philadelphia: Lippincott Williams Wilkins; 2003.
16. Buschbacher RM. Reference values for peroneal nerve motor conduction to the tibialis anterior and for peroneal vs. tibial latencies. Am J Phys Med Rehabil 2003;82:296-301.
17. Lawlor T, Wells DG. Metabolic hazards of fasting. Am J Clin Nutr 1969;22:1142-9.
18. Verdy M. Fasting in obese females. I. A study of thyroid function tests, serum proteins and electrolytes. Can Med Assoc J 1968;98:1031-3.
19. Katirji B. Peroneal neuropathy. Neurol Clin 1999;17:567-91.
20. Gilchrist JM, Sachs GM. Electrodiagnostic studies in the management and prognosis of neuromuscular disorders. Muscle Nerve 2004;29:165-90.

Original Article

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# Psychosocial Adjustment, Depression, Anxiety, and Stress in Pregnancy Following Assisted Reproductive Treatment and Spontaneous Conception

## Yardımcı Üreme Tedavi ve Spontan Gebelik Sonrası Kadınların Gebeliğe Uyumları, Depresyon, Anksiyete ve Stres Durumlarının Karşılaştırılması

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## ABSTRACT

**Objective:** This study aimed to determine the psychosocial adjustment, depression, anxiety, and stress levels between women who conceived through assisted reproductive treatment (ART) and women who were fertile and conceived spontaneously.

**Methods:** This prospective, comparative, and descriptive study enrolled 69 women who presented to İstanbul University's İstanbul Medical Faculty Reproductive Endocrinology and Infertility Department and conceived through ART between June 2015 and June 2016 and 139 women who presented to the antenatal policlinic for pregnancy. Data were obtained using the Personal Identification Form, Prenatal Self-Evaluation Questionnaire, and Depression, Anxiety, And Stress scale in each trimester.

**Results:** The adaptation of spontaneously pregnant women (spontaneous group) was better than that of women who became pregnant by ART (ART group) in the first trimester. The psychosocial adjustment of all women to pregnancy was the highest in the second trimester, followed by the third and first trimesters. Infertility time, infertility treatment duration, number of ART attempts, duration of wanting to have a child, pregnancy loss experience, and cause of infertility did not affect pregnancy adjustment in all trimesters. In the first and third trimesters, depressive symptoms are more common in the spontaneous group than in the ART group. In the first and third trimesters, the anxiety and stress levels were higher in the ART group than in the spontaneous group.

## ÖZ

**Amaç:** Üremeye yardımcı tedavi uygulamaları (ÜYTU) sonrası gebe kalan kadınlar ile spontan gebe kalan kadınların, gebeliğe uyumları ile depresyon, anksiyete ve stres durumlarını belirlemektir.

**Yöntemler:** Prospektif tipte, karşılaştırmalı-tanımlayıcı bir araştırmadır. Araştırmaya Haziran 2015-2016 tarihleri arasında İstanbul Üniversitesi İstanbul Tıp Fakültesi Üreme Endokrinolojisi ve İnfertilite Anabilim Dalı'na başvuran ve ÜYTU ile gebe kalan 69 kadın ile doğum öncesi polikliniğine başvuran spontan gebe kalan 139 kadın dahil edilmiştir. Veriler; Tanıtıcı Bilgi Formu, Prenatal Kendini Değerlendirme Ölçeği, Depresyon-Anksiyete-Stres Ölçeği uygulanarak her üç trimesterde elde edilmiştir. Analizlerde sayı, yüzde, ortalama, standart sapma, ki-kare, bağımsız örneklem t testi ve tek yönlü varyans analizi kullanılmıştır.

**Bulgular:** Spontan gebe kalan kadınların gebeliğe uyumları birinci trimesterde ÜYTU sonrası gebe kalan kadınlara göre daha iyi düzeyde olduğu belirlenmiştir. Tüm kadınların gebeliğe psikososyal uyumu en fazla ikinci trimesterde iken; bunu üçüncü ve birinci trimester izlemiştir. İnfertilite süresi, infertilite tedavi süresi, ÜYTU deneme sayısı, çocuk sahibi olma isteme yılı, gebelik kaybı deneyimi ve infertilite nedeni değişkenlerinin her üç trimesterde de gebeliğe uyumu etkilemediği belirlenmiştir. Spontan gebe kalan kadınlarda depresif belirtiler birinci ve üçüncü trimesterde ÜYTU sonrası gebe kalan kadınlara kıyasla daha fazla iken, ÜYTU sonrası gebe kalan kadınlarda anksiyete ve stres belirtileri birinci ve üçüncü trimesterde

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**Conclusion:** Psychosocial support programs should be organized for women who conceived through ART in infertility clinics. Moreover, routine pregnancy monitoring should cover the psychosocial evaluation of pregnant women, including adjustment, depression, anxiety, and stress.

**Keywords:** Psychosocial adjustment, assisted reproductive treatment methods, depression, anxiety, stress

spontan gebe kalan kadınlara kıyasla daha fazla olduğu saptanmıştır.

**Sonuç:** İnfertilite kliniklerinde ÜYTU ile gebe kalan kadınlara psikososyal destek programları düzenlenmelidir. Ayrıca kadınların rutin gebe izlemleri psikososyal değerlendirmeyi de (uyum, depresyon, anksiyete, stres) kapsamalıdır.

**Anahtar Sözcükler:** Psikososyal uyum, üremeye yardımcı tedavi uygulamaları, depresyon, anksiyete, stres

## Introduction

Infertility is defined as the absence of pregnancy despite regular sexual intercourse for at least 1 year without any contraceptive method (1). Infertility is not only a gynecological disorder but also a health problem that has negative biological, social, cultural, and psychological dimensions and can affect the couples' quality of life (2). Pregnancy is considered a physiological event in the life of the woman and an important life event that requires serious biopsychosocial adaptation by the pregnant woman and her family. Many studies have defined the pregnancy period as a developmental crisis or a critical phase. While many women easily adapt to the physiological, psychological, and social changes caused by pregnancy, some may have psychological illnesses at mild, moderate, and severe levels. Especially, in women who conceived for the first time after infertility treatment, this process is described as a psychological risk, stressful, and expensive (3-5).

Studies have suggested that many women with infertility who conceived after chronic infertility treatment do not have the chance to renew their psychological resources that were consumed during the treatment process and have a more difficult experience with the pregnancy process and parenting roles and therefore need more support (6,7). Similar studies have reported that women who conceived for the first time following infertility treatment had a higher level of stress, had difficulty adapting to the pregnancy, and experienced lower psychological well-being than women who became pregnant spontaneously (8-11).

Considering that women who conceived after infertility treatment have attained their desired pregnancy, health workers may overlook or care less about the negative emotional situations of pregnant women. Some pregnant women may have difficulty recognizing the negative symptoms they have experienced. Others may be ashamed of expressing negative symptoms after their long struggle to having a baby, while some may disagree when they learn about symptoms of maladaptation, depression, anxiety, or stress. Although infertility treatment may result in pregnancy, women's adaptation to pregnancy and their emotional states may be affected. Therefore, health professionals should evaluate the adaptation of women to pregnancy and examine their depression, anxiety, and stress situations. Some studies about adaptation to pregnancy have been performed in Turkey, but they do not include the three trimesters or comparative groups (7,12,13).

## Subjects and Methods

This prospective, comparative, and descriptive study focused on women who presented to İstanbul University, İstanbul Medical Faculty Reproductive Endocrinology and Infertility Department and conceived through assisted reproductive treatment (ART) and all women who presented to the antenatal polyclinic for pregnancy follow-up between June 2015 and June 2016. The study sample consists of women who participated in the study voluntarily and met the inclusion criteria. Of these women, 69 conceived through ART and 139 conceived spontaneously (Figure 1).

Ethical approval was obtained from the Ethics Committee of Medipol University Faculty of Medicine (approval no: 108400987-292, date: 11.05.2015).

Women aged >18 years who were in the first trimester of pregnancy, were not diagnosed with any psychiatric illness, had no symptoms indicative of fetal illnesses, do not have any literacy problem, did not have mental or communication disorder, volunteered to participate in the study, conceived for the first time through at least one of the ARTs (ART group), and conceived naturally without any treatment for the first time (spontaneous group) were included in this study.

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Study flow diagram is presented in Figure 1.

**Data Collection Tools**

Data were collected using a sociodemographic Questionnaire/ Personal Identification Form, Prenatal Self-Evaluation Questionnaire (PSEQ), and Depression, Anxiety, Stress scale (DASS).

The personal identification form was used to determine the descriptive characteristics of the women. PSEQ was used to evaluate their adaptation to pregnancy, and DASS was used to evaluate their depression, anxiety, and stress levels. The Personal Identification Form-2$^{nd}$ Trimester and Personal Identification Form-3$^{rd}$ Trimester were used to evaluate changes that may occur in the second and third trimesters, respectively.

The PSEQ was developed by Ledermanin 1979 to evaluate adaptation to motherhood in antenatal women and was adapted into Turkish by Beydağ and Mete (14). The PSEQ has a 4-point Likert scale with 79 items and seven subscales. The total scores range from 79 to 316 points. Lower scores indicate better adaptation to pregnancy, while higher scores mean poor adaptation (14).

The DASS was developed by Lovibond and Lovibond (15) to measure the negative emotional states of depression, anxiety, and stress, and it was adapted into Turkish by Akın and Çetin (16). The DASS is a 42-item questionnaire that includes three (depression, anxiety, and stress) self-reporting scales. High scores from each dimension indicate a problem about the corresponding state (16).

**Statistical Analysis**

Statistical analyses were performed using SPSS 21.0 for Windows (IBM Corp., Armonk, NY, USA). Number, percentage, mean, standard deviation, chi-square, Independent samples t-test, and One-Way variance analysis were used in the analysis of data. The significance level was determined at a 95% confidence interval and $p<0.05$.

## Results

The mean age of the participants (ART: 33.0±4.38 years; spontaneous: 28.76±4.52 years) and their partners' mean age (ART: 35.94±5.01; spontaneous: 32.24±4.95) ($p<0.001$) were significantly higher in the ART group than in the spontaneous group. In terms of the gestational week, a significant difference was found in the spontaneous group (ART: 10.74±2.21; spontaneous: 11.4±1.57). No significant difference was found between the ART and spontaneous groups in the number of pregnancy ($t=0.378$), miscarriage ($t=1.912$), and abortion ($t=0.020$), ($p>0.05$). Data on the descriptive characteristics of the participants are shown in Table 1.

In the first trimester, the average scores in the ART group were higher in the spontaneous group ($p<0.05$). Moreover, the adaptation of the spontaneous groups to pregnancy is better than that of the ART group in the first trimester (Table 2).

As shown in Table 3, an evaluation of the ART and spontaneous groups separately reveals that the depression levels of the ART group were not significantly different among the trimesters, while the depression levels of the spontaneous group appear higher during the first trimester than during the second trimester. Moreover, infertility duration, infertility treatment duration, number of ART trials, duration of desire to have children, pregnancy loss experience, and cause of infertility did not affect pregnancy adaptation in all trimesters.


**Figure 1.** Study flow diagram

ART: Assisted reproductive treatment

**Table 1.** Description and comparison of the participants (n=208)

| Variables | Groups | ART, (n=69) | | Spontaneous,(n=139) | | Statistic | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | $\chi^2$ | p-value |
| Education level | Literate | 0 | 0 | 1 | 0.07 | 26,769 | 0.001*** |
| | Primary school | 18 | 26.1 | 4 | 2.9 | | |
| | Secondary school | 5 | 7.2 | 16 | 11.5 | | |
| | High school | 12 | 17.4 | 32 | 23.0 | | |
| | Bachelor's degree | 34 | 49.3 | 86 | 61.9 | | |
| Income | Lower than expenditure | 3 | 4.3 | 6 | 4.3 | 7,589 | 0.022* |
| | Equal to expenditure | 59 | 85.5 | 96 | 69.1 | | |
| | Higher than expenditure | 7 | 10.1 | 37 | 26.6 | | |
| Working status | Housewife | 33 | 47.8 | 43 | 30.9 | 5,673 | 0.017* |
| | Employee or retired | 36 | 52.2 | 96 | 69.1 | | |
| Family type | Elementary family | 65 | 94.2 | 125 | 89.9 | 1,066 | 0.302 |
| | Extended family | 4 | 5.8 | 14 | 10.1 | | |
| Number of pregnancies | Never | 26 | 37.7 | 85 | 61.2 | 11,947 | 0.003** |
| | Once | 20 | 29.0 | 32 | 23.0 | | |
| | Twice or more | 23 | 33.3 | 22 | 15.8 | | |
| Number of miscarriage | Never | 40 | 58.0 | 91 | 65.5 | 5,749 | 0.056 |
| | Once | 15 | 21.7 | 36 | 25.9 | | |
| | Twice or more | 14 | 20.3 | 12 | 8.6 | | |
| Number of abortion | Have not had abortion | 57 | 82.6 | 116 | 83.5 | 0.023 | 0.878 |
| | Has had for at least once | 12 | 17.4 | 23 | 16.5 | | |
| Getting informed for pregnancy | Yes | 23 | 33.3 | 76 | 54.7 | 8,421 | 0.004** |
| | No | 46 | 66.7 | 63 | 45.3 | | |

*p<0.05; **p<0.01; ***p<0.001 $\chi^2$: chi-square test, f: Fisher's exact test, ART: Assisted reproductive treatment

## Discussion

In this study, the participants were 19-46 years old, which corresponds to the expectation that women who conceived through ART have a significantly higher average age than women who are fertile and conceived spontaneously (ART: 33.0±4.38; spontaneous: 28.76±4.52). These results indicate the effect of age on infertility. It was also expected that the average age of partners of women who conceived through ART is significantly higher than those who conceived spontaneously. The guideline published by the American College of Obstetricians and Gynaecologists (ACOG) stated that the fertility of women and men decreased with age, emphasizing that age was a major factor of infertility (17).

Studies have emphasized the importance of prenatal care, and arranging training during this period to increase physical and psychological adaptation of the pregnant woman is necessary (18). While 66.7% of the pregnant women in the ART group did not receive any information, 54.7% of the pregnant women of the spontaneous group were informed about pregnancy. The women in the spontaneous group were thought to be more open to education considering their younger age and higher education levels. Despite the older age and lower education levels of women who are not well informed in the ART group, we think that the intensive knowledge they have received during the ART process may be effective in increasing consciousness.

In the comparison of total PSEQ scores, the spontaneous group demonstrated better adaptation than did the ART group during the first trimester. Women who conceived with moral and material difficulties may find it difficult to believe the pregnancy, so they may find themselves having constant repetitive pregnancy tests, ultrasound imaging, and examinations (19). This finding will inevitably contribute to the literature.

In the evidence-based guideline published by the European Society of Human Reproduction and Embryology (ESHRE), women who conceived through in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) were reported to have no worse depression symptoms compared with women who conceived spontaneously (level of evidence, A) and that no difference was found between the groups, or the symptoms of depression were lower for women who conceived after treatment (20). In this study, the ART group showed milder depressive symptoms than the spontaneous group. This situation was interpreted by Harf-Kashdaei and Kaitz (21) as "enjoying the success" achieved after a long struggle with ART. These results can also be explained

**Table 2.** Comparison of groups in total and subscales scores of the Prenatal Self-Evaluation Questionnaire (n=208)

| Mean | | ART (n=69) | | Spontaneous (n=139) | | Test value (t) | p-value |
|---|---|---|---|---|---|---|---|
| | | SD | Mean | SD | | | |
| Sense of well-being for baby and self | 1st trimester | 30.29 | 6.55 | 21.58 | 6.28 | 9,283 | **0.001*** ** |
| | 2nd trimester | 23.80 | 6.13 | 20.48 | 5.84 | 3,792 | **0.001*** ** |
| | 3rd trimester | 28.02 | 6.20 | 22.22 | 6.09 | 6,429 | **0.001*** ** |
| Acceptance of pregnancy | 1st trimester | 24.68 | 6.62 | 20.09 | 5.58 | 4,947 | **0.001*** ** |
| | 2nd trimester | 16.68 | 2.92 | 19.19 | 5.13 | 4,482 | **0.001*** ** |
| | 3rd trimester | 16.86 | 2.81 | 18.79 | 4.61 | 3,745 | **0.001*** ** |
| Identification of a motherhood role | 1st trimester | 22.68 | 4.65 | 23.23 | 4.63 | 0.804 | 0.423 |
| | 2nd trimester | 21.38 | 3.83 | 22.88 | 4.80 | 2,264 | **0.025*** |
| | 3rd trimester | 20.75 | 3.96 | 22.58 | 4.33 | 2,938 | **0.004**** |
| Preparation for labor | 1st trimester | 18.55 | 4.23 | 19.32 | 5.02 | 1,164 | 0.246 |
| | 2nd trimester | 17.99 | 4.02 | 18.79 | 4.20 | 1,321 | 0.188 |
| | 3rd trimester | 17.44 | 3.90 | 18.82 | 4.34 | 2,239 | **0.026*** |
| Fear of labor | 1st trimester | 17.42 | 4.85 | 20.50 | 4.40 | 4,599 | **0.001*** ** |
| | 2nd trimester | 17.57 | 4.25 | 19.59 | 4.41 | 3,157 | **0.002**** |
| | 3rd trimester | 25.29 | 5.13 | 19.14 | 3.89 | 8,794 | **0.001*** ** |
| Relationship with her mother | 1st trimester | 15.07 | 5.09 | 15.47 | 4.91 | 0.540 | 0.590 |
| | 2nd trimester | 14.73 | 6.42 | 15.45 | 5.80 | 0.815 | 0.416 |
| | 3rd trimester | 14.33 | 4.80 | 15.06 | 4.98 | 1,000 | 0.319 |
| Relationship with her partner | 1st trimester | 14.74 | 4.36 | 14.72 | 4.33 | 0.031 | 0.975 |
| | 2nd trimester | 13.90 | 3.67 | 14.63 | 4.66 | 1,240 | 0.217 |
| | 3rd trimester | 13.91 | 3.28 | 14.74 | 4.52 | 1,503 | 0.135 |
| Total scores | 1st trimester | 142.41 | 19.91 | 134.17 | 23.37 | 2,508 | **0.013*** |
| | 2nd trimester | 126.03 | 18.99 | 131.01 | 23.97 | 1,506 | 0.134 |
| | 3rd trimester | 136.59 | 16.10 | 131.34 | 22.51 | 1,932 | 0.055 |

*P<0.05; **p<0.01; ***p<0.001; t: Student's t-test, ART: Assisted reproductive treatment, SD: Standard deviation

**Table 3.** Comparison of Depression, Anxiety. Stress Scale scores by groups and trimesters

| DASS | Groups | 1st Trimester[a] | | 2nd Trimester[b] | | 3rd Trimester[c] | | Test value (F) | p-value |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | Mean | SD | | |
| Depression | ART (n=69) | 3.36 | 4.26 | 3.13 | 4.74 | 3.71 | 5.34 | 0.393 | 0.676 |
| | Spontaneous (n=139) | 5.37 | 5.75 | 3.83 | 4.50 | 4.68 | 4.33 | 6.319 | **0.002**[**, a>b] |
| | Total (n=208) | 4.70 | 5.38 | 3.60 | 4.58 | 4.36 | 4.70 | 4.830 | **0.008**[**, a>b] |
| Anxiety | ART (n=69) | 10.12 | 4.83 | 5.55 | 5.26 | 12.46 | 6.67 | 37.552 | **0.001**[***, c>a>b] |
| | Spontaneous (n=139) | 7.91 | 5.79 | 6.73 | 5.66 | 9.19 | 5.44 | 12.888 | **0.001**[***, c>a, b] |
| | Total (n=208) | 8.64 | 5.58 | 6.34 | 5.55 | 10.28 | 6.06 | 41.632 | **0.001**[***, c>a>b] |
| Stress | ART (n=69) | 15.80 | 6.62 | 9.72 | 7.83 | 21.81 | 8.05 | 65.155 | **0.001**[***, c>a>b] |
| | Spontaneous (n=139) | 11.88 | 6.88 | 9.86 | 6.63 | 12.66 | 5.97 | 11.829 | **0.001**[***, a, c>b] |
| | Total (n=208) | 13.18 | 7.03 | 9.81 | 7.03 | 15.70 | 7.98 | 53.411 | **0.00**[***, c>a>b] |

**p<0.01, F: Variance analysis

by several factors such as the end of material and spiritual exhaustion, disappearance of social pressure, or end of a difficult treatment period.

Moreover, ESHRE (20) reported that anxiety levels of pregnant women after IVF/ICSI may be higher than that of women who conceived spontaneously (level of evidence, B). Related qualitative studies have also emphasized that miscarriage risk increases the anxiety levels in the first trimester of the women who conceived through ART, that their anxiety levels decreased when they felt the baby's movements in the second trimester, that

the fear of labor and thought of deficiencies in the baby increased the anxiety levels, and that the pregnant women experienced nightmares in the third trimester (13,19).

In the present study, the anxiety levels of the ART group are higher than those of the spontaneous group. This result is in line with the literature. In a comparative study, Baor and Soskolne (22) revealed that the ART group had higher stress levels than the spontaneous group. Similar results were also reported by Darwiche et al. (23) who compared pre-pregnancies before Down syndrome screening in the first trimester. Similarly, in the present study, the stress levels of the ART group were higher than those of the spontaneous group.

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In the comparison of total PSEQ scores, the spontaneous group demonstrated better adaptation than did the ART group during the first trimester. Women who conceived with moral and material difficulties may find it difficult to believe the pregnancy, so they may find themselves having constant repetitive pregnancy tests, ultrasound imaging, and examinations (19). This finding will inevitably contribute to the literature.

In the evidence-based guideline published by ESHRE, women who conceived through IVF/ICSI were reported to have no worse depression symptoms compared with women who conceived spontaneously (level of evidence, A) and that no difference was found between the groups, or the symptoms of depression were lower for women who conceived after treatment (20). In this study, the ART group showed milder depressive symptoms than the spontaneous group. This situation was interpreted by Harf-Kashdaei and Kaitz (21) as "enjoying the success" achieved after a long struggle with ART. These results can also be explained by several factors such as the end of material and spiritual exhaustion, disappearance of social pressure, or end of a difficult treatment period.

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### Study Limitations

In the present study, the anxiety levels of the ART group are higher than those of the spontaneous group. This result is in line with the literature. In a comparative study, Baor and Soskolne (22) revealed that the ART group had higher stress levels than the spontaneous group. Similar results were also reported by Darwiche et al. (23) who compared pre-pregnancies before Down syndrome screening in the first trimester. Similarly, in the present study, the stress levels of the ART group were higher than those of the spontaneous group.

## Conclusion

The results of this study indicate that pregnancy adaptations of the spontaneous group are better than those of the ART group in the first trimester. Moreover, the anxiety and stress levels of the ART group were higher than those of the spontaneous group in the first and third trimesters. In line with these results, psychosocial support programs should be organized for women who conceived through ART in infertility clinics. In addition, routine pregnancy monitoring should cover the psychosocial evaluation of pregnant women, including adjustment, depression, anxiety, and stress. Further studies with a larger number of participants (women and their partners) will contribute to developing specific guidelines about psychosocial care. These guidelines will help nurses in providing psychosocial support to patients, which will eventually improve the quality of care.

### Ethics

**Ethics Committee Approval:** Ethical approval was obtained from the Ethics Committee of Medipol University Faculty of Medicine (approval no: 108400987-292, date: 11.05.2015).

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

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## References

1. Dilek N, Beji NK. Determining the emotional reactions of couples undergoing assisted reproductive procedures. HEAD 2012;9:24-9.
2. Yılmaz T, Oskay ÜY. Methods to cope with ınfertility stress and nursing attitudes. HSP 2015;2:100-12.
3. HaCohen N, Amir D, Wiseman H. Women's narratives of crisis and change: Transitioning from infertility to pregnancy. J Health Psychol 2018;23:720-30.
4. Bayram GO. İnfertilitenin yaşam kalitesi ve evlilik uyumu üzerine etkisi. Istanbul Üniversitesi Sağlık Bilimleri Enstitüsü. Doktora Tezi; 2009.
5. Gameiro S, Moura-Ramos M, Canavarro MC, Soares I. Psychosocial adjustment during the transition to parenthood of Portuguese couples who conceived spontaneously or through assisted reproductive technologies. Res Nurs Health 2010;33:207-20.
6. Fisher JR, Hammarberg K, Baker HW. Assisted conception is a risk factor for postnatal mood disturbance and early parenting difficulties. Fertil Steril 2005;84:426-30.
7. Seven M, Akyüz A. An under-recognized factor in the development of postpartum depression: infertility. HEAD 2013;10:7-11.
8. Gourounti K. Psychological stress and adjustment in pregnancy following assisted reproductive technology and spontaneous conception: A systematic review. Women Health 2016;56:98-118.
9. Ataman H, Arslan H. Psycho-social care needs in pregnancies experienced naturally and pregnancies with as a result of infertility treatment. J Fam Soc 2010;6:75-86.
10. Ellison MA, Hall JE. Social stigma and compounded losses: quality-of-life issues for multiple-birth families. Fertil Steril 2003;80:405-14.
11. Monti F, Agostini F, Fagandini P, La Sala GB, Blickstein I. Depressive symptoms during late pregnancy and early parenthood following assisted reproductive technology. Fertil Steril 2009;91:851-7.
12. Lepecka-Klusek C, Jakiel G. Difficulties in adaptation to pregnancy following natural conception or use of assisted reproduction techniques: a comparative study. Eur J Contracept Reprod Health Care 2007;12:51-7.
13. Redshaw M, Hockley C, Davidson LL. A qualitative study of the experience of treatment for infertility among women who successfully became pregnant. Hum Reprod 2007;22:295-304.
14. Beydağ KD, Mete S. Prenatal kendini değerlendirme ölçeğinin geçerlik ve güvenirlik çalışması. Journal of Anatolia Nursing and Health Sciences 2008;11:16-24.
15. Lovibond PF, Lovibond SH. The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behav Res Ther 1995;33:335-43.
16. Akın A, Çetin B. The depression, anxiety and stress scale (DASS): The study of validity and reliability. Educational Sciences: Theory and Practice 2007;7:260-8.
17. The American College of Obstetricians and Gynecologists- ACOG-Treating Infertility. 2017; [cited 2016 Des 14]. Available from: https://www.acog.org/Patients/FAQs/Treating-Infertility
18. Demirbaş H, Kadıoğlu H. Adaptation of pregnancy in prenatal period women and factors associated with adaptation. MÜSBED 2014;4:200-6.
19. Covington SN, Burns LH. Pregnancy after infertility. In: Infertility CounselingA Comprehensive Handbook for Clinicians. 2nd ed. UK: Cambridge University Press; 2006. p. 440-58.
20. The European Society of Human Reproduction and Embryology - ESHRE. Psychology and Counselling Guideline Development Group, Routine psychosocial care in infertility and medically assisted reproduction A guide for fertility staff. 2015; [cited 2016 Jan 20]. Available from: https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Psychosocial-care-guideline.aspx
21. Harf-Kashdaei E, Kaitz M. Antenatal moods regarding self, baby, and spouse among women who conceived by in vitro fertilization. Fertil Steril 2007;87:1306-13.
22. Baor L, Soskolne V. Mothers of IVF and spontaneously conceived twins: a comparison of prenatal maternal expectations, coping resources and maternal stress. Hum Reprod 2010;25:1490-6.
23. Darwiche J, Lawrence C, Vial Y, Wunder D, Stiefel F, Germond M, et al. Anxiety and psychological stress before prenatal screening in first-time mothers who conceived through IVF/ICSI or spontaneously. Women Health 2014;54:474-85.

Original Article

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# The Mediating Role of Perceived Organizational Support in the Effects of Job Stress on Occupational Commitment: Research on Nurses Working in a Foundation University Hospital

## İş Stresinin Mesleki Bağlılık Üzerindeki Etkisinde Algılanan Örgüt Desteğinin Aracılık Rolü: Bir Vakıf Üniversitesi Hastanesinde Çalışan Hemşireler Üzerine Araştırma

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## ABSTRACT

**Objective:** This study aimed to reveal the relationship between the concepts of job stress, perceived organizational support, and occupational commitment on nurses, who are one of the occupational groups most affected by the coronavirus 2019. Only a few academic studies on the relationships between these concepts were carried out in the literature. Therefore, this study aimed to fill the gap mentioned in the literature.

**Methods:** This study is a quantitative research conducted on 270 nurses working in a foundation university hospital in Istanbul. the data in this study were collected using the questionnaire method, and statistical analyses were performed using SPSS. The participants' demographic characteristics, factor and reliability analyses of job stress, perceived organizational support and occupational commitment variables, mean values of variables, and regression analysis to determine the effects of variables were conducted within the scope of the research.

**Results:** According to the research results, there are significant relationships between job stress, perceived organizational support, and occupational commitment. Perceived organizational support plays a full-mediating role on the effects of job stress, and occupational commitment is another result of the study.

## ÖZ

**Amaç:** İş stresi, algılanan örgüt desteği ve mesleki bağlılık kavramları arasındaki ilişkiyi ortaya koymak için gerçekleştirilen bu çalışma corona virüs hastalığı-2019 salgınından en çok etkilenen meslek gruplarından biri olan hemşireler üzerine gerçekleştirilmiştir. Yapılan literatür taramasında, bahsi geçen kavramlar arasındaki ilişkilere yönelik akademik çalışmaya pek fazla rastlanılmamıştır. Dolayısıyla, bu araştırmanın orijinalliği literatürde bahsi geçen boşluğu doldurmasıdır.

**Yöntemler:** Bu çalışmada, İstanbul'da bir vakıf üniversitesi hastanesinde çalışan 270 hemşire ile nicel bir araştırma gerçekleştirilmiştir. Araştırmada veriler anket yöntemiyle toplanmış olup SPSS ile istatistiksel analizler gerçekleştirilmiştir. Araştırma kapsamında katılımcıların demografik özellikleri, iş stresi, algılanan örgüt desteği ve mesleki bağlılık değişkenlerine ait faktör ve güvenilirlik analizleri, değişkenlere ilişkin ortalama değerler ve değişkenler arası etkiyi belirlemeye yönelik analizler yapılmıştır.

**Bulgular:** Araştırma sonucuna göre, iş stresi, algılanan örgüt desteği ve mesleki bağlılık arasında anlamlı ilişkiler olduğu belirlenmiştir. İş stresini mesleki bağlılık üzerindeki etkisinde algılanan örgüt desteğinin tam aracı role sahip olması araştırmanın bir diğer sonucudur.

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**Conclusion:** In this study, the relationships between the concepts of job stress, perceived organizational support, and occupational commitment are determined. According to the research results, although nurses are exposed to job stress due to working conditions, their occupational commitment increases with the support they receive from their organizations.

**Keywords:** Job stress, perceived organizational support, occupational commitment, COVID-19

**Sonuç:** Bu çalışmada, iş stresi, algılanan örgüt desteği ve mesleki bağlılık kavramları arasındaki ilişki ortaya konmuştur. Araştırma sonucuna göre, hemşireler çalışma koşullarından kaynaklı iş stresine maruz kalmalarına rağmen örgütlerinden almış oldukları destek ile mesleki bağlılıkları artmaktadır.

**Anahtar Sözcükler:** İş stresi, algılanan örgüt desteği, mesleki bağlılık, COVID-19

## Introduction

Today, ensuring the sustainability of employees who have occupational commitment is an important problem faced by organizations. Occupational commitment is the psychological link between individuals and professions (1). Another definition of occupational commitment is that “it provides a more complete understanding of a person’s tie to his/her occupation” (2). According to Meyer et al. (2), occupational commitment has been handled in three dimensions as follows: affective commitment, continuance commitment, and normative commitment. Affective commitment is a person’s emotional commitment to their profession (3,4). Meyer et al. (2) expressed affective commitment as "individuals' encountering satisfactory experiences while performing their profession.” Continuance commitment is the evaluation of the costs associated with leaving the profession of the individual (3,4). According to Meyer et al. (2), continuance commitment is “the loss or decrease of the value of the investments that individuals have made in their profession until that day when they change their jobs”. Normative commitment is the feeling of an obligation to remain in one’s profession (3,4). According to Meyer et al. (2), normative commitment is “the attachment of individuals to their profession due to normative pressures.”

Occupational commitment may be negatively affected because it develops under or beyond the organizations’ control. One of these reasons is job stress (5-8), which is “the individual’s awareness or feeling of functional impairment as a result of conditions or events arising from the work environment” (9). Researchers considered job stress in the two following dimensions: time stress and anxiety stress (9-11). Time stress occurs because of crisis management, time pressure at the workplace, too much work to do, but not enough time, and experiences with managers (9). Anxiety stress is when individuals feel emotionally uncomfortable because of the stress they have experienced (9). In other words, anxiety stress is the stress caused by the anxiety and tension arising from the workplace and work conditions (12).

On the other hand, organizations want to change employees' attitudes and behaviors in order to increase their employees' occupational commitment. Organizational support is one of the attitudes that affect employees' commitment to their occupation (13,14). Organizational support means that the organization deals with its employees (15). In other words, it is "employees' perception concerning the extent to which the organization values their contribution and cares about their well-being." (16). In addition, organizational support also reduces the job stress experienced by employees. Employees who have a perception of organizational support may have a low perception of job stress since they believe that their organizations are by their side even if they experience job stress due to working conditions (17,18).

In recent years, the coronavirus-2019 (COVID-19) pandemic has been a major threat to the whole world and humanity. Almost all sectors were adversely affected, although the health sector comes first among these sectors. In this period, healthcare professionals are serving humanity by struggling to survive, and this situation causes job stress. Despite this, almost all healthcare professionals worldwide are committed to serving humanity and working with great devotion. This shows that the occupational commitment of healthcare professionals is high. In addition, another factor that can affect the occupational commitment of healthcare professionals is the support they receive from the organizations they work for. With the support they receive from their organizations, healthcare professionals feel that their organizations are always with them; thus, their occupational commitment increases, and job stress can be reduced.

This study was conducted on nurses working in a foundation university hospital in Istanbul, and the role of perceived organizational support in the effects of job stress on occupational commitment was discussed. When related literature was examined, studies involving the concepts of job stress, perceived organizational support, and occupational commitment were rarely encountered before, and this has been the source of motivation for this study. In addition, this study has gained originality because it was conducted on nurses, which is one of the groups most affected by the COVID-19 pandemic that affected the whole world and humanity. For this reason, it is thought that this study will contribute to the related literature.

## Methods

### Purpose and Importance of the Research

Recently, the COVID-19 pandemic has been a major threat to the whole world and humanity. Day by day, the working conditions of healthcare professionals are getting more and more difficult, and this situation causes job stress. Despite this, healthcare professionals devote themselves to serve humanity and work with intense labor, effort, and devotion at the cost of their lives. This situation shows that the occupational commitment of healthcare workers is high. In addition, another factor that can

affect the occupational commitment of healthcare professionals is the support they receive from the organizations they work for. With the support they receive from their organizations, healthcare professionals feel that their organizations are always with them; thus, their occupational commitment increases, and job stress can be reduced. Therefore, this study was carried out to reveal the relationship between the concepts mentioned earlier. Thus, this study aimed to examine the role of perceived organizational support in the effects of job stress on occupational commitment of nurses, who are one of the most important groups of healthcare professionals.

**Participants and Sampling of the Research**

This research was conducted on nurses working in a foundation university hospital in İstanbul. According to the information obtained from its human resources department, there were 417 nurses working in the university hospital. The sample size was 201 employees for a population of 417 employees, at a 95% confidence interval and 5% significance level. A convenience sampling method was used. The surveys were distributed and collected by the researchers. The research was conducted on a voluntary basis, and the data were obtained from 270 respondents.

**Research Model, Variables, and Hypothesis of the Study**

The model developed in line with the purpose of the research is based on the social change theory, which attempts to explain employees' attitudes at work (19). The independent, dependent, and mediating variables of the study were job stress, occupational commitment, and perceived organizational support, respectively.

The model of the research was created to determine the role of perceived organizational support in the effects of job stress on occupational commitment as shown in Figure 1.

For the purpose of this study, the research hypothesis is determined as follows:

$H_1$: Perceived organizational support mediates the relationship between job stress and occupational commitment.

**Measurement Instrument of the Research Variables**

In this research, surveys were used as a means of data collection. The questionnaire used in this research consisted of four main parts. The first part contained questions about the respondents' demographic features.

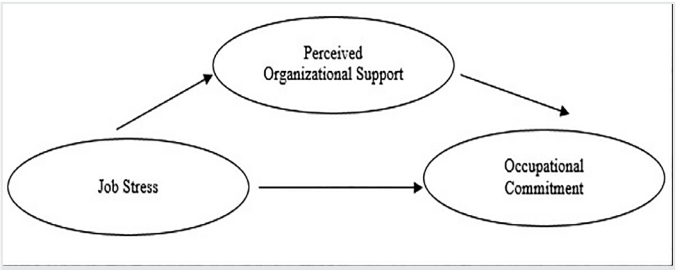


**Figure 1.** Research model

The second part of the questionnaire form, developed by Parker and Decotiis (9), was a scale with 13 expressions and used to determine the job stress of employees. The job stress scale consisted of the two following dimensions: "anxiety stress" and "time stress". In the literature review, the short form of the scale, consisting of nine statements, was used in this study (20-23). The shortened version was first used by Jamal and Baba (1992) who measured job stress as one construct (10).

The third part of the questionnaire form consisted of statements regarding the perceived organizational support scale. To measure, the shortened version of the scale, which was developed by Eisenberger, Huntington, Hutchison, and Sowa, with eight statements with the highest factor load was used (16). In addition, expressions 2, 3, 5, and 7 in the scale were in the reverse direction, and scoring was made in reverse.

The fourth part of the questionnaire comprised expressions about occupational commitment scale, which was developed by Meyer et al. (2). The scale consisted of 18 statements and 3 dimensions. The first six statements measured affective commitment, the next 6 measured continuance commitment, and the last 6 measured normative commitment. Expressions 2, 4, 5, 11, and 14 of the scale are in the reverse direction, and these expressions are scored in reverse.

The questionnaire form was graded using a 5-point Likert scale, except for demographic expressions, ranging from Strongly Disagree (1) to Strongly Agree (5).

## Results

**Descriptive Statistics**

The percentages of the respondents' demographic features are as follows: 77% were women, and 23% were men. Of the respondents, 35% were married, and 30% had children. Their ages ranged from under 25 years (56%), 26-30 (19%), 31-35 (10%), and 36 and above (15%). Of the respondents, 88% were nurses, 6% were chief nurses, and 6% were supervisor nurses. Of the respondents, 50% had a high school degree, 16% had vocational high school, 30% had bachelor's degree, and 4% had a master's degree. Before the COVID-19 pandemic, 83% stated that they lived with their family, 6% with their friends, 2% with others, and 9% alone. After the COVID-19 pandemic, 82% of the participants stated that they lived with their family, 6% with their friends, 2% with others, and 10% alone. Meanwhile, most of the participants (80%) stated that their daily working hours was 10 h, and 20% stated that they worked 10 h or more. Of the participants, 91% stated that they received their overtime pay, whereas 9% did not. The participants stated that they had a monthly seizure of 30% at 1-3 days, 13% at 4-6, 24% at 7-9, and 33% at 10 or more. The number of years that the participants had been involved in the job experience is 9% under 1 year, 44% at 1-5, 20% at 6-10, 14% at 11-15, and 13% at 16 or more. The number of years that the participants had been involved in their current hospital ranged from under 1 year (24%), 1-5 (44%), 6-10 (24%), and 11 or longer (8%).

**Factor and Reliability Analysis of Variables**

In this section, the factor and reliability analyses of the research variables were provided.

**Job Stress Factor and Reliability Analysis**

In the factor analysis of job stress scale, the Kaiser-Meyer-Olkin (KMO) value was 0.86 and was significant at 0.000 level. This indicated an excellent value, and data gathered through respondents were suitable for factor analysis (24). By conducting exploratory factor analysis, it was found that job stress scale has created a one dimensional structure. According to the results of the reliability analysis on the job stress scale, the Cronbach alpha was 0.86, which indicates a high reliability value (26). As a result, after the factor and reliability analyses, the latest job stress scale has one dimension and nine items.

**Perceived Organizational Support Factor and Reliability Analysis**

In the factor analysis of perceived organizational support scale, the KMO value was 0.91, and this found significant at 0.000 level. This indicates an excellent value, and data gathered through respondents were suitable for factor analysis (24). By conducting an exploratory factor analysis, it was found that perceived organizational support created a one dimensional structure. According to the results of the reliability analysis regarding the perceived organizational support scale, the Cronbach alpha was 0.95, which indicates a high reliability value (26). As a result, after the factor and reliability analyses, the latest perceived organizational support scale is the same as the original one, consisting of one dimension and eight items.

**Occupational Commitment Factor and Reliability Analyses**

In the factor analysis of the occupational commitment scale, the KMO value was 0.86. This indicates an excellent value, and data gathered through respondents were suitable for factor analysis (24). According to Hair et al. (25), factors with high cross loadings must be excluded. For this reason, three items are eliminated as follows: "I have put too much into the nursing profession to consider changing now," "I believe people who have been trained in a profession have a responsibility to stay in that profession for a reasonable period of time," and "I am in nursing because of a sense of loyalty to it."

The original occupational commitment scale consisted of three dimensions as follows: affective commitment, continuance commitment," and "normative commitment". By conducting a factor analysis, it is found that occupational commitment scale is measured with three dimensions as in the original scale in this study. The affective commitment, normative commitment, and continuance commitment factor-loading values were 0.89-0.50, 0.82-0.72, and 0.76-0.62, respectively. Explained variances of the three factors and the total explained variance of the scale are as follows: "affective commitment" as the first factor explains 26% of the variance, "normative commitment" as the second factor explains 19% of the variance, and "continuance commitment" as the third factor explains 17% of the variance. The total explained variance is 62%. According to the result of the reliability analysis on the occupational commitment scale, the Cronbach alpha was 0.88, which indicates a high reliability value (26). As a result, after the factor and reliability analyses, the latest occupational commitment scale is the same as the original one, consisting of three dimensions.

**Descriptive Statistics and Correlation Analysis of Variables**

The correlations between variables, mean, and standard deviations are reported in Table 1.

Table 1 shows that job stress has a significant negative correlation with perceived organizational support ($r=-0.521$, $p<0.01$), occupational commitment ($r=-0.130$, $p<0.05$), and affective commitment ($r=-0.305$, $p<0.01$). Perceived organizational support has a significant positive correlation with occupational commitment ($r=0.391$, $p<0.01$), affective commitment ($r=0.433$, $p<0.01$), and normative commitment ($r=0.342$, $p<0.01$). Occupational commitment has a significant positive correlation with affective commitment ($r=0.727$, $p<0.01$), continuance commitment ($r=0.724$, $p<0.01$), and normative commitment ($r=0.806$, $p<0.01$). Affective commitment has a significant positive correlation with continuance commitment ($r=0.167$, $p<0.01$) and normative commitment ($r=0.402$, $p<0.01$). Continuance commitment has a significant positive correlation with normative commitment ($r=0.487$, $p<0.01$)

**Hypothesis Testing: Measuring Mediating Effect**

This study aimed to demonstrate that there is a mediating effect of perceived organizational support on the relationship between job stress and occupational commitment.

**Table 1.** Descriptive statistics and correlations for variables

| | M | SD | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|---|
| Job stress | 2.74 | 1.30 | 1 | -0.521** | -0.130* | -0.305** | 0.111 | -0.75 |
| Perceived organizational support | 2.85 | 1.12 | | 1 | 0.391** | 0.433** | 0.098 | 0.342** |
| Occupational commitment | 3.36 | 1.04 | | | 1 | 0.727** | 0.724** | 0.806** |
| Affective commitment | 3.64 | 1.08 | | | | 1 | 0.167** | 0.402** |
| Continuance commitment | 3.19 | 1.06 | | | | | 1 | 0.487** |
| Normative commitment | 3.26 | 1.00 | | | | | | 1 |

*Correlation is significant at the 0.05 level (two-tailed), **Correlation is significant at the 0.01 level (two-tailed), SD: Standard deviation

The research hypothesis for this study was determined as follows:

$H_1$: Perceived organizational support mediates the relationship between job stress and occupational commitment.

To measure the mediating effect, regression analysis was performed in three steps as suggested by Baron and Kenney (27). Table 2 shows that, in the first step of regression, job stress and occupational commitment were added to the model. According to regression analysis findings, there is a significant effect of job stress on occupational commitment (p=0.033 and <0.05). In the second step of the hypothesis, job stress and perceived organizational support were added to the model. According to regression analysis findings, there is a significant effect of job stress on perceived organizational support (p=0.000 and <0.05). In third and last step of hypothesis testing, to determine the mediating role of perceived organizational support on the relationship between job stress and occupational commitment, both steps were examined. The effect of perceived organizational support on occupational commitment is still significant (p=0.000 and <0.05). The result explained that perceived organizational support significantly affects occupational commitment. Also, the effect of job stress on occupational commitment when controlling perceived organizational support is insignificant. It can be stated that there is a fully mediating effect.

Accordingly, it can be concluded that there is a fully mediating effect of perceived organizational support on the relationship between job stress and occupational commitment. Also, it can be stated that if nurses have perceived organizational support, even if they experience job stress, their occupational commitment may increase. Thus, this reveals that $H_1$ is accepted.

## Discussion

This study included a quantitative study of nurses working in a foundation university hospital and aimed to examine the mediating role of perceived organizational support in the effects of job stress on occupational commitment.

According to the results of this study, there is a negative relationship between job stress and occupational commitment. This result is consistent with previous studies in the literature, which were conducted by Barouch Gilbert et al. (5), Jepson and Forrest (6), Klassen and Chiu (7), and Klassen et al. (8). When nurses are exposed to job stress, their occupational commitment may decrease as they cannot work peacefully and happily because of the pressure they have experienced.

Another result of this study is that there is a negative relationship between job stress and perceived organizational support. The studies by Adan-Gök et al. (28), Chen et al. (17), Dawley et al. (18), and Higazee et al. (29) supported this result. Job stress is usually the pressure that occurs on employees because of unfavorable working conditions. Stress caused by negative working conditions is actually an indicator that employees do not receive support from their organizations. In other words, when hospitals support their nurses, their perceptions of job stress may decrease as they will improve their working conditions.

Another result of this study is that there is a positive relationship between occupational commitment and perceived organizational support. This result is also supported with previous studies in the literature, which were conducted by Aydın and Kalemci Tüzün (13), Darolia et al. (14), Kuo et al. (30), and Singh et al. (31). Occupational commitment of employees who receive support from their organizations may increase. In other words, if nurses trust their hospitals and feel that they are by their side under all circumstances, their occupational commitment may increase.

The general result of the study is that perceived organizational support fully mediates the relationship between job stress and occupational commitment. In other words, results of this research claimed that although nurses work under job stress, their occupational commitment will be high when they receive support from their hospitals.

### Study Limitations

The fact that this study was conducted only on nurses working in a foundation university hospital does not mean that the findings will reflect on all nurses. In other words, the results obtained in the research are valid only for the limited universe participating in the research. For this reason, it is impossible to make a generalization about the results of the research beyond this. Another limitation of this study is that it was evaluated using a subjective approach based on nurses' opinions.

**Table 2.** Regression analysis

| Regression model<br>independent variable<br>mediating variable | Model 1<br>dependent variable<br>occupational commitment | | Model 2<br>dependent variable<br>perceived organizational support | | Model 3<br>dependent variable:<br>occupational commitment | |
|---|---|---|---|---|---|---|
| | β | p | β | P | β | p |
| Job stress | -0.130 | 0.033 | -0.521 | 0.000 | 0.101 | 0.126 |
| Perceived organizational support | | | | | 0.443 | 0.000 |
| R | 0.130 | | 0.521 | | 0.400 | |
| F | 4.606 | | 99.607 | | 25.476 | |
| T | -2.146 | | -9.980 | | 1.535<br>6.751 | |
| R2 | 0.013 | | 0.268 | | 0.154 | |

## Conclusion

Today, one of the most important problems faced by organizations is to ensure the sustainability of the employment of their employees who are committed to their occupations. Occupational commitment is the psychological link between employees and their profession, and it is the desire of individuals to continue their profession. Occupational commitment decreases because of the unfavorable working conditions that employees often encounter while performing their profession. At the same time, the unfavorable working conditions cause employees to experience job stress, which is a functional disorder that could arise from unfavorable work environment. In other words, employees may lose their commitment to their occupation because of the job stress they have experienced.

Organizations strive to increase the occupational commitment of their employees and use various factors. One of these factors is organizational support, which is the way organizations value and care for their employees. At the same time, organizational support reduces the job stress experienced by employees. In other words, employees who think that their organizations are by their side under all circumstances may have a low perception of job stress if they believe that they receive support from their organization.

Recently, the COVID-19 pandemic has been a major threat to the whole world and humanity. One of the occupational groups that took the first place in combating the epidemic was healthcare professionals. They are serving humanity by risking their own lives. As the pandemic still continues, the working conditions of healthcare professionals are getting harder with each passing day, and this situation causes job stress. Despite this, healthcare professionals worldwide serve humanity by dedicating themselves to their profession. This situation shows that the occupational commitment of healthcare professionals is high. In addition, another factor that may affect the occupational commitment of healthcare professionals is the support they receive from the hospitals they work for. With the support they receive in their hospitals, healthcare professionals feel that their hospitals are always with them and their occupational commitment increases, and job stress can be reduced. Therefore, the general result of this research is that although nurses are exposed to job stress, their occupational commitment will be high when they get support from their hospitals.

In this study, some suggestions were made for organizations and researchers. Organizations should develop policies that will increase the occupational commitment and perceived organizational support of their employees and reduce their job stress. For example, employees should be empowered, and their participation in decisions should be increased. Opportunities such as wage, rewards, and promotions should be done fairly, and equal opportunities to all employees should be provided. In addition, job descriptions of the employees should be reviewed and clearly stated. For example, bureaucratic workloads of nurses should be reduced, and they should be ensured to perform their professions. Moreover, organizations should carry out activities that will increase the motivation of employees. Various social activities should be organized to increase interaction and communication within the organization, such as celebrating employees' birthdays and organizing family picnics to attend together.

In future studies, the concepts of the leadership style, perceived supervisor support, personality, job satisfaction, motivation, organizational commitment, organizational justice, emotional labour, organizational culture and organizational climate should be addressed. In addition, it is thought that considering the distinction between private and public sectors will contribute to the field of social sciences.

### Ethics

**Ethics Committee Approval:** Bezmialem Vakıf University Rectorate Non-interventional Research Ethics Committee (number: E-54022451-050.05.04-15487/date: 06.05.2021).

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

### Authorship Contributions

Concept: M.K.S., Z.G., Design: M.K.S., Z.G., Data Collection or Processing: Z.G., Analysis or Interpretation: M.K.S., Literature Search: M.K.S., Z.G., Writing: M.K.S., Z.G.

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## References

1. Lee K, Carswell JJ, Allen NJ. A meta-analytic review of occupational commitment: relations with person- and work-related variables. J Appl Psychol 2000;85:799-811.
2. Meyer J, Allen NJ, Smith CA. Commitment to organizations and occupations: Extension and test of a three-component conceptualization. Journal of Applied Psychology 1993;78:538-51.
3. Blau G. On assessing the construct validity of two multidimensional constructs: Occupational commitment and occupational entrenchment. Human Resource Management Review 2001;11:279-98.
4. Blau G. Testing for a four-dimensional structure of occupational commitment. Journal of Occupational and Organizational Psychology 2003;76:469-88.
5. Barouch Gilbert R, Adesope OO, Schroeder NL. Efficacy beliefs, job satisfaction, stress and their influence on the occupational commitment of English-medium content teachers in the Dominican Republic. Educational Psychology 2014;34:876-99.
6. Jepson E, Forrest S. Individual contributory factors in teacher stress: the role of achievement striving and occupational commitment. Br J Educ Psychol 2006;76:183-97.
7. Klassen RM, Chiu MM. The occupational commitment and intention to quit of practicing and pre-service teachers: Influence of self-efficacy, job stress, and teaching context. Contemporary Educational Psychology 2011;36:114-29.

8. Klassen R, Wilson E, Siu AF, Hannok W, Wong MW, Wongsri N, et al. Preservice teachers' job stress, self-efficacy, and occupational commitment in four countries. European Journal of Psychology of Education 2013;28:1289-1309.
9. Parker DF, Decotiis TA. Organizational determinants of job stress. Organizational Behavior and Human Performance 1983;32:160-77.
10. Jamal M. Job stress and employee well-being: A cross-cultural empirical study. Stress & Medicine 1999;15:153-8.
11. Yıldız H, Koçoğlu Sazkaya M. Duygusal emek ile iş stresi ilişkisinin incelenmesi: kamu çalışanlarına yönelik bir araştırma. İstanbul Gelişim Üniversitesi Sosyal Bilimler Dergisi 2021;8:29-50.
12. Arshadi N, Damiri H. The relationship of job stress with turnover intention and job performance: Moderating role of OBSE. Procedia-Social and Behavioral Sciences 2013;84:706-10.
13. Aydın E, Kalemci Tüzün I. Organizational support sources and job performance relations: what about occupational commitment? Anatolia 2019;30:1-11.
14. Darolia CR, Kumari P, Darolia S. Perceived organizational support, work motivation, and organizational commitment as determinants of job performance. Journal of the Indian Academy of Applied Psychology 2010;36:69-78.
15. Koçoğlu M. Cynicism as a mediator of relations between job stress and work alienation: A study from a developing country-Turkey. Global Business and Management Research 2014;6:24-36.
16. Eisenberger R, Huntington R, Hutchison S, Sowa D. Perceived organizational support. Journal of Applied Psychology 1986;71:500-7.
17. Chen Z, Eisenberger R, Johnson KM, Sucharski IL, Aselage J. Perceived organizational support and extra-role performance: which leads to which? J Soc Psychol 2009;149:119-24.
18. Dawley DD, Andrews MC, Bucklew NS. Mentoring, supervisor support, and perceived organizational support: what matters most? Leadership & Organization Development Journal 2008;29:235-42.
19. DeConinck JB. The effect of organizational justice, perceived organizational support, and perceived supervisor support on marketing employees' level of trust. Journal of Business Research 2010;63:1349-55.
20. Fields DL. Taking the measure of work: a guide to validated scales for organizational research and diagnosis. Thousand Oaks CA: Sage Publications; 2002.
21. Jamal M, Baba VV. Shiftwork and department-type related to job stress, work attitudes and behavioral intentions: A study of nurses. Journal of Organizational Behavior 1992;13:449-64.
22. Koçoğlu M. Çalışanların örgütlerine yönelik girişimcilik yönelimi algıları, örgüt desteği, kariyer tatminleri ve işten ayrılma niyetleri arasındaki ilişkinin incelenmesi: Otomotiv sektöründe bir araştırma. Akademik Bakış Uluslarası Hakemli Sosyal Bilimler Dergisi 2013;35:1-20.
23. Nair P K. A Path Analysis of relationships among job stress, job satisfaction, motivation to transfer, and transfer of learning: perceptions of occupational safety and health administration outreach trainers (dissertation). Texas A&M University College Station: 2007.
24. Durmuş B, Yurtkoru ES, Çinko M. Sosyal bilimlerde SPSS'le veri analizi. Istanbul: Beta Yayıncılık; 2011.
25. Hair Jr F. Joseph, Anderson, E. Rolph, Tatham, L. Ronald, and Black, C. William. multivariate data analysis. Upper Saddle River, NJ: Prentice Hall Inc.; 1998.
26. Sekaran U. Research method for business: A skill building approach. USA: John Wiley & Sons; 1992.
27. Baron RM, Kenney DA. The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. Journal of Personality and Social Psychology 1986;51:1173-82.
28. Adan-Gök Ö, Akgündüz Y, Alkan C. The effects of job stress and perceived organizational support on turnover intentions of hotel employees. Journal of Tourismology 2017;3:23-32.
29. Higazee MZA, Rayan A, Khalil M. Relationship between job stressors and organizational support among Jordanian nurses. American Journal of Nursing Research 2016;4:51-5.
30. Kuo MHC, Chang Y, Chang WC. Perceived organizational support as a mediator of managerial coaching skills and occupational commitment. Public Administration Research 2014;3:17-32.
31. Singh R, Zhang Y, Wan M, Fouad NA. Why do women engineers leave the engineering profession? The roles of work–family conflict, occupational commitment, and perceived organizational support. Human Resource Management 2018;57:901-14.

Original Article

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# Comparison of Knowledge Levels of Nursing Students and Clinical Nurses Related to Hemogivigilance: Preliminary Work to Develop a Measurement Tool

## Hemşirelik Öğrencileri ve Klinik Hemşirelerin Hemovijilans ile İlgili Bilgi Düzeylerinin Karşılaştırılması: Ölçüm Aracı Geliştirme Ön Çalışması

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## ABSTRACT

**Objective:** In this study, it was aimed to evaluate the knowledge level of the nursing students and clinical nurses who have applied the clinical practice related to hemogivigilance.

**Methods:** This research was comparative and cross-sectional in design. The measurement tool consisted of two parts in the collection of research data. The first part included the demographic variables, and the second part consisted of "hemovigilance information index" created by the researcher. The sample was completed with 146 nursing students and 137 clinical nurses working in the hospital for clinical practice, who volunteered to participate in the research. Ethical permissions were obtained from the Ankara Yıldırım Beyazıt University Ethics Committee to conduct the research.

**Results:** It was concluded that there was a significant relationship between having knowledge about hemovigilance or hemovigilance nursing, thinking of being competent about hemovigilance, self-sufficiency about blood transfusion, having knowledge about the meaning of the term "near miss" about hemovigilance, knowledge about the transfusion follow-up form, late and early reactions that might occur as a result of blood transfusion, and the number of correct answers ($p<0.05$).

**Conclusion:** It was concluded that the knowledge level increased as the clinical experience increased in nursing student. It was

## ÖZ

**Amaç:** Bu araştırmada, klinik ders uygulamasını yapmış hemşirelik öğrencilerinin ve klinik hemşirelerinin hemovijilans ile ilgili bilgi düzeylerinin değerlendirilmesi amaçlanmıştır.

**Yöntemler:** Bu araştırma karşılaştırılmalı ve kesitsel olarak tasarlanmıştır. Araştırma verilerinin toplanmasında kullanılan ölçüm aracı iki bölümden oluşmaktadır. Birinci bölüm demografik değişkenleri içermekte, ikinci bölüm ise araştırmacı tarafından oluşturulmuş "hemovijilans bilgi indeksi" tamamlanmıştır. Klinik uygulama için hastanede çalışan, araştırmaya katılımı gönüllü olan 146 hemşirelik öğrencisi ve 137 klinik hemşiresi ile örneklem tamamlanmıştır. Araştırmanın yapılabilmesi için etik izinler Ankara Yıldırım Beyazıt Üniversitesi Beşeri ve Sosyal bilimler Etik Kurulu'ndan alınmıştır.

**Bulgular:** Hemovijilans ya da hemovijilans hemşireliği hakkında bilgi durumu, hemovijilans konusu hakkında yeterli olduğunu düşünme, konu ile ilgili eğitim gerekliliği, hemovijilans ile ilgili "ramak kala" teriminin anlamı, transfüzyon izlem formu hakkında bilgi durumu ve kan transfüzyonu sonucunda oluşabilecek reaksiyonlar hakkında bilgi sahibi olma durumu ile doğru sayısı arasında anlamlı farklılık olduğu sonucuna ulaşılmıştır ($p<0,05$).

**Sonuç:** Öğrenci hemşirelerde klinik deneyim arttıkça bilgi düzeyinin arttığı sonucuna varılmıştır. Klinik hemşirelerin hemovijilans ile

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determined that clinical nurses had a high level of knowledge related to hemovigilance and students did not. In-service trainings were found to be sufficient in this regard.

**Keywords:** Hemovigilance, nurse, blood and blood products, transfusion, hemovigilance nursing

ilgili bilgi düzeylerinin yüksek olduğu, öğrencilerin ise istenen düzeyde olmadığı belirlenmiştir. Hizmetiçi eğitimlerin bu konuda yeterli olduğu görülmüştür.

**Anahtar Sözcükler:** Hemovijilans, hemşire, kan ve kan ürünleri, transfüzyon, hemovijilans hemşireliği

## Introduction

Since collecting, storing, transporting and transfusing blood and blood products for therapeutic purposes within the scope of health care services is an important service, it should be carried out in accordance with the standards (1). In our country, the current regulations regarding the blood supply system have been made within the scope of the main directive numbered 2002/98/EC, which is also included in the closing criteria of the 28th chapter titled "Protection of the Consumer and the Health of the Consumer" (2). Establishing standardized definitions for adverse events is crucial to achieving the goal of all surveillance systems (3). In this direction, in the main directive, hemovigilance is defined as "a series of surveillance that covers the entire transfusion chain, including the follow-up after blood collection and delivery to the recipient, collecting and evaluating all kinds of undesirable and unexpected effects arising from the use of blood products, preventing these events and preventing their reoccurrence" (4).

The first official studies on hemovigilance started with the establishment of the blood monitoring system by the "Blood Transfusion Committees" in France in 1991. It was implemented in Canada in 1997 after the Krever report. With the establishment of SHOT (serious hazards of transfusion) in 1997 in England, notifications of hemovigilance began. With the establishment of European Hemovigilance Network in 1998, an international analysis platform was formed. The European Blood Directive 2002/98/EC was published on 8 February 2003 (4). In this directive, on October 1, 2005, regulations were made on traceability, serious side effects and quality and standards of blood institutions. In 2005, many countries outside of Europe developed their national hemovigilance systems and became involved in this communication network. In 2006, a hemovigilance program was established in the USA with the American Association of Blood Banks. Hemovigilance information exchange has been continuing at the international level with International Hemovigilance Network since 2009 (5). Studies have been initiated in our country in line with the "EU legislation to adapt", and the National Hemovigilance Guide was created in 2013 and published in 2016 (2).

The aim of hemovigilance is to determine the cause of unexpected situations in blood transfusion and to prevent their reoccurrence, and as a result, to ensure safe blood transfusion (6). For this purpose, issues such as inadequate blood supply structure, insufficient blood supply, increased need, unequal distribution, weak quality systems, risks of infection transmitted by transfusion, and inappropriate use of blood products are priorities in ensuring blood transfusion safety, especially in healthcare services in developing countries (7). Hemovigilance is an important part of the quality system for blood transfusion. It includes methods for identifying errors, adverse events, and reactions, such as alert systems, complaint investigation, traceability systems, notification systems, and application controls (6).

Situations related to the collection, testing, processing, storage, distribution of blood and blood products and which can cause death, permanent and significant disability, disability, hospitalization or prolonged hospital stay in individuals as a result of transfusion of affected products are defined as serious adverse events. Serious undesirable effects and adverse events that occur in the patient during and after blood and blood product transfusion form the basis of the hemovigilance system and must be reported (8) These are;

- Early undesirable serious effects are hemolysis during transfusion, non-hemolytic fever reaction, rash, erythema, urticaria, anaphylactic shock, bacterial contamination, and transfusion-induced acute lung injury.
- Delayed undesirable serious effects are hemolysis, transfusion-associated graft versus host disease, post-transfusion purpura, and elevation in ALT level.
- Virus, parasite or prion contamination.
- Development of alloimmunization against erythrocyte, human leukocyte antigen or platelet antigens. At the same time, undesirable events may occur in the donor (9).
- Hemovigilance is a control system that every healthcare worker responsible for transfusion of blood and blood products should know. Nurses are active members of this system. The role of nurses in hemovigilance is clearly stated in the "National Guide to Hemovigilance" published in 2016. These roles are;
- Every personnel with duties and responsibilities related to transfusion can make notifications about hemovigilance. The hemovigilance officers of the relevant clinics and the hospital hemovigilance nurse are responsible for making these notifications appropriately.
- The hemovigilance nurse checks whether the forms submitted to him/her are filled in appropriately and completely and reports the situation to the hemovigilance committee.

- In case of a problem with transfusion, if the hemovigilance nurse receives information from the responsible physician that the problem is due to non-transfusion reasons, he/she notifies the hemovigilance committee.
- The nurse or doctor working in the relevant clinic is responsible for the hemovigilance clinic. He/she is responsible for transmitting the Transfusion Monitoring Form of the patients and other data requested for the sustainability of the hemovigilance system to the hemovigilance nurse.
- The hemovigilance nurse organizes trainings.
- The hemovigilance nurse informs the hemovigilance committee about the activities (2).

**Definition of the Problem**

Definitions are available for a better understanding of hemovigilance. These are adverse event, serious adverse event, serious uneventful transfusion errors, incorrect transfusion, near miss, adverse reaction, serious adverse reaction, patient-to-donor tracking (Trace-back), donor-to-patient tracking (Look-back), recall, return, and association (2). Clear definitions of the concept of hemovigilance are important for both reporters and those who will analyze reports. Reporting adverse events as soon as possible is essential for quality assurance. Serious adverse events should be reported promptly. Hemovigilance systems provide rapid assessment of serious reports by the hemovigilance task group and additional information requested shortly after reporting. The reporter sometimes needs advice on root cause analyzes and corrective and preventive measures. Health professionals in the hemovigilance committee can provide advice and assistance (10).

It is clear that hemovigilance systems and staff can help collect and analyze the necessary data. Training of hospital transfusion committees, transfusion workers, clinicians and laboratory personnel play an important role in controlling the hemovigilance systems of transfusion units. In summary, optimal use of the hemovigilance system, consensus, common criteria, analysis and regulatory measures are required for the periodic evaluation of hemovigilance studies. At the same time, these studies can support developments (11).

Due to the recent history of hemovigilance, there is a lack of information among healthcare professionals (12). In the healthcare field, the term hemovigilance focuses on transfusion. However, the transfusion constitutes a part of the hemovigilance (4). Studies in the literature focuse on transfusion. Studies involving all components of hemovigilance are insufficient. For this reason, the level of knowledge of healthcare workers on hemovigilance in studies is compared with studies on transfusion (13). Studies emphasized that the knowledge levels of both nurses and nursing students about hemovigilance were insufficient (13-15). Similar results were observed in studies conducted with physician groups (16). For this reason, effective training of healthcare professionals on hemovigilance during clinical or school periods is necessary for quality systems, patient safety, and reduction of malpractices. A structured measurement tool is needed to monitor the process, to feed back when necessary, and to measure the success of the trainings. In this study, it was aimed to determine the knowledge levels of nursing students and clinical nurses who practiced clinical courses for knowledge, skills and experience, and to create an applicable semi-structured scale. Hemovigilance is accepted as a new term in the world and in our country. For this reason, the literature on this subject is not sufficient. In this direction, our study question was "How is the knowledge level of nursing students and clinical nurses about hemovigilance and related concepts?".

## Methods

**Research Type**

In this study, a comparative, cross-sectional study was conducted in order to evaluate the knowledge levels of nursing students and clinical nurses about hemovigilance who did clinical course practice.

**Universe Sample Selection**

The population of the research consisted of all nursing students studying at a state university in Ankara and all clinical nurses working in a public hospital. In the study, 146 nursing students and 137 clinical nurses who agreed to participate in the study on a voluntary basis were included without choosing a sample.

**Data Collection Tool**

**Demographic Data Form:** The data form created by the researchers was used. In this form; age, gender, presence of smart device, duration of daily use of smart device, monthly internet usage quota, research related to the occupation, information about hemovigilance and where this information was obtained, and level of knowledge about hemovigilance and training on this subject, were recorded. In the form, nursing students were asked what grade they were in, while nurses were asked in which clinic they worked.

**Hemovigilance Information Index:** It was created by the researchers in line with the literature. Seven of the questions (1,2,12,13,15,17,20) were asked to measure attitude. The remaining questions were directed to the students in order to measure the level of knowledge. The answers given to these questions, which we directed to determine the level of knowledge, were evaluated.

**Obtaining Expert Opinion/Scope Validity Index:** Items created for the hemovigilance information index were examined by a total of 10 experts in the field of nursing. The SVI values of the expressions for the created knowledge index were found to be between 0.80 and 1.00, and the average SVI value was found to be 0.92. In line with expert opinions; some of the items that were not understood, had similar meanings, contained more than one judgment and were stated not to measure attitude were corrected, and some items were removed completely. The form took its final version after expert opinions.

### Application

Data collection tools were applied at the end of a suitable course determined according to the curriculum of the students and it took approximately 20 minutes for each form to collect the data. It was applied to the nurses in a face-to-face manner during working hours after obtaining the institutional permissions. It took about 10 minutes to fill out the questionnaire.

### Ethical Aspect of Research

In order to carry out the research, permission was obtained from the institution where the study was conducted and approval from the Ankara Yıldırım Beyazıt University Ethics Committee (29.05.2019/decision no: 51) was obtained. Data were collected in accordance with the Declaration of Helsinki. Participants were informed about the purpose of the research, its content and the way the data were collected. Participants were given confidence that their participation in the study was voluntary, that their information would be kept confidential, and that they could withdraw from the study at any time.

### Statistical Analysis

The IBM SPSS Statistics 22.0 (IBM Corp. Released 2014. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) was used to evaluate the data. Non-parametric tests were used for statistical analysis since the data did not show normal distribution. Percentage, frequency and mean were used for descriptive statistics Kruskal-Wallis H, Mann-Whitney U, t-test and chi-square test were used to evaluate the data. The results were evaluated within the 95% confidence interval. Statistical significance level was accepted as $p<0.05$.

## Results

The ages of the nurses participating in the study ranged from 20 to 54, with an average of 32.17±8.43. The demographic data of the participants are given in Table 1. Women constitute the majority of the participants in both groups. Of the students 32.19% were first year students, and 43.06% of the nurses were working in internal medicine units. The highest use of smart devices by both groups was found in 2-4 hours, and the database they used for professional research was Google scholar. While the monthly internet usage quota of the students was 4-6 gb (Gigabytes), it was 10 gb or above in the nurses. Nurses had more knowledge about hemovigilance or hemovigilance nursing, and while students obtained this information via the internet, nurses obtained this information via in-service training. Both groups stated that the students did not have sufficient knowledge about hemovigilance and that education on this subject was important. The numbers of correct answers of clinical nurses and student nurses regarding hemovigilance are given in Table 2.

When the nursing students were examined, it was determined that there was a significant difference between the class variable and the number of correct answers. It was determined as a result of statistical tests that this difference was due to the fact that the number of correct answers of 1st year students was lower than that of 3rd and 4th year students. It was concluded that there was a significant relationship between having knowledge about hemovigilance or hemovigilance nursing, thinking of being competent about hemovigilance, self-sufficiency about blood transfusion, having knowledge about the meaning of the term "near miss" about hemovigilance, knowledge about the transfusion follow-up form, late and early reactions that might occur as a result of blood transfusion, and the number of correct answers ($p<0.05$).

When the clinical nurses were examined, it was determined that there was a significant difference between the units they worked in and the number of correct numbers. It was determined as a result of statistical tests that this difference was due to the fact that the correct number of answers of the nurses working in emergency service was higher than those working in surgical units and intensive care units. It was concluded that there was a significant relationship between having knowledge about hemovigilance or hemovigilance nursing, thinking of being competent about hemovigilance, self-sufficiency about blood transfusion, having knowledge about the meaning of the term "near miss" about hemovigilance, knowledge about the transfusion follow-up form, late and early reactions that might occur as a result of blood transfusion, and the number of correct answers ($p<0.05$).

## Discussion

Individuals who agreed to participate in our study were examined in two groups as nursing students and clinical nurses. Nursing students made up 51.59% of the sample, while clinical nurses made up 48.41% of the sample. Students participating in the study covered all classes, while nurses were working in internal medicine units (43.06%), surgical units (30.66%), intensive care (13.87%) and emergency services (12.41%). In the study conducted by Jimenez-Marco et al. (17) on hemovigilance, they reported that the nurses worked in surgery service (27.27%), internal medicine service (22.04%), emergency service (16.8%), blood bank (11.85%) and intensive care unit (11.29%). In another study on hemovigilance nursing by Gün et al. (13), the working units of the nurses were as follows: Intensive care unit (35.0%), emergency room (6.9%), internal medicine service (6.9%), pediatrics service (7.6%), gynecology service (6.3%), general surgery service (5.8%) and laboratory (7.9%).

Nursing students' knowledge levels were evaluated based on the number of correct answers, and it was found that the range of number of correct answers was 0-13, and the mean level of knowledge was 4.00±3.72. It was found that the number of correct answers for the knowledge level of clinical nurses was between 2 and 13, and the mean of correct answers was 10.36±2.00. It was determined that there was a significant difference in terms of the means of the correct answers between nurses and nursing students. This difference led us to conclude that in-service training in the hospital was effective, while nursing students were lacking in education on this subject. It was determined that 64.23% of the nurses within the scope of the study received hemovigilance training in in-service training.

**Table 1.** Comparison of demographic data of nursing students and clinical nurses

| | | Nursing student | | Clinical nurse | |
|---|---|---|---|---|---|
| Variables | Groups | Sample (n=146) | Percentage (%) | Sample (n=137) | Percentage (%) |
| Gender | Woman | 131 | 89.73 | 119 | 86.86 |
| | Man | 15 | 10.27 | 18 | 13.14 |
| Class | 1st class | 47 | 32.19 | - | - |
| | 2nd class | 40 | 27.40 | | |
| | 3rd class | 35 | 23.97 | | |
| | 4th class | 24 | 16.44 | | |
| Work place | Surgery unit | - | - | 42 | 30.66 |
| | Internal medicine unit | | | 59 | 43.06 |
| | Intensive care unit | | | 19 | 13.87 |
| | Emergency | | | 17 | 12.41 |
| Daily smart device usage | 0-2 hours | 9 | 6.16 | 31 | 22.63 |
| | 2-4 hours | 46 | 31.51 | 41 | 29.92 |
| | 4-6 hours | 41 | 28.08 | 29 | 21.17 |
| | 6-8 hours | 34 | 23.29 | 25 | 18.25 |
| | 8-10 hours | 11 | 7.53 | 11 | 8.03 |
| | 10 hours or above | 5 | 3.42 | 0 | 0 |
| Monthly internet usage quota | 0-2 gb | 6 | 4.11 | 12 | 8.76 |
| | 2-4 gb | 30 | 20.55 | 12 | 8.76 |
| | 4-6 gb | 33 | 22.60 | 30 | 21.90 |
| | 6-8 gb | 29 | 19.86 | 17 | 12.41 |
| | 8-10 gb | 18 | 12.33 | 30 | 21.90 |
| | 10 gb or above | 30 | 20.55 | 36 | 26.27 |
| The database used for professional research | Google Schoolar | 72 | 49.32 | 82 | 59.85 |
| | Youtube Videos | 15 | 10.27 | 37 | 27.00 |
| | Pubmed-Medline | 8 | 5.48 | 20 | 14.60 |
| | Any website | 51 | 34.93 | 46 | 33.58 |
| | Other | 0 | 0 | 17 | 12.41 |
| Do you know about hemovigilance or hemovigilance nursing? | Yes | 28 | 19.18 | 131 | 95.62 |
| | No | 118 | 80.82 | 6 | 4.38 |
| Where did you get this information? | Internet | 19 | 13.01 | 30 | 21.90 |
| | Undergraduate courses | 8 | 5.48 | 50 | 36.50 |
| | Television | 0 | 0 | 2 | 1.46 |
| | Friend shares | 0 | 0 | 12 | 8.76 |
| | In-service training | 0 | 0 | 88 | 64.23 |
| | Other | 6 | 4.11 | 4 | 2.92 |
| Do you think you have enough knowledge about hemovigilance? | Yes | 3 | 2.05 | 75 | 54.74 |
| | No | 143 | 97.95 | 62 | 45.26 |
| Do you think it is necessary and important to receive training on hemovigilance? | Yes | 127 | 86.99 | 132 | 96.35 |
| | No | 19 | 13.01 | 5 | 3.65 |

**Table 2.** Evaluation of knowledge attitudes of nursing students and clinical nurses

| | Mean of correct answers | Correct answers (min-max) |
|---|---|---|
| **Nursing student** | 4.00±3.72 | 0-13 |
| **Clinical nurse** | 10.36±2.00 | 2-13 |

Min: Minimum, Max: Maximum

**Table 3.** Statistics on the average of various variables and correct numbers of nursing students and clinical nurses

| | | Nursing student | Clinical nurse |
|---|---|---|---|
| Variable | Group | Mean of correct answers | Mean of correct answers |
| Gender | Woman | 3.58±3.22 | 10.38±1.81 |
| | Man | 4.47±4.10 | 10.22±3.04 |
| | | Z=-0.738; p=0.460 | t=0.307; p=0.759 |
| Class | 1st class | 2.68±2.87 | |
| | 2nd class | 3.88±3.24 | |
| | 3rd class | 4.51±3.74 | - |
| | 4th class | 4.04±3.31 | |
| | | **$x^2$=7.818; p=0.049** | |
| Wok place | Surgery unit | | 9.95±1.82 |
| | Internal medicine unit | | 10.73±1.78 |
| | Intensive care unit | - | 9.53±2.97 |
| | Emergency | | 11.00±1.37 |
| | | | **F=3.068; p=0.030** |
| Daily smart device usage | 0-2 hours | 2.89±3.86 | 10.94±1.61 |
| | 2-4 hours | 3.28±2.86 | 10.34±2.25 |
| | 4-6 hours | 4.10±3.82 | 10.00±2.17 |
| | 6-8 hours | 3.94±3.22 | 10.16±1.67 |
| | 8-10 hours | 3.54±3.30 | 10.18±2.18 |
| | 10 hours or above | 3.60±3.44 | - |
| | | $x^2$=1.506; p=0.912 | x2=4.456; p=0.348 |
| Monthly internet usage quota | 0-2 gb | 3.17±3.60 | 10.17±1.80 |
| | 2-4 gb | 3.80±3.20 | 10.67±1.15 |
| | 4-6 gb | 4.10±3.28 | 9.93±2.35 |
| | 6-8 gb | 4.72±3.57 | 10.58±1.62 |
| | 8-10 gb | 2.11±2.30 | 10.50±2.11 |
| | 10 gb or above | 3.10±3.45 | 10.44±2.09 |
| | | $x^2$=9.222; p=0.101 | $x^2$=1.917; p=0.860 |
| Do you know about hemovigilance or hemovigilance nursing? | Yes | 7.82±2.60 | 10.67±1.56 |
| | No | 2.69±2.64 | 6.82±2.99 |
| | | **Z=-6.594; p=0.000** | **Z=-4.154; p=0.000** |
| Do you think you have enough knowledge about the subject? | Yes | 9.00±1.73 | 10.89±1.48 |
| | No | 3.56±3.25 | 9.71±2.34 |
| | | **Z=-2.433; p=0.015** | **t=3.598; p=0.000** |
| Is training required on the subject? | Yes | 3.95±3.35 | 10.38±1.90 |
| | No | 1.79±2.39 | 9.80±4.15 |
| | | **Z=-2.904; p=0.004** | Z=-0.310; p=0.756 |
| I do not consider myself sufficient about blood transfusion. | Yes | 3.87±3.27 | 9.70±2.36 |
| | No | 3.90±3.52 | 10.75±1.73 |
| | Not sure | 3.13±3.28 | 10.21±1.97 |
| | | $x^2$=2.152; p=0.341 | **F=3.575; p=0.031** |
| I know what "near miss" means as a hemovigilance term. | Yes | 6.71±3.69 | 10.86±1.65 |
| | No | 4.87±3.66 | 9.79±2.46 |
| | Not sure | 2.35±2.81 | 9.68±1.94 |
| | | **$x^2$=17.892; p=0.000** | **F=5.676; p=0.004** |

**Table 3.** contiuned

| Variable | Group | Nursing student<br>Mean of correct answers | Clinical nurse<br>Mean of correct answers |
|---|---|---|---|
| I have information about the transfusion follow-up form. | Yes | 4.88±3.27 | 10.48±1.84 |
| | No | 3.77±3.46 | - |
| | Not sure | 1.83±2.37 | 8.38±3.29 |
| | | **$x^2$=30.743; p=0.000** | **Z=-1.970; p=0.049** |
| I know what are the early and delayed reactions that may occur as a result of blood transfusion. | Yes | 4.73±3.41 | 10.41±1.97 |
| | No | 3.23±3.14 | 8.00±5.20 |
| | Not sure | 2.40±2.75 | 10.41±1.44 |
| | | **$x^2$=17.753; p=0.000** | **$x^2$=0.985; p=0.611** |

Z: Mann-Whitney U, F: One-way ANOVA, t: Independent groups t test, x2: Kruskal-Wallis H

In a study on hemovigilance, the knowledge level of 135 health personnel was evaluated out of 24 points, and they scored 16.30±3.16. They concluded that the highest score among the groups belonged to nurses and the lowest score belonged to nursing students (14). In another study, they reported that the scores of the group they worked with (nurse, doctor, other health worker) varied between 1 and 19 (out of 20) and their average was 9.7±4.2. In the same study, they found that the mean knowledge of nurses was 10.0±4.2 (13). In another study on blood transfusion with midwives in a maternity hospital, the rate of correct answers was found to be between 5% and 98%, depending on the questions (18). In the study conducted by Shamshirian et al. on nursing students, it was found that only 25.9% of nursing students had knowledge and awareness about blood transfusion (15). In another study, care standards for hemovigilance were evaluated instead of knowledge level, and as a result, neonatal clinics reported that the compliance rate of nurses working in neonatal intensive care units was 56% (19).

It was determined that there was a statistically significant difference between the class years and knowledge levels of nursing students (p=0.049). As a result of the statistics, it was determined that the difference was due to the fact that the knowledge levels of the 3rd and 4th year students were higher than the other students. In our study, it was found that there was a statistically significant difference between the unit they worked in and their level of knowledge (p=0.030). As a result of the statistics, it was determined that the knowledge levels of nurses working in the intensive care unit were lower than the other units. In the study of Gün et al. (13), it was found that there was no significant difference between the working units and the level of knowledge of hemovigilance. In a study conducted in a group of physicians, they reported that those working in the internal medicine achieved highest score and those working in the anesthesia department achieved the second highest score (16). In a study conducted by Rudrappan, it was found that there was no relationship between the clinical experience of the nurse and their knowledge and practices (20). We think that the fact that students take more active roles in the clinic with the following years has a positive effect on their level of knowledge. In the findings, the distribution of in-service training according to the units was examined. As a result, it was determined that only 36.84% (n=7) of the nurses working in the intensive care unit participated in in-service training. It was determined that more than half of the nurses working in other clinics participated in hemovigilance training. It was thought that the result was due to the low rate of participation in in-service training on hemovigilance.

In our study, it was concluded that there was a significant difference between those who answered "yes" to the question "Do you have information about hemovigilance or hemovigilance nursing?" and those who answered "no" in both groups. The percentage of those who answered this question was 19.18% among nursing students and 95.62% among clinical nurses. According to the research sources, it was determined that nursing students obtained the most information about hemovigilance from the internet t, and clinical nurses obtained the most from in-service training. In a study, 55.55% of the doctors and 9.09% of the nurses who participated in the study reported that they knew the term hemovigilance (21). In a study by Aneke et al. (22), it was reported that the majority of the participants were not aware of the transplant units or committees for hemovigilance. In the literature, when the nurses were questioned whether they participated in training programs such as in-service training and seminars related to hemovigilance, 9.24-10% of them stated that they participated (23,24). In the study of Jimenez-Marco et al. (17), 76.03% of the nurses stated that they did not receive any formal training on transfusion before starting to work at the workplace, and that 83.75% of the nurses did not receive in-service training during their work in their hospitals. Unlike the literature, the clinical nurses participating in our study received in-service training on the subject with a rate of 64.23%. In our study, the insufficient knowledge of nursing students on this subject made us think that it was not included in the core curriculum followed in undergraduate nursing programs in our country. Given that the most common source for student nurses to learn about hemovigilance was the internet, it was believed that they could obtain insufficient, incomplete and incorrect information from the internet.

The question "Do you think you have enough knowledge about the subject?" was directed to the participants of the study. It was found that the knowledge levels of the group who

answered "yes" to the questions "I know what "near miss" means as a hemovigilance term" and "I have information about the transfusion monitoring form" were statistically significant in both groups ($p<0.05$). It was determined that the knowledge level of the group who answered "yes" was higher. In line with this result, it was thought that the group who thought that they had inadequate knowledge on the subject could increase their awareness on this issue. At the same time, with this result, it was determined that individuals could correctly identify their deficiencies in terms of knowledge and were aware of these deficiencies. In a study where nurses were asked a different question "Do you think the reactions are dangerous?", 70% of the nurses answered "yes" to the question (25). In the study of Jimenez-Marco et al. (17), it was found that nurses who received transfusion training felt that they had a better level of knowledge than those who did not receive training. It was found that the level of knowledge of those who answered "yes" to the statement "I don't have enough knowledge about blood transfusion" was lower than those who answered "no". In line with the literature, this result suggests that the level of knowledge of nurses affects their self-confidence in practice.

In our study, it was questioned whether education about hemovigilance was necessary. Of the students, 86.99% and 96.35% of the nurses reported that they thought education was necessary and important. At the same time, it was found that there was a significant difference between the knowledge levels of nursing students who answered "yes" to this question and those who answered "no" ($p=0.004$). There was no significant difference in nurses. In a study conducted with midwives, their knowledge of blood transfusion was questioned, and 99.2% of midwives reported that education was necessary (18). In another study, 63% of nurses reported that they had participated in a blood bank training program before (20). In the studies in the literature, the effects of the education on the level of knowledge were evaluated by making a pre- and post-education evaluation, and they found that the trainings were effective and positive (13,26). Raising awareness about hemovigilance through in-service training will lead to improved reporting of transfusion reactions (23). Most of the graduates have a positive attitude towards transfusion reaction reporting, but their knowledge of the hemovigilance program is weak and the reporting procedure is less common in recent graduates (24). Reporting and data collection should not be the sole purpose of the hemovigilance system, and the use of hemovigilance data sources in practice may be beneficial to increase transfusion safety (17).

### Study Limitations

The groups compared in our study were studied as a single center in their own universe. The universe was accepted as a sample and all individuals who voluntarily agreed to participate in the study were included in the study. Therefore, power analysis was not performed. One of the limitations of our study was that our results could only be generalized to the sample group.

## Conclusion

It was determined that clinical nurses had a high level of knowledge about hemovigilance, while students did not. It was concluded that as the clinical experience of nursing students increased, the level of knowledge increased. The database in which both groups used for research was determined as any website after Google scholar. Due to the low level of hemovigilance knowledge of nursing students, necessary studies can be done to include this subject in the nursing education curriculum. It is recommended to support nurses with continuous training after graduation in terms of the directly proportional development of behavior, attitude and clinical skills. It is thought that in-service trainings are functional in this regard, and their awareness and knowledge about hemovigilance will increase by working integrated with the clinic and including nursing students in in-service training. The applicability of the HII was found to be effective, but it was recommended to update it in terms of measurement and evaluation and develop a fully structured scale in similar groups.

### Ethics

**Ethics Committee Approval:** In order to carry out the research, permission was obtained from the institution where the study was conducted and approval from the Ankara Yıldırım Beyazıt University Ethics Committee (29.05.2019/decision no: 51) was obtained.

**Informed Consent:** Obtained.

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

### Authorship Contributions

Concept: A.K., E.T., Design: A.K., E.T., Data Collection or Processing: A.K., E.T., Analysis or Interpretation: A.K., E.T., Literature Search: A.K., E.T., Writing: A.K., E.T.

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## References

1. Transfüzyon öncesi uygunluk testleri. In: Uluhan R, Berkem R, Emekdaş G, Bayık M, editors. Temel Kurs kitabı. 1st ed. İstanbul, Şan Ofset. 2010:76-84.
2. T.C. Sağlık Bakanlığı. Ulusal Hemovijilans Rehberi. 2016:6.
3. Whitaker BI, Belov A, Anderson SA. Progress in US hemovigilance: can we still learn from others? Transfusion 2019;59:433-6.
4. European Union. Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety forthe collection, testing, processing, storage and distribution of human blood and blood component sandamending Directive 2001/83/EC. Official Journal of the European Union 2003;33:30.
5. Atilla E, Arslan Ö. Hemovigilance. Türkiye Klinikleri Hematology-Special Topics 2013;6:7-15.

6. de Vries RR, Faber JC, Strengers PF; Board of the International Haemovigilance Network. Haemovigilance: an effective tool for improving transfusion practice. Vox Sang 2011;100:60-7.
7. Chew E, Benjamin RJ, McDonald CP, Wiersum-Osselton JC, WoodEM, International Society of Blood Transfusion Working Parties on Transfusion-Transmitted Infectious Diseases (Bacterialsubgroup) and Haemovigilance. International survey on definitions and current practices in prevention, diagnosis, management and reporting of transfusion-transmittedbacterialinfections. ISBT Science Series 2015;10:31-40.
8. T.C. Erciyes Üniversitesi Sağlık Uygulama ve Araştırma Merkezi. Hemovijilans Kapsamında Kan ve Kan Ürünlerinin Transfüzyon Endikasyonları ve Transfüzyon Reaksiyonlarına Yaklaşım Kılavuzu. Temmuz 2017.
9. T.C. Sağlık Bakanlığı. Ulusal kan ve kan ürünleri rehberi. Türkiye Kan Merkezleri ve Transfüzyon Derneği, Çesa Basım Hizmetleri 2011:1-329.
10. Steinsvåg CT, Espinosa A, Flesland Ø. Eight years with haemovigilance in Norway. What have we learnt? Transfus Apher Sci 2013;49:548-52.
11. Reesink HW, Panzer S, Gonzalez CA, Lena N, Muntaabski P, Gimbatti S, et al. Haemovigilance for the optimal use of blood products in the hospital. Vox Sang 2010;99:278-93.
12. Ait Bouchrim SA, Haddad A, Bou Assi T, Oriol P, Guyotat D, Bois C, et al. Residents' knowledge in transfusion medicine and educational programs: A pilot study. Transfus Clin Biol 2020;27:18-24.
13. Gün R, Öz S, Altındiş S, Uyutan Y, Köroğlu M, Altındiş M. Hemovijilans hemşireliği ve transfüzyon güvenliğine katkısı. Turk Hij Den Biyol Derg 2019;76:405-14.
14. Jafari E, Koohestani S, Ghaziizade M. Knowledge among health care workers about hemovigilance in hospitals of Kerman in 2018. Scientific Journal of Iran Blood Transfus Organ 2019;16:280-8.
15. Shamshirian A, Alirahimi Z, Ghorbanpour A, Motamen S, Maadi N, Zamani P, et al. Knowledge and Awareness of Nursing Students on Blood Transfusion. Int J Med Invest 2017;6:129-34.
16. Philip J, Kumar S, Chatterjee T, Mallhi RS. Knowledge of Transfusion Medicine Among Resident Doctors in Clinical Specialities: A Cross-Sectional Study from a Tertiary Care Centre. Indian J Hematol Blood Transfus 2015;31:374-7.
17. Jimenez-Marco T, Clemente-Marin G, Girona-Llobera E, Sedeño M, Muncunill J. A lesson to learn from Hemovigilance: The impact of nurses' transfusion practice on mistransfusion. Transfus Apher Sci 2012;47:49-55.
18. Grolleau N, Liétard C, Lebdiri B, Le Niger C. Évaluation des connaissances transfusionnelles des sages-femmes dans les maternités publiques et privées de la région Bretagne en 2014 [Evaluation of midwives transfusion knowledge in Brittany public and private maternities, 2014]. Transfus Clin Biol 2015;22:318-25.
19. Tajalli S, Nourian M, Rassouli M, Baghestani AR. Clinical assessment of nursing care regarding hemovigilance in neonatal wards and neonatal intensive care units in selected hospitals affiliated to Shahid Beheshti University of Medical Sciences (2013-2014). Iranian Red Crescent Medical Journal 2015;17:e19987.
20. Rudrappan RB. Evaluating the knowledge and practices of nurses and paramedics in blood transfusion services–A survey in thestates of Tamil Nadu and Pondicherry, India. J Educ Health Promot 2019;8:48.
21. Sireesha N, Reddy KP, Sravani J, Rani S, Rathinavelu M. Assessment of Healthcare Professional Awareness towards Haemovigilance (HvPI) Programme of India in South India. IOSR JPBS 2015;10:13-7.
22. Aneke JC, Ezeama N, Okocha CE, Onyeyili AN, Onah CE, Ibeh NC, et al. Knowledge, attitude and practice of haemovigilance among health care professionals in a Nigerian Tertiary Hospital. The Egyptian Journal of Haematology 2017;42:108.
23. Shivgunde PP, Besekar SM, Bhojwani KM, Bhojwani DG. Knowledge, attitude and practice of haemovigilance amongst healthcare professionals in Nashik, Maharashtra, India. International Journal of Basic & ClinicalPharmacology 2018;7:986.
24. HimaBindu K, Sudha J. Knowledge, attitude, perception of Hemovigilance among post-graduates in tertiary care hospital, King George Hospital, Visakhapatnam, Andhra Pradesh.IOSR Journal of Dental and Medical Sciences 2020;19:28-31.
25. Roshi, Tandon VR. Knowledge, attitude and practices about hemovigilance among practitioners: a cross-sectional study. International journal of basic and clinical pharmacology 2019;8:2553-6.
26. Mirzaee MS, Karimi M. The Assessment of the Effect of the Haemovigilance Education by the Conceptual Map on the Knowledge of Nursing Students. Pajouhan Scientific Journal 2018;17:51-6.

Original Article

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# The Frequency of Restless Legs Syndrome and Its Relationship with the Level of Addiction in Smokers

## Sigara İçen Bireylerde Huzursuz Bacaklar Sendromu Sıklığı ve Bağımlılık Düzeyi ile İlişkisi

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## ABSTRACT

**Objective:** In this study; it was aimed to determine the frequency of Restless Legs Syndrome (RLS) in smokers and to investigate the relationship with the level of addiction.

**Methods:** This prospective study was designed as a descriptive and single-centered study. Following the ethics committee's approval, the study was conducted with the smokers who applied to a tertiary hospital for any reason between 01/03/2017 and 01/07/2017. The Restless legs syndrome diagnosis form consisting of the International Restless Leg Syndrome Study Group (IRLSSG) consensus criteria was applied to all cases. Those who had all five criteria were diagnosed with RLS. The Fagerström Test for Nicotine Dependence (FTND) was applied to evaluate the nicotine addiction of the participants. Significance was accepted at the level of $p<0.05$.

**Results:** Most of the 3,011 people included in the study were male (52.3%; n=1.579). According to the FTND, 68.4% (n=2.059) of the participants had medium and high dependence levels. RLS was detected in 9.8% (n=296) of all participants. While the presence of RLS was 6.9% (n=66) in the group with a low level of dependence, it was found to be 11.2% (n=230) in the group with a medium-high level of dependence and this difference was found statistically significant (p=0.02).

**Conclusion:** In this study, the rate of RLS was found to be higher in smokers than the general population, and it was found that the incidence of RLS increased as the level of addiction increased.

**Keywords:** Cigarette, fagerström test for nicotine dependence, restless legs syndrome, smoking

## ÖZ

**Amaç:** Bu çalışmada; sigara içenlerde huzursuz bacaklar sendromu (HBS) görülme sıklığının belirlenmesi ve bağımlılık derecesi ile ilişkisinin araştırılması amaçlandı.

**Yöntemler:** Bu prospektif çalışma, tanımlayıcı ve tek merkezli bir çalışma olarak tasarlandı. Çalışma etik kurul onayı alındıktan sonra; 01/03/2017 ile 01/07/2017 tarihleri arasında herhangi bir nedenle üçüncü basamak bir hastaneye başvuran sigara içicileri ile yapıldı. Tüm olgulara Uluslararası Huzursuz Bacaklar Sendromu Çalışma Grubu (IRLSSG) tarafından geliştirilen huzursuz bacaklar tanı formu uygulandı. Beş kriterin tamamına sahip olanlara HBS tanısı konuldu. Katılımcıların nikotin bağımlıklarını değerlendirmek için Fagerström Nikotin Bağımlılık Testi (FNBT) uygulandı. Anlamlılık $p<0,05$ düzeyinde kabul edildi.

**Bulgular:** Çalışmaya dahil edilen 3011 kişinin çoğu erkek (%52,3; n=1,579) idi. FNBT'ye göre katılımcıların %68,4'ü (n=2,059) orta ve yüksek derecede bağımlı idi. Toplamda tüm katılımcıların %9,8'inde (n=296) HBS saptandı. Düşük derecede bağımlılığı olan grupta HBS varlığı %6,9 (n=66) iken orta-yüksek derecede bağımlılığı olan grupta %11,2 (n=230) bulundu ve aradaki bu farklılık istatistiksel olarak anlamlı bulundu (p=0,02).

**Sonuç:** Bu çalışmada, sigara içenlerde HBS görülme oranı genel popülasyona göre yüksek bulunmuş olup bağımlılık düzeyi arttıkça HBS görülme sıklığının arttığı saptandı.

**Anahtar Sözcükler:** Fagerström nikotin bağımlılık testi, huzursuz bacaklar sendromu, sigara, sigara içme

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## Introduction

Restless leg syndrome (RLS) is a neurological disorder characterized by an abnormal sensation and dysesthesia in the extremities, especially in the legs. It is characterized by motor restlessness, periodic limb movements, and sleep disturbance, mostly occurring during rest or at night, partially or temporarily disappearing with activity and can be seen at any age (1,2). Sir Thomas Willis made the first definition of RLS in 1685, and in 1945, it was named "RLS" by Ekbom (3,4). The prevalence of RLS was reported as 1-15% worldwide, while in Turkey was reported to be 2.5-7% (5-7).

RLS has two clinical forms as primary (idiopathic) and secondary. RLS, not caused by another disorder, is called Idiopathic RLS. The other form that develops due to iron deficiency, pregnancy, obesity, low iron level, use of certain medications, such as antidepressants, neuropathy or smoking is called secondary RLS (8,9). There is no specific diagnostic test for RLS, so diagnosis is made based on diagnostic criteria. All five key criteria determined by the International RLS Study Group (IRLSSG) must be observed for a definitive diagnosis (8). There are non-pharmacological and pharmacological approaches in the treatment of RLS. Dopamine agonists, alpha 2-delta ligands and opioids should be considered in pharmacological treatment, especially to reduce symptoms in moderate to severe primary RLS (10-12).

Smoking results in severe illnesses and deaths and is defined as the most critical public health problem by the World Health Organization (WHO). Approximately 19.9 % of the entire population, over 15 years of age, was found to smoke worldwide (13). In our country, the smoking rate in the general population is approximately 27.5 % (14).

In the literature, various studies have reported a significant relationship between smoking and RLS (15-19). To our knowledge, although there are studies on the rate of smoking and the effect of smoking on the severity of the disease in those with RLS, there are not many studies showing the relationship between RLS and level of addiction in smokers.

This study aimed to determine the frequency of RLS in smokers and the relationship of the frequency with the level of addiction.

## Methods

This study was designed as a prospective, descriptive and single-centered study. After the ethics committee's approval, the study was conducted between 01/03/2017 and 01/07/2017 in a tertiary hospital. Smokers who applied to the hospital for any reason were included in the study. The patients with polyneuropathy, pregnants, those who use SSRI, lithium, antiepileptic, antihistamine, antidopaminergic drugs, and individuals with physical and mental communication problems were excluded from the study. Participants were informed about the purpose of the study before being included in it.

### Data Collection Tools

After obtaining the participants' verbal consent, their socio-demographic data and health status were interrogated by the face-to-face interview technique. Fagerström Test for Nicotine Dependence (FTND) was applied to all cases to evaluate their nicotine dependence. The scoring was as follows in this test consisting of 6 questions: 0-3 as a low level of dependence, 4-6 as a medium level of dependence, and 7-10 as a high level of dependence.

Besides, all participants were tested with the Restless Leg Diagnosis Form developed by the IRLSSG. Those who had all five criteria in the diagnostic form were diagnosed with RLS. The results were recorded.

### Statistical Analysis

Average and standard deviation, frequency and ratio values were used to analyze the obtained numerical data, and the chi-square test was used in the analysis of the qualitative data. Significance was accepted at the level of $p<0.05$. The analyzes were done using NCSS 10 (2015. Kaysville, Utah, USA) software program.

## Results

Three thousand eleven people were included in the study, most of whom were male (52.3%; n=1,579). The participants' ages ranged between 18 and 70, and the mean age was 39±11.49. Most of the participants were between the ages of 35-49 (44.8%, n=1,353).

In total, RLS (n=296) was found in 9.8% of all participants. As shown in Table 1, 55.4 % (n=164) of those with RLS were female and 44.6 % (n=132) were male. This difference between gender was found to be statistically significant (p=0.04) (Table 1).

According to FTND, while the level of nicotine dependence was low in 31.6% (n=952) of the participants, 68.4% (n=2,059)

**Table 1.** The distribution of RLS according to patients' gender

| | RLS (+) (n=296; 9.8%) | | RLS (–) (n=2715; 90.2%) | | p* |
|---|---|---|---|---|---|
| Gender | N | % | N | % | |
| Male (n=1,579; 52.3%) | 132 | 44.6 | 1447 | 53.3 | 0.04 |
| Female (n=1,432;47.7%) | 164 | 55.4 | 1268 | 46.7 | |

Data presented as number (%) of participants. RLS: Restless legs syndrome
*T-test was used

were medium and high. While 22.3% (n=66) of the participants with RLS had low level of addiction, 77.7% (n=230) of them had medium-high level of addiction. It was determined that the incidence of RLS increased as the dependency increased, which was found statistically significant (p=0.02). Table 2 presents the differences in the RLS status of participants according to the level of addiction (Table 2).

The prevalence of RLS in smokers was 8.2% in the 18-34 age group (n=88), 9.6% in the 35-49 age group (n=130), 11.8% in the 50-64 age group (n=62), and 25.8% (n=16) at the age 65 and over.

While 18.2% of the participants with RLS had a family history (n=54), 9.0% of those without RLS had a family history (n=244). The rate of family history in the RLS group was significantly higher than the group without RLS (p<0.001).

The mean age (34.4±15.2 years) of the participants with RLS with a family history was lower than the average of those without a family history (37.9±14.7 years), and this difference between the ages in groups was found statistically significant (p=0.05).

## Discussion

RLS is one of the less-known but common diseases and remains untreated for a long time. In recent years, there has been an increase in studies investigating the RLS. In this study, the frequency of RLS was found higher in smokers than the general population, and the incidence of RLS increased as the level of addiction increased. Female gender, advanced age, family history were also determined as risk factors for RLS in smokers.

In previous studies, RLS has been shown to be more common in women than in men. Park et al. showed that the prevalence of RLS was twice higher in women than in men (20). In the study conducted by Tasdemir et al. (10), the disease was reported to be 3.5 times more common in women than in men, and the prevalence increased proportionally with age. In our study, the prevalence of RLS in smokers was found to be higher in women, which was similar to that in the general population. Therefore, our results were compatible with other studies in the literature.

In the literature, the relationship between age and RLS is not certain. Some studies reported that RLS increases with age (21), while some reported that RLS increases the rate up to the age of 60 years and then decreases with increasing age (10). On the contrary, some studies found that prevalence did not increase with age (22). For example, Cho et al. (23) reported that the disease increased with age; most of them started before the age of 45, peaked at the age of 50-59 and reached 9.1% in this age group. In our study, it was found that there was a significant relationship between the prevalence of RLS and age in accordance with some studies in the literature.

In previous studies, it was observed that most people with RLS had a history of RLS in at least one family member, and it was emphasized that the age of onset of the disease was early in people with a positive family history (24). The age of onset of RLS was found bimodal; it has been suggested that the form with an early onset is associated with familial factors, and the RLS form with late-onset is associated with secondary factors (25). In another study, the rate of family history in person with RLS was found to be 28.3% (26). In our study, family history was found in 18.2% of the participants with RLS. The mean age of those with RLS with a family history was found to be significantly lower than the average age of those without a family history, and these findings were consistent with the literature.

The prevalence of RLS has varied in studies using the IRLSSG criteria without addressing differential diagnoses. Vogl et al. (27) found that the prevalence of RLS was 8.9%, Berger et al. (17); 10.6%; Allen et al. (28);7.2%.

In this study, we evaluated the frequency of RLS in smokers by using the IRLSSG criteria without mentioning the differential diagnosis, and RLS prevalence was found as 9.8%. This rate was higher than the general population-prevalence studies conducted in Turkey. This high rate supported the fact that smoking has been a risk factor for RLS.

Although some studies reported the existence of a significant relationship between smoking and RLS, some studies provided the opposite data (21,29).

In the study conducted by Phillips et al. (15), it was found that there was a significant relationship between smoking at least 20 cigarettes daily and RLS, but no significant relationship was observed between less than 20 cigarettes and RLS. In another study, it was determined that 44.7% of patients diagnosed with RLS smoked, and 73.9% of them smoked more than ten cigarettes per day. Active smokers were found to be significantly higher in the patient group than in the control group, and smokers of more than ten cigarettes per day were more likely to have RLS (16). It was also observed a significant relationship between smoking and RLS in the study conducted by Liu et al. (30).

**Table 2.** Evaluation of RLS status according to the level of addiction

| | RLS (-) (n=2,715; 90.2%) | | RLS (+) (n=296; 9.8%) | | Total (n=3,011) | | p* |
|---|---|---|---|---|---|---|---|
| Level of dependence | N | % | N | % | N | % | |
| Low | 886 | 32.7 | 66 | 22.3 | 952 | 31.6 | **0.02** |
| Medium-high | 1,829 | 67.3 | 230 | 77.7 | 2059 | 68.4 | |

Data presented as number (%) of participants. RLS: Restless legs syndrome
*T-test was used

In another study, compared to those who have never smoked, those who reported currently smoking more than 15 pieces have been shown to have an increased risk of RLS. However, this relationship was found only in women. In contrast, no significant association was noted between smoking and the risk of RLS among men in this study (31). Similar to this study, we also found that the female gender is a risk factor for RLS.

Unless the results obtained from these studies, in an epidemiological study searching for the association between RLS and cardiovascular disease, no differences were observed in the percentages of current and former smokers between subjects with or without RLS (32). In one of the studies conducted in our country, Ceylan et al. (33) found that 28% of patients with RLS were smokers, but the rate was also not significant compared to non-smokers. Similarly, in another study, no difference was found in terms of smoking when the RLS group was compared with the control group (34).

In our study, as a contribution to all these studies in the literature, which yielded different results regarding the relationship between smoking and RLS, we evaluated the addiction levels of smokers, in addition to smoking status, and found that the rate of RLS was higher in those with high addiction levels.

As is known, smoking increases symptoms in RLS. In a study conducted in the USA, patients were divided into two groups according to the frequency of RLS, and the rate of smoking was found higher in the group experiencing frequent symptoms. However, although at least 20 cigarette smoking per day was found to have a significant relationship with RLS symptoms, this relationship had not been detected in smokers who smoke less than 20 cigarettes (24).

Oksenberg (35) reported that a 75-year-old woman who smoked 25 cigarettes daily for 50 years had a decrease in RLS symptoms by sudden cessation of smoking. In a study investigating the relationship between RLS and smoking by Dündar (18), it was observed that smoking and RLS severity were directly related. In another study by Didriksen et al. (19), the relationship between RLS severity and cigarette consumption was observed. In our study, we examined the prevalence and the frequency of RLS in smokers, but not the effect of smoking on RLS severity, and we found that the frequency of RLS was higher in smokers than the general population. The results of our study are mostly similar to the literature.

### Study Limitations

While collecting the participants' data, scales reporting personal status were used by the face-to-face interview technique. This condition could lead to individual prejudices, and individuals may not share accurate information.

The strengths of the study were that there are not many studies that reveal the relationship between RLS and level of addiction in smokers in the literature.

## Conclusion

In this study, we concluded that the RLS frequency was higher in smokers than in the general population. Our study highlighted the potential impact of high levels of addiction on RLS as well as smoking status in smokers. In those who describe symptoms of restless legs syndrome, smoking status and level of addiction should be investigated. Large-scale studies are needed to examine the causal relationship between smoking and the development of RLS.

### Ethics

**Ethics Committee Approval:** After the ethics committee's approval, the study was conducted between 01/03/2017 and 01/07/2017 in a tertiary hospital.

**Informed Consent:** Smokers who applied to the hospital for any reason were included in the study.

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

### Authorship Contributions

Surgical and Medical Practices: O.G., O.B., Concept: O.G., O.B.,Design: O.G., O.B., Data Collection or Processing: O.G., Analysis or Interpretation: O.G., S.T.K., O.B., Literature Search: O.G., S.T.K., O.B., Writing: O.G., S.T.K., O.B.

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## References

1. Garcia-Borreguero D, Williams A-M. An update on restless legs (Willis-Ekbomdisease): clinical features, pathogenezis and treatment. Curr Opin Neurol 2014;27:493-501.
2. Mungan S, Ozcan M, Orhan G, Titiz A, Arli B, Koseoglu S, et al. Clinical and polysomnographic features of patients with Restless Legs Syndrome. J Pak Med Assoc 2016;66:568-73.
3. Willis T. The London Practice of Physic. Bassett and Crook, London. 1685.
4. Ekbom KA. Restless legs: a clinical study. Acta Med Scand Suppl 1945;158:1-123.
5. Yilmaz K, Kilicaslan A, Aydin N, Kor D. Prevalence and correlates of restless legs syndrome in adolescents. Dev Med Child Neurol 2011;53:40-7.
6. Demir AU, Ardic S, Firat H, Karadeniz D, Aksu M, Ucar ZZ, et al. Prevalence of sleep disorders in the Turkish adult population epidemiology of sleep study. Sleep and Biological Rhytmes 2015;13:298-308.
7. Altunayoglu Cakmak V, Koc B, Nuhoglu I, Topbas M, Ucuncu SY, Deger O, et al. Prevalence of restless legs syndrome in Trabzon in the northeast Black Sea Region of Turkey: co-morbidities, socioeconomic factors and biochemical parameters. Neurol Res 2015;37:751-62.

8. Allen RP, Picchietti DL, Garcia-Borreguero D, Ondo WG, Walters AS, Winkelman JW, et al. Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria - history, rationale, description, and significance. Sleep Med 2014;15:860-73.
9. Sayin S, Atilla FD. Overlooked clinical presentation of iron deficiency; Restless Leg Syndrome. Ankara Med J. 2019;19-3.
10. Tasdemir M, Erdogan H, Börü UT, Dilaver E, Kumas A. Epidemiology of restless legs syndrome in Turkish adults on the western Black Sea coast of Turkey: A door to-door study in a rural area. Sleep Medicine 2010;11:82-6.
11. Manconi M, Ferri R, Zucconi M, Clemens S, Rundo F, Oldani A, et al. Effects of acute dopamine-agonist treatment in restless legs syndrome on heart rate variability during sleep. Sleep Med 2011;12:47-55.
12. Yalınay Dikmen P. Restless legs syndrome treatments in adults: practice guideline summary of American Academy of Neurology. Journal of Turkish Sleep Medicine 2017;4:59-64.
13. World health statistics overview 2019: monitoring health for the SDGs, sustainable development goals. Geneva: World Health Organization; 2019 (WHO/DAD/2019.1). Licence: CC BY-NC-SA 3.0 IGO.
14. WHO global report on trends in prevalence of tobacco smoking 2000-2025, second edition. Geneva: World Health Organization;2018.
15. Phillips B, Young T, Finn L, Asher K, Hening WA, Purvis C. Epidemiology of restless legs symptoms in adults. Arch Intern Med 2000;160:2137-41.
16. Sevim S, Dogu O, Kaleagasi H, Aral M, Metin O, Camdeviren H. Correlation of anxiety and depression symptoms in patients with restless legs syndrome: a population based survey, J Neurol Neurosurg Psychiatry 2004;75:226-30.
17. Berger K, Luedemann J, Trenkwalder C, John U, Kessler C. Sex and risk of RLS in the general population. Arch İntern Med 2004;164:196-202.
18. Dündar F. Huzursuz bacaklar sendromu ve sigara, Ankara Üniversitesi/ Tıp Fakültesi / Nöroloji Anabilim Dalı, 443683, 2016.
19. Didriksen M, Rigas AS, Allen RP, Burchell BJ, Di Angelantonio E, Nielsen MH, et al. Prevalence of restless legs syndrome and associated factors in an otherwise healthy population: results from the Danish Blood Donor Study. Sleep Med 2017;36:55-61.
20. Park YM, Lee HJ, Kang SG, Choi HS, Choi JE, Cho JH, et al. Prevalence of idio-pathic and secondary restless legs syndrome in Korean women. Gen Hosp Psychiatry 2010;32:164-8.
21. Hadjigeorgiou GM, Stefanidis I, Dardiotis E, Aggellakis K, Sakkas GK, Xiromerisiou G, et al. Low RLS prevalence and awareness in central Greece: an epidemiological survey. Eur J Neurol. 2007;14:1275-80.
22. Benediktsdottir B, Janson C, Lindberg E, Arnardóttir ES, Olafsson I, Cook E, et al. Prevalence of restless legs syndrome among adults in Iceland and Sweden: lung function, comorbidity, ferritin, biomarkers and quality of life. Sleep Med 2010;11:1043-8.
23. Cho YW, Shin WC, Yun CH, Hong SB, Kim JH, Allen RP, et al. Epidemiology of restless legs syndrome in Korean adults. Sleep 2008;31:219-23.
24. Phillips B, Hening W, Britz P, Mannino D. Prevalence and correlates of restless legs syndrome: results from the 2005 National Sleep Foundation Poll. Chest 2006;129:76-80.
25. Winkelmann J, Muller-Myhsok B, Wittchen HU, Hock B, Prager M, Pfi ster H, et al. Complex seregation analysis of restless legs syndrome provides evidence for an autosomal dominant mode of inheritance in early age at onset families. Ann Neurol 2002;52:297-302.
26. Haba-Rubio J, Marti-Soler H, Marques-Vidal P, Tobback N, Andries D, Preisig M, et al. Prevalence and determinants of periodic limb movements in the general population. Ann Neurol 2016;79:464-74.
27. Vogl FD, Pichler I, Adel S, Pinggera GK, Bracco S, De Grandi A, et al. Restless legs syndrome: epidemiological and clinicogenetic study in a South Tyrolean population isolate. Mov Disord. 2006;21:1189-95.
28. Allen RP, Walters AS, Montplaisir J, Hening W, Myers A, Bell TJ, et al. Restless Legs syndrome prevalance and impact: REST General Population Study. Arch Intern Med 2005;165:1286-92.
29. Sevim S, Dogu O, Camdeviren H, Bugdayci R, Sasmaz T, Kaleagasi H, et al. Unexpectedly low prevalence and unusual characteristics of RLS in Mersin, Turkey. Neurology 2003;61:1562-9.
30. Liu Y, Liu G, Li L, Yang J, Ma S. Evaluation of cardiovascular risk factors and restless legs syndrome in women and men: A preliminary population-based study in China. J Clin Sleep Med 2018;14:445-50.
31. Batool-Anwar S, Li Y, De Vito K, Malhotra A, Winkelman J, Gao X. Lifestyle factors and risk of restless legs syndrome: prospective cohort study. J Clin Sleep Med 2016;12:187-94.
32. Winkelman JW, Shahar E, Sharief I, Gottlieb DJ. Association of restless legs syndrome and cardiovascular disease in the Sleep Heart Health Study. Neurology 2008;70:35-42.
33. Ceylan M, Aygül R, Yalçın A. Investigation of restless leg syndrome prevalence and assosiated sociodemographic features in province of Erzurum. J Contemp Med 2019;9:48-54.
34. Aydın Ş, Özdemir C, Sökücü SN.The Relationship Between Restless Legs Syndrome and Cardiovascular Risk Factors. Journal of Turkish Sleep Medicine 2019;1:29-36.
35. Oksenberg A. Alleviation of severe restless legs syndrome (RLS) symptoms by cigarette smoking. J Clin Sleep Med. 2010;6:489-90.

Case Report

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# Concomitant Abdominal Aortic Aneurysm and L2-L3 Disk Herniation: Is There a Relationship Between Them?

## Abdominal Aort Anevrizması ve L2-L3 Disk Hernisi Birlikteliği: Aralarında Bir İlişki Var Mı?

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**ABSTRACT**

Abdominal aortic aneurysm (AAA) is a critical disease and is often asymptomatic. It can cause diminished lumbar blood flow. Impaired blood flow in the lumbar arteries is significantly associated with decreased diffusion in lumbar disks and may lead to progressive disk damage. AAA can clinically mimic upper lumbar disk herniation. Disk herniation is rarely seen in the upper lumbar region since the upper part of the lumbar spine is less mobile than the lower region. To the best of our knowledge, no reports have presented concomitant AAA and L2-L3 disk herniation. We describe a 48-year-old man treated for symptomatic AAA followed by L2-L3 disk herniation at an interval of 3 months.

**Keywords:** Low back pain, abdominal aortic aneurysm, disk herniation, disk degeneration

**ÖZ**

Abdominal aort anevrizması (AAA) önemli bir hastalıktır ve sıklıkla asemptomatiktir. Lomber kan akışında azalmaya neden olabilir. Lomber arterlerdeki bozulmuş akış, lomber disklerdeki difüzyonun belirgin şekilde azalmasıyla ilişkilidir ve ilerleyici disk hasarına yol açabilir. AAA klinik olarak üst lomber disk hernilerini taklit edebilir. Lomber omurganın üst kısmı alt bölgeden daha az hareketli olduğundan, disk herniasyonu üst lomber bölgede nadiren görülür. Bildiğimiz kadarıyla, literatürde abdominal aort anevrizması ve L2-L3 disk herniasyonu birlikteliği ile ilgili daha önce herhangi bir rapor bulunmamaktadır. Biz üç ay arayla semptomatik AAA ve L2-L3 disk hernisi nedeniyle tedavi edilen 48 yaşında bir erkek hastayı sunuyoruz.

**Anahtar Sözcükler:** Bel ağrısı, abdominal aort anevrizması, disk hernisi, disk dejenerasyonu

## Introduction

Low back pain (LBP) is most commonly caused by mechanical dysfunction. However, 1-2% of cases are caused by nonmechanical spinal disorders or visceral disease, such as abdominal aortic aneurysm (AAA) (1). Factors potentially involved in chronic LBP in patients with AAA include the size of the aneurysm, increased pressure on the vascular wall and surrounding neural elements, and erosion of the vertebral body (2). Several cross-sectional studies have suggested that vascular diseases in the lumbar area are associated with disk degeneration (DD) and LBP (3-5). The correlation of atherosclerotic changes to DD was stronger in the upper levels of the lumbar spine than in the lower ones (5). AAA can cause lumbar DD and clinically mimic upper lumbar disk herniation. The incidence of herniated upper lumbar disks is less than that of lower disks (6). Pathological fractures due to osteoporosis, bone metastasis, and spinal tumors must be

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considered alternatively when assessing upper lumbar pathology. AAA and L2-L3 disk herniation are rarely concomitant, as they were in the present case.

## Case Report

A 48-year-old man, a current smoker, with a previous diagnosis of hypertension first presented with severe localized LBP after walking 200 m. The pain made walking difficult but was relieved by resting for at least 5 min. It persisted for two months and was not ameliorated by analgesics or myorelaxant agents. The pain was rated 9/10 on a visual analog scale (VAS), and the patient reported no night pain or morning stiffness. The patient is a maintenance technician and had moderate physical activity levels. He had no trauma history. At physical examination, the range of motion testing of the lumbar spine was normal but painful, and palpation of the lumbar spinous process segments and paravertebral muscles also elicited pain. The straight leg raise test was negative. The range of motion of the hip joints was normal, and no pain and restriction were detected at the hip joints in the flexion-abduction-external rotation test and flexion-adduction-internal rotation test. Sacroiliac joint provocation tests were negative. Gait analysis was normal, and no pelvic asymmetry was detected. Neurological examination was unremarkable, and the patellar reflex was normoactive. Arterial pulses in the lower limbs were normal. Edema, leg diameter difference, and discoloration were not observed in the lower extremities. The patient did not report systemic symptoms such as fever, muscle pain, fatigue, or weight loss. Results of the systemic examination were normal. The patient had not sought medical assistance for any systemic disease, except for hypertension. Results of laboratory investigations (such as complete blood count, erythrocyte sedimentation rate, and C-reactive protein) were within the normal limits. Magnetic resonance imaging (MRI) revealed a thrombosed aneurysmatic dilatation (68x60 mm in the widest part) of the wall in an approximately 12 cm segment of the abdominal aorta and L2-3 left paracentral extruded disc herniation with lateral recess stenosis. Loss of signal intensity due to degeneration was also detected in the intervertebral discs and more markedly in the upper lumbar disks (Figure 1). The patient was referred to the cardiovascular surgery department where an endovascular stent graft was inserted in the aortoiliac position (Figure 2). No complication was observed during or after the intervention, and the clinical symptoms improved significantly. Following surgery, the patient started walking 30 min to 1 h daily. At six weeks following surgery, the patient did not report any episodes of low back or abdominal pain.

Three months later, the patient was readmitted to our clinic again with LBP extending to the left lower extremity. Physical examination revealed tenderness over the lumbar spinous process segments, and the *femoral nerve stretch* test was positive on the left side. The lumbar lordosis had decreased, and antalgic gait was present. The cardiovascular surgery department was consulted in terms of contraindication before treatment. Since the case was compatible with discogenic LBP, 15 sessions of physiotherapy including superficial and deep heating and burst-type transcutaneous electrical nerve stimulation were applied. McKenzie and stabilization exercises were performed. The radiating LBP improved, and the VAS score decreased from 8 to 2 points.

## Discussion

The pathogenesis of LBP is multifactorial. AAA can induce LBP. It is mainly caused by arterial stenosis, which results in the reduction of blood flow in the affected area. Initially, no symptoms were observed at rest, but patients may experience claudication during exercise. It may also play an important role in the mechanism of painful degenerative disc diseases. In this case, the patient presented early with claudication and lately with lower radiating back pain.

AAA is defined as a weakening of the aortic wall involving progressive, full-thickness local dilation >150% of the normal diameter. Diameters exceeding 3 cm are clinically significant. Larger aneurysms expand at a faster rate than smaller aneurysms. The risk of spontaneous rupture increases exponentially with

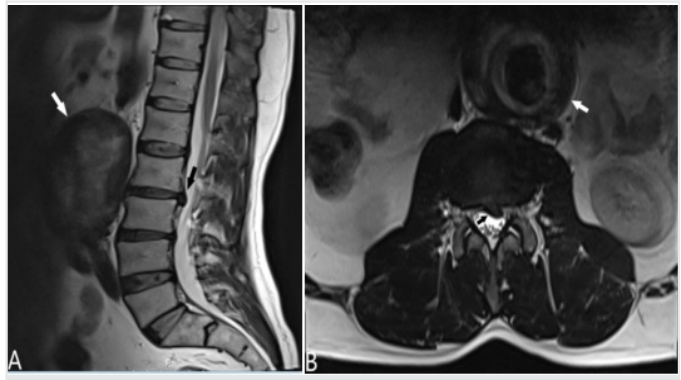


**Figure 1.** Preoperative T2-sagittal (A) and T2-axial (B) magnetic resonance images showing abdominal aortic aneurysm (AAA) (white arrow) and L2–3 extruded disk herniation (black arrow)

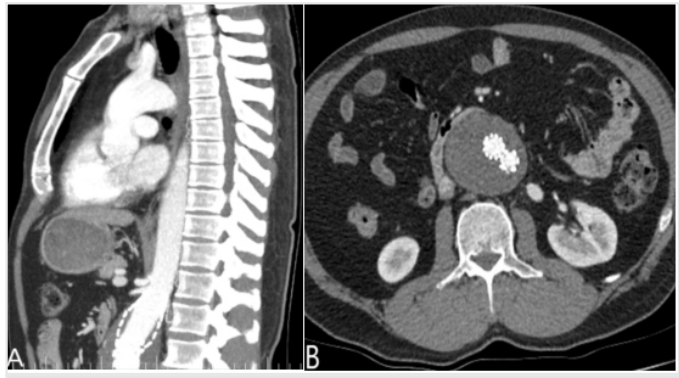


**Figure 2.** Postoperative sagittal (A) and axial (B) computed tomography (CT) angiography sections showing stent material in the abdominal aorta starting from the renal level and extending into both the common iliac arteries. In contrast to the upper vertebral arteries, the second pair of the lumbar arteries did not appear normal

the aortic diameter. Rupture accounts for more than 40% of mortality cases (7). Thus, surgery is generally recommended when the AAA exceeds >5.5 cm in diameter in men and >5.0 cm in women, in the presence of symptoms, and in the case of a rapid increase in size (8). In the present case, endovascular aneurysm repair was performed since the risk of rupture was high and symptoms developed. Previous studies have suggested that arterial surgery (when possible) is effective for LBP symptoms in patients with AAA (9).

Although the etiology of an AAA is still not completely understood, major risk factors for an AAA include hypertension, age >60 years, male gender, smoking history, atherosclerosis, coronary artery disease, and a genetic/family history of AAA (10). AAA is not normally screened for unless the patient has these specific risk factors. In a male patient aged >60 years with one or more additional risk factors, abdominal ultrasonography is initially recommended. In the present case, AAA had been diagnosed incidentally during the investigation of other spinal pathologies.

Autopsy and radiology studies have documented a correlation between vascular disease and DD. Lumbar artery stenosis is significantly associated with decreased diffusion of the lumbar disks. Intervertebral discs receive nutrients by diffusion mainly through the vertebral endplates. Diminished blood flow to the vertebrae may therefore reduce diffusion of nutrients and oxygen to the disk and hamper the disposal of harmful metabolites. Beckworth et al. (11) also found an association with other degenerative changes such as facet arthritis and lumbar canal stenosis. Interestingly, the correlation was strongest in patients aged ≤61 years. Various contributing factors may emerge with advancing age. Similar to vascular diseases, DD begins early in life. Asymptomatic individuals therefore commonly exhibit degenerative changes (12). Trompeter and Paremain reported a case series of four patients who had incidental AAA detected on lumbosacral MRI. All patients had degenerative spinal diseases. Kim et al. (13) reported a case in which AAA with mural thrombus coexisted with aggravated L3-L4 intervertebral disc extrusion. Surgery was performed for both pathologies in that case (14).

The upper three segments of the lumbar spine are supplied only by the segmental lumbar arteries, originating from the posterior wall of the abdominal aorta. The L1, L2, and L3 arteries mainly go to the L1-2, L2-3, and L3-4 disk spaces, respectively. Stenosis of the ostia of the lumbar arteries may trigger degenerative changes. With its location at the end of the nutrient chain, the disk is affected earliest by poor circulation. Insufficient blood supply may render the disks more vulnerable to mechanical stress and thus result in disk damage (5). AAA is frequently associated with diminished lumbar blood flow, and 95% of AAAs are located in the infrarenal region (L1-4 level). The prevalence of complicated lesions associated with atheromatous plaques (i.e., plaques with necrosis, thrombus, and calcification) increases rapidly at age 44-65 years. Either atheromatous plaques or thrombotic layers accumulate gradually inside the aneurysm. This then gradually obstructs the corresponding lumbar arteries but allows sufficient time for collateral pathways to develop. Therefore, ischemic symptoms in the lumbar region are rarely found even after AAA surgery. Symptoms may be observed only during exertion when reduced blood supply fails to meet demand (15). In the present case, degeneration was particularly marked in the upper lumbar disks, and symptoms developed following exertion.

The upper lumbar disks are generally defined as the L1-L2 and L2-L3 levels. Disk herniation is rarely seen in this region since the upper part of the lumbar spine is less mobile than the lower region. Upper lumbar disk herniations constitute 1-2% of all herniated lumbar disks and are mostly seen in the older population (16). Clinical signs associated with upper lumbar disk herniation are nonspecific, with most patients reporting low back and leg pain. The radicular pattern of back pain may not be clear and not reflect the true level of the disease. The *femoral nerve stretch* test, also known as reverse straight raise test, is positive in 84-95% of the patients with upper lumbar disk herniation, as in the present case (17). The nerve root in the upper lumbar spine does not innervate any specific muscles. In some cases, the clinical signs of radiculopathy do not match the electromyographic signs, so electromyography has no absolute diagnostic value. Accurate diagnosis is often difficult without radiological findings. Surgical outcomes of upper lumbar disk herniation are less satisfactory than those involving lower disks (18). Therefore, conservative treatment was applied in the present case. In the management of patients with upper lumbar degenerative disk diseases, the possibility of comorbidities such as an AAA should not be overlooked because a delayed diagnosis of AAA puts the patient at risk of aneurysmal rupture.

AAA is a rare entity that may be asymptomatic. An advanced disease has been correlated with LBP and DD, in which a degenerative "cascade" of events is triggered. A gradual decrease in disk flexibility and increased ruptures in annulus fibrosis may lead to herniation of the nucleus pulposus. AAA can therefore present with localized back pain or radiculopathy. Further studies are needed to confirm the causal association.

**Ethics**

**Informed Consent:** An informed consent was obtained from the patient.

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

**Authorship Contributions**

Surgical and Medical Practices: Y.E., R.S., Concept: Y.E., R.S., E.Y., Design: Y.E., R.S., E.Y., Literature Search: Y.E., E.Y., Writing: Y.E., E.Y.

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## References


1. Jarvik JG, Deyo RA. Diagnostic evaluation of low back pain with emphasis on imaging. Ann Intern Med 2002;137:586-97.
2. Tsuchie H, Miyakoshi N, Kasukawa Y, Nishi T, Abe H, Takeshima M, et al. High prevalence of abdominal aortic aneurysm in patients with chronic low back pain. Tohoku J Exp Med 2013;230:83-6.
3. Kurunlahti M, Tervonen O, Vanharanta H, Ilkko E, Suramo I. Association of atherosclerosis with low back pain and the degree of disc degeneration. Spine (Phila Pa 1976) 1999;24:2080-4.
4. Kurunlahti M, Karppinen J, Haapea M, Niinimäki J, Autio R, Vanharanharanta H, et al. Three-year follow-up of lumbar artery occlusion with magnetic resonance angiography in patients with sciatica: associations between occlusion and patient-reported symptoms. Spine (Phila Pa 1976) 2004;29:1804-8.
5. Kauppila LI, Penttilä A, Karhunen PJ, Lalu K, Hannikainen P. Lumbar disc degeneration and atherosclerosis of the abdominal aorta. Spine (Phila Pa 1976) 1994;19:923-9.
6. Adamec I, Prutki M, Habek M. Abdominal aortic aneurysm mimicking L2-L3 disc herniation. Acta Neurol Belg 2016;116:695-7.
7. Sakalihasan N, Limet R, Defawe OD. Abdominal aortic aneurysm. Lancet 2005;365:1577-89.
8. Kent KC. Clinical practice. Abdominal aortic aneurysms. N Engl J Med 2014;371:2101-8.
9. Takeyachi Y, Yabuki S, Arai I, Midorikawa H, Hoshino S, Chiba K, et al. Changes of low back pain after vascular reconstruction for abdominal aortic aneurysm and high aortic occlusion: a retrospective study. Surg Neurol 2006;66:172-6.
10. Forsdahl SH, Singh K, Solberg S, Jacobsen BK. Risk factors for abdominal aortic aneurysms: a 7-year prospective study: the Tromsø Study, 1994-2001. Circulation 2009;119:2202-8.
11. Beckworth WJ, Holbrook JF, Foster LG, Ward LA, Welle JR. Atherosclerotic Disease and its Relationship to Lumbar Degenerative Disk Disease, Facet Arthritis, and Stenosis With Computed Tomography Angiography. PM R 2018;10:331-7.
12. Miller JA, Schmatz C, Schultz AB. Lumbar disc degeneration: correlation with age, sex, and spine level in 600 autopsy specimens. Spine (Phila Pa 1976) 1988;13:173-8.
13. Kim NS, Kang SH, Park SY. Coexistence of expanding abdominal aortic aneurysm and aggravated intervertebral disc extrusion -a case report-. Korean J Anesthesiol 2013;65:345-8.
14. Trompeter AJ, Paremain GP. Incidental abdominal aortic aneurysm on lumbosacral magnetic resonance imaging - a case series. Magn Reson Imaging 2010;28:455-7.
15. Kauppila LI. Atherosclerosis and disc degeneration/low-back pain--a systematic review. Eur J Vasc Endovasc Surg 2009;37:661-70.
16. Kim DS, Lee JK, Jang JW, Ko BS, Lee JH, Kim SH. Clinical features and treatments of upper lumbar disc herniations. J Korean Neurosurg Soc 2010;48:119-24.
17. Porchet F, Fankhauser H, de Tribolet N. Extreme lateral lumbar disc herniation: clinical presentation in 178 patients. Acta Neurochir (Wien) 1994;127:203-9.
18. Karaaslan B, Aslan A, Börcek AÖ, Kaymaz M. Clinical and surgical outcomes of upper lumbar disc herniations: a retrospective study. Turk J Med Sci 2017;47:1157-60.

Review

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# Probiotics and Relationship Between Probiotics and Cancer Types

## Probiyotikler ve Probiyotiklerin Kanser Türleriyle İlişkisi

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### ABSTRACT

Cancer is a disease with a high mortality rate worldwide. Moreover, this rate is increasing day by day. It is expected to rise to first place by 2030, leaving cardiovascular diseases behind, which is the most common cause of death in the world. Today, it is known that cancer is the second most common cause of death. The process of cancer and its treatment reducethe quality of life. To improve this process, the effects of probiotics on some types of cancer, especially colorectal cancer, are examined in studies conducted today. Studies are showing that probiotics provide positive results in cancer prevention and treatment. However, some studies argue that they should not be used, putting forward the fact they may cause infection in patients with very weak immunity. The mechanisms for the antitumor properties of probiotics have not been fully explained yet. It is associated with some pathways which mainly focus on the gut microbiota. The opinion that the effects of probiotics on cancer are dependent on dose, strain, and species is accepted as a general conclusion. Besides, probiotics must be consumed regularly and the consumed product must contain the minimum number of microorganisms (approximately 100 g/day) to provide the intended effect. In this review, the effects of probiotics, of which positive and negative effects on individuals with cancer are still being discussed, on different types of cancer are presented in the light of current literature.

**Keywords:** Probiotics, cancer, cancer types

### ÖZ

Kanser, dünya genelinde ölüm oranı oldukça yüksek olan bir hastalıktır. Üstelik bu oran her geçen gün yükselmektedir. Öyle ki, 2030 yılına kadar dünyada görülen en yaygın ölüm nedeni olan kardiyovasküler hastalıkları geride bırakarak birinci sıraya yükselmesi beklenmektedir. Günümüzde kanserin ikinci en yaygın ölüm nedeni olduğu bilinmektedir. Kanser süreci ve tedavisi hayat kalitesini düşürmektedir. Bu süreci iyileştirmek adına, günümüzde yapılan çalışmalarda, kolorektal kanser başta olmak üzere bazı kanser türlerinde probiyotiklerin etkisi incelenmektedir. Probiyotiklerin kanseri önlemede ve kanser tedavisinde olumlu sonuçlar verdiğine dair çalışmalar bulunmaktadır. Ancak, bağışıklığı çok zayıf olan hastalarda infeksiyona neden olabileceği gibi sebepler öne sürülerek kullanılmaması gerektiğini savunan çalışmalar da mevcuttur. Probiyotiklerin antitümör özelliklerine dair mekanizmalar, henüz tam anlamıyla açıklanamamıştır. Merkezinde barsak mikrobiyotasının bulunduğu bazı yolaklarla ilişkilendirilmektedir. Probiyotiklerin kanser üzerine olan etkilerinin doza, suşa ve türe bağlı olduğu görüşü, genel bir sonuç olarak kabul edilmektedir. Ayrıca, probiyotiklerin istenilen etkiyi sağlayabilmeleri için düzenli bir şekilde tüketilmesi ve tüketilen ürünün minimum mikroorganizma sayısını (yaklaşık olarak 100 g/gün) içermesi gerekmektedir. Bu derlemede, kanserli bireyler üzerindeki olumlu ve olumsuz etkileri hala tartışılmakta olan probiyotiklerin farklı kanser türleri üzerine etkileri güncel literatür ışığında sunulmaktır.

**Anahtar Sözcükler:** Probiyotikler, kanser, kanser türleri

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## Introduction

The concept of probiotic, which means "for life" in Greek, is used to describe living microorganisms that do not have disease-causing effects and their effects on hosts (1). According to the international FAO/WHO definition, probiotics are defined as "live microorganisms that provide health benefits to the host when administered in adequate amounts" (2). Thanks to their metabolic activities, probiotic microorganisms play an important role in the use of nutrients in the body. Moreover, probiotics greatly affect the development and performance of the immune system and other functions. In the production of probiotic foods, Lactobacillus and Bifidobacterium species are often preferred among probiotic bacteria (3). *Enterococcus*, *Streptococcus* and *Leuconostoc* bacteria are rarely used in probiotic food production.

Probiotic products may contain one or more strains (1). The benefits of a probiotic formulation also differ according to the patient group. Limited studies have shown greater efficacy when multiethnic probiotics are used. Probiotics exert their benefits in a variety of ways, such as lowering the intestinal pH, reducing the colonization of pathogenic microorganisms, and altering the host immune response (4). In order for probiotics to provide targeted health benefits, probiotic foods must contain the minimum number of viable microorganisms required during consumption (5).

According to the oldest known records, cancer is a serious health problem that has been seen since 3,000 BC and its incidence continues to increase even today (6). Cancer is a difficult disease to fight because of the many physical, social, material and spiritual ailments it carries with it. Approximately one million patients are newly diagnosed as having cancer in the world every year (7). Cancer, a disease characterized by uncontrolled proliferation in cells, causes millions of deaths every year and is seen as one of the biggest health problems that humanity struggles with (8). For this reason, a wide variety of methods are being tried to be produced by countless scientists for the treatment of cancer today.

Studies on the inclusion of probiotics among the adjunct applications to traditional cancer treatments have increased significantly in recent years (9). Probiotics exert their cancer-preventing and therapeutic effects mainly by regulating the intestinal microbiota, improving the physico-chemical conditions of the colon, increasing the intestinal barrier function, modulating intestinal bacterial metabolism and enzymes, thus preventing carcinogenics, secreting anticancer metabolites and reducing inflammation (10,11). More studies are needed to determine how and to what extent the positive effects of probiotics affect the cancer rate (12).

### Probiotics

In the human gut, the microbiota interacts intensely with nutrients and host cells. This process is a complex biosystem that is important for intestinal homeostasis and helps human development. The intestinal microbiota plays an important role in the use of nutrients in the body, thanks to its metabolic activities (2). Moreover, it greatly affects the development and performance of the immune system and other functions. The interaction between the gut microbiota and the host organism provides many benefits for both. The useful basic functions of the microbiota in the host organism are:

1- Participation in the formation of the intestinal wall

2- Providing resistance to colonization

3- Production of short chain fatty acids

4- Vitamin synthesis: Especially B group and K vitamins

5- Interacting with the mucosal immune system

6- Degradation of xenobiotics with genes capable of synthesizing enzymes with catabolic activity against these compounds.

Metabolism, barrier effect and trophic functions, which are the main functions of the microbiota, are accepted as active components of intestinal physiology (3). The bacterial imbalance that can cause various diseases that occur here is called dysbiosis. It is known that the microbiota changes positively with the intake of live bacteria (probiotics) or indigestible substrates (prebiotics) for the prevention and even treatment of some diseases. Today, it is accepted that the intestinal microbiota interacts with human health and is changed by probiotics.

According to the experts of the World Health Organization (WHO) and the Food and Agriculture Organization (FAO), a bacterial strain to be considered a probiotic; first of all, the species must reach the region of influence and withstand the physiological stress (acid, stomach and intestinal pH value and bile salts) to which it will be exposed in the body. Also, a probiotic must have proven beneficial effects for the host and must not pose any risk, and must preserve its properties during the production process and storage. Microorganisms used as probiotics can be obtained from different genera and species (13). Yeast *(Saccharomyces cerevisiae)* and bacteria; *lactic acid bacteria* (such as Lactobacillus, *Streptococcus* and *Enterococcus species*), *Bifidobacterium*, *Propionibacterium*, *Bacillus* and *Escherichia coli* species are used as probiotics. They can be natural (used in foods for everyone) or genetically modified for a specific effect. Among the probiotic strains, those belonging to the *Enterococcus* genus have a higher risk potential. Although rare, they can cause systemic infections and antibiotic resistance in the host. Probiotic products may contain one or more strains (1). The benefits of a probiotic formulation also differ according to the patient group. Limited studies have shown greater efficacy when multiethnic probiotics are used. The WHO and FAO have developed joint guidelines. FAO/WHO guidelines on probiotics are used as a global standard for the evaluation of probiotics in food. Required instructions for the directive are as follows:

1. Strain definition.

2. Functional characterization of strain(s) for safety and probiotic properties.

3. Confirmation of health benefits in human studies.

4. Honest, non-misleading efficacy claims and ingredient labeling for the entire shelf life.

The main benefits of probiotics are: Protection against gastrointestinal pathogens, strengthening the immune system, lowering serum cholesterol and blood pressure, anti-carcinogenic activity, improving nutrient utilization and bioavailability (5). Probiotics exert their benefits in a variety of ways by lowering intestinal pH, reducing colonization and invasion of pathogenic organisms, and altering the host immune response (4). In order for probiotics to provide the targeted health benefit, they must contain the minimum number of viable microorganisms required at the time of consumption (5). Generally, the minimum level recommended by the food industry is 106 c.f.u (colony forming unit)/mL. The FDA also supports this. Daily 108-109 c.f.u/mL probiotic is necessary to be effective in humans. In addition, probiotic foods should be consumed regularly in an amount of about 100 g/day to deliver approximately $10^9$ living cells to the intestines. In particular, probiotics involving the gastrointestinal tract appear to be effective in the prevention and treatment of various medical conditions. Studies supporting its effects in other conditions are often contradictory.

Probiotic bacteria belonging to the *Lactobacillus* and *Bifidobacterium* genera are considered part of the normal human microbiota (14). *Lactobacillus* and *Bifidobacterium* are generally considered safe. Some data suggest that probiotics may contribute to the strengthening of the intestinal mucosal barrier function, particularly by affecting intestinal epithelial cells and macrophages (2). The primary effect of probiotics is the barrier effect, which is related to the modulation of the host microbiota. It creates resistance to colonization by preventing or limiting colonization of pathogenic bacteria. This barrier effect can also act in different ways, such as inhibition of adhesion and competition for binding sites. Improving the barrier function of the intestinal mucosa is also a secondary mode of action of probiotics. This barrier function is related to the tightness of the connections between intestinal epithelial cells. It also produces mucus with antimicrobial peptides (defensins, lysozyme) and Paneth cells and mucus cells. Thus, it participates in the barrier function by acting as a protective layer that prevents direct contact of the intestinal lumen with bacteria. The third mode of action of probiotics is the modulation of the immune system. More than 70% of the immune cells make up the gut-associated lymphoid tissue, particularly in the small intestine. Among probiotic bacteria, especially lactic bacteria, have local or systemic effects depending on their cytokine profile. The mechanism of action of probiotics must be perfectly determined. The properties of the probiotic strain should not change during the production process and storage before use. It must not contain any disease-causing factors.

Probiotics, especially *Bifidobacterium* and *Lactobacillus*, have a long history in terms of safety. In addition, these bacteria and especially *Lactobacillus* are frequently encountered in nature. *Lactobacillus, Bifidobacteria, Lactococcus*, and yeasts are generally in the category of "Generally recognised as safe" organisms. However, a few infections have been reported, mostly in immunocompromised patients. Not all probiotics used are included in this category. It must be scientifically proven whether probiotics are effective and safe (14). The probiotic effect of each strain is unique. Therefore, each strain of bacteria should be individually tested for its associated health benefit. Its efficacy has not been proven due to very low quality studies, microbiota variability and response to modulation attempts, and the diversity of probiotic strains used (3). It is necessary to be able to work on large cohorts to account for inter-patient variability. There should be a global approach to the microbiota. It is also important to select the correct probiotic strain for a particular application, because the effect of the probiotic is strain dependent. All these indicators pave the way for research focusing on the benefits of modulation and its relationship to the microbiota and host health.

There are several risk theories regarding the use of probiotics. It is thought that probiotics may cause infections due to translocation. Some strains appear to have the capacity to reduce or increase translocation of gut bacteria. Another negative effect of probiotics may be due to the production of metabolites with toxic potential. D-lactate production during bacterial fermentation, which is responsible for lactic acidosis, is one of the possible risks. In children with short bowel syndrome, administration of a microbiota abnormally rich in lactobacilli or the administration of probiotic *Lactobacillus* strains was associated with acidosis resulting in encephalopathy or hyperventilation. However; no complaint of lactic acidosis is reported in healthy children. One of the most important risks is the transfer of antibiotic resistance genes between the host's common bacteria and probiotic strains in the host digestive tract. Gene transfers may occur in the microbiota in the gut and the diversity of bacteria in this area may increase. Therefore, probiotic strains can be vectors of resistance genes that act as donors or recipients. It is recommended to use probiotic strains that do not contain acquired and potentially transferable resistance genes. This raises the problem of using probiotic strains belonging to the species that naturally carry virulence and/or resistance to antibiotics such as enterococci or *E. coli*. Genomic analyzes of probiotic enterococci strains proved that these strains lacked virulence factors.

**Prebiotics**

Prebiotics are fibers, which are generally indigestible food components, and they positively affect host health by stimulating the growth and/or activity of some microorganisms in the colon (1). FAO and WHO define prebiotics as food ingredients that confer health benefits on the host associated with modulation of microbiota. Prebiotics consist of various carbohydrate components that are not well understood according to their origin, fermentation profile and appropriate dosage for health effects. Some sources of prebiotics are; breast milk, soybeans, sources of inulin (such as jerusalem artichoke, chicory root, etc.), raw oats, unrefined wheat, unrefined barley, black cumin, non-digestible carbohydrates and especially non-digestible oligosaccharides.

**Synbiotics**

Gibson and Roberfroid, when introducing the concept of prebiotics, have stated that prebiotics have additional benefits

when combined with probiotics to form what they call synbiotic (1). Synbiotics were developed to overcome possible survival challenges for probiotics. An improvement in the survival of probiotic bacteria in the passage through the upper intestinal tract was observed when synbiotics were used.

**Cancer**

According to the oldest known records, cancer is a serious health problem that has been seen since 3,000 BC and its incidence continues to increase even today (6). Cancer is a difficult disease to fight because of the many physical, social, material and spiritual ailments it carries with it. Approximately one million patients are newly diagnosed as having cancer in the world every year (7). Cancer formation is caused by the formation of abnormal cells (neoplasia) that can multiply uncontrollably in any part of the body. As these cells continue to multiply, they become a mass called a tumor. Although the formation of these neoplastic masses, which are independent of control mechanisms, can be dangerous, they are mostly harmless (8). As a matter of fact, in order to be able to talk about cancer, the features of invasion and metastasis along with uncontrolled proliferation must be present in the cell (7). When a normal cell acquires each of these malignant properties, it is considered to have passed into the next stage of carcinogenesis. These four stages are as follows: Stage 1 (initiation, progressing very slowly, also called latent stage), Stage 2 (promotion, much faster growing cell groups, promoters are effective), Stage 3 (progression, acting independently of the surrounding tissue, genetic mutations are now irreversible) and Stage 4 (invasion and metastasis, very difficult to heal) (8). Cancer development can be stopped by intervention in cells in the early stages of mutation. For this reason, diagnostic tests without risk factors are important for each individual. Especially people with a family history of cancer are expected to be more sensitive about routine controls (6). Despite the efforts to develop standard approaches for certain types of cancer, it is known that cancer is a disease specific to the individual. Chemotherapy, radiotherapy and surgical methods are frequently used in cancer treatment and constitute the most important parts of the treatment.

In summary, cancer, which is a disease characterized by uncontrolled proliferation in cells, causes millions of deaths every year and is one of the biggest health problems that humanity struggles with (7). For this reason, a wide variety of methods are being tried to be produced by countless scientists for the treatment of cancer today.

**Mechanism of Effect of Probiotics in Cancer**

Studies on the inclusion of probiotics among the adjunct applications to traditional cancer treatments have increased significantly in recent years (9). However, the mechanisms related to the antitumor properties of probiotics are still not fully elucidated and remain partially unclear. The gut microbiota is associated with a number of pathways that are considered to play a central role in this process. Some of these pathways are (7);

1. Regulating the microbiota by inhibiting pathogens that produce cancer-promoting agents

2. Inhibition of pathogenic microorganisms and activation of immunomodulatory cells by production of antimicrobial substances

3. Reduction of DNA damage and genotoxicity

4. Production of anti-cancer metabolites

Probiotics exert their cancer-preventing and therapeutic effects mainly by regulating the intestinal microbiota, improving the physico-chemical conditions of the colon, increasing the intestinal barrier function, modulating intestinal bacterial metabolism and enzymes, thus preventing carcinogens, secreting anticancer metabolites, and reducing inflammation (10,11[th]]. More studies are needed to determine how and to what extent the positive effects of probiotics affect the cancer rate (12).

**The Relationship of Probiotics with Some Kinds of Cancer**

**Cancers of the Gastrointestinal System**

Of all cancers in the World, 25% are cancers of the digestive system. Of cancer-related deaths, 9% are due to gastrointestinal (GI) cancer types (15). GI cancers are defined as multifactorial diseases and are associated with complex pathways such as genetics, epigenetics, immunity, environmental factors, diet and vital changes, which have a known effect on the gut microbiota. Studies show that probiotics have positive effects on GI cancers. Important studies have shown that probiotics have anti-proliferative or pro-apoptotic activities (16). Colon cancer and stomach cancer are the most commonly studied cancers among GI cancers. Although lactic acid bacteria and *Bifidobacterium* are frequently used among probiotics, *Streptococcus thermophilus*, *Enterococcus*, *Escherichia coli* and *Saccharomyces boulardii* species are also included in the studies (16,17). Recent studies have shown the anti-proliferative role of *L. rhamnosus* GG strain in human gastric cancer (GC) and colon cancer cells (18). Another probiotic product, *Bifidobacterium adolescentis* SPM0212, inhibits the proliferation of colon cancer cell lines including HT-29, SW 480 and Caco-2 (17). With this; *Bacillus polyfermenticus*, *L. acidophilus 606*, *LGG/Bb12* and *LGG/Bifidobacterium animalis subsp. lactis* is shown among other probiotic products and strains known for their apoptotic effects on human colon cancer cells.

**Colorectal Cancer**

Evidence shows that intake of probiotics is an effective method for proper protection of the healthy gut microbiota and reducing the risk of colon cancer (18). Many *in vitro* and *in vivo* studies on this subject have been applied in animal models and human cancer cell lines. In contrast, there are few randomized placebo-controlled studies (RCTs) reporting that probiotics have an effect on the prevention and inhibition of intestinal carcinogenesis. Probiotics have intraluminal, systemic and direct effects on the intestinal mucosa (19). Among the mentioned intraluminal effects are competitive exclusion of pathogenic intestinal flora, alteration of intestinal microflora enzyme activity, reduction of carcinogenic secondary bile acids, binding of carcinogens and mutagens, and increased production of short-chain fatty acids.

It is clearly supported by the available evidence that probiotics have a versatile immunomodulatory role in colorectal cancer (CRC), and particularly probiotics have ability to regulate intestinal inflammation, which is considered a major risk factor for CRC. Probiotics may show their benefits in this area, not only by preventing CRC, but also by improving side effects in patients undergoing colorectal surgery and being treated for CRC (17). A few of the randomized controlled studies have clearly demonstrated that the use of probiotics is an effective method that can be used in patients with CRC (20,21). Studies have shown that, in patients undergoing abdominal surgery, the use of probiotics can prevent post-operative superficial incision surgical site infections and improve the integrity of the intestinal mucosal barrier. In addition, the use of probiotics improves the quality of life of patients, shortens the time spent in the hospital after surgery and the time needed for antibiotic administration.

Administration of probiotics as a mixture of one or more strains before surgery (preoperatively) in patients with CRC may reduce dysbiosis and similar bowel-related side effects (22). Gianotti et al. (22) showed that *L. johnsonii* (La1) modulated the gut microbiota by adhering to the colonic mucosa after its preoperative administration, by reducing pathogen concentration, and by reducing local immunity. The study also showed that La1 was more effective than another probiotic, B. longum (BB536).

Liu et al. (23) showed in two studies that administration of probiotics (*L. plantarum*, *L. acidophilus*, and *B. longum*) before colorectomy improved intestinal mucosal barrier integrity, decreased the rate of post-surgical infection and septicemia, shortened the duration of antibiotic treatment, inhibited the p38-MAPK signaling pathway, decreased serum serum level of zonulin, and also protected the liver barrier from metastasis (24). Zonulin is a protein synthesized by liver and intestinal cells, and when the regulation of this pathway is disrupted, autoimmune, inflammatory and neoplastic disorders may occur. Pala et al. (25) included 45,241 volunteers recruited from the The European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. As a result of such a comprehensive study, it was reported that there was a decrease in the risk of CRC with yogurt consumption. In the study of Gao et al. (26), *Lactobacillus reuteri* was shown to suppress colon cancer due to inflammation by providing luminal histamine production, and it was observed that histamine-producing probiotic reduced the number of tumors in the colon and shrunk tumors. It is known that traditional methods used in cancer treatment such as chemotherapy and radiotherapy cause changes in the intestinal microbiota, and these methods can cause mucositis, bacteremia and especially diarrhea (17). Promising results were observed in studies that followed the use of probiotics for the prevention of mucositis in individuals with cancer. In studies in patients with CRC undergoing chemotherapy and radiotherapy, administration of a mixture of eight probiotics, including *L. rhamnosus GG*, significantly reduced the incidence of diarrhea. Prevention of CRC by probiotics depends on the type of microorganism (19). With this, there are also studies stating that viability in probiotics to be used is not one of the conditions sought for anticancer mechanisms. It is predicted that the opportunity to discover new strains with probiotic properties and anti-CRC activities will arise in the coming period with the understanding developed from advanced techniques and gut microbiome research (27).

**Gastric Cancer**

GC ranks fourth among the most common cancer types in the world and third among the main causes of death from cancer (28). The fifth most common type of malignant tumors is GC and surgical intervention is used as the main method for treatment. Studies in patients with GC show that early postoperative enteral nutrition (EN) may aid recovery. However, EN can also cause some complications. Diarrhea, the most common among them, causes fluid and electrolyte loss. The use of probiotics in patients with GC may reduce the incidence of diarrhea. With the administration of a combination of EN and probiotics, positive responses such as improved immune function and decreased inflammatory response can be seen in patients with GC in the postoperative period. A RCT by Zhao et al. (29) supports the effects of probiotic use in ameliorating the complications of EN. Considering the results, it appears that the combination of probiotics and fiber reduces the incidence of diarrhea, increases bowel motility and reduces bowel disorders in patients with GC in the postoperative period.

Most of the studies investigating the relationship between probiotics and GC are mainly directed at fighting *Helicobacter pylori* (*H. Pylori*) infection, which has properties such as disrupting the acid mucus barrier and colonizing the gastric epithelium (17). Positive inhibitory effects of probiotics including *B. bifidum, L. acidophilus, L. rhamnosus, L. salivarius* and several other probiotics to abolish *H. pylori* infection can be observed in animal models (30). Another study investigated the administration of kimchi, a Korean probiotic, in humans and mice with GC due to *H. pylori* (31). In the study, *H. pylori*-infected C57BL/6 mice were treated with anti-cancer kimchi (cpKimchi) mixed in water for 36 weeks, and standard kimchi and specially prepared kimchi were compared for their anti-inflammatory and anti-mutagenesis properties. Significant reduction in tumorigenesis in the *H. pylori* infected group were noted in those using cpKimchi. As a result, it is stated that cpKimchi administration provides significant changes in fecal microbiota and anti-cancer activities.

**Other Gastrointestinal Cancers**

Although less numerous than studies on CRC and GC, studies have also been conducted to show the relationship of probiotics to other types of GI cancer, such as esophageal, pancreatic, and liver cancers (17). In some previous studies, it is supported that probiotics exert their effects on pancreatic cancer through many different mechanisms by controlling risk factors such as, diabetes, pancreatic necrosis, inflammation and obesity. Among all cancers, liver cancer is less common (7). Its origin is liver cells, which are often referred to as hepatocytes. For this reason, a significant portion of liver cancers are called hepatocellular cancer (HCC). There are limited studies investigating the effects of probiotics on liver cancer. However, it is supported by studies that probiotics reduce hepatocyte damage, inflammation and proinflammatory

cytokines, while increasing antioxidant activity. In these ways, it can be determined that probiotics have a role in preventing the formation of liver cancer. In another study by Li et al. (32), in which probiotics were reported to inhibit HCC progression in mice, the results of feeding tumor-injected mice with a probiotic mixture were compared with the control group. As a result, it is suggested that probiotics can alter the composition of the microbiota and reduce the size of liver tumors. In addition, it has been shown in the study that angiogenic factors can also be regulated by probiotic administration.

**Bladder Cancer**

Although *Bacillus calmette guerin* (BCG) is the current gold standard immunotherapy for bladder cancer, the rate of responders is 50-70% and it has side effects (33). In a study, it was investigated whether *Lactobacillus rhamnosus GG* (LGG) could be as effective in bladder cancer as BCG. In this study, it was observed that LGG treatment greatly (p=0.006) increased the treatment response in mice, restored XCL1 levels in bladders, and recruited large numbers of macrophages and neutrophils to the tumor site. When cure rates of LGG and BCG immunotherapies were compared with cure rate in untreated mice, cure rates was 20% in untreated mice, 89% in LGG group, and 77% in BCG group, indicating that LGG may have the potential to replace BCG immunotherapy in the treatment of bladder cancer. Another study indicated that probiotics increased the activity of dendritic cells, which had a significant effect on immune manipulation by causing the mobilization of natural killer cells (34). It suggests that it may be possible to minimize the risk of bladder cancer with probiotic supplements.

**Prostat Cancer**

Tumor necrosis factor-associated apoptosis-inducing ligand (TNFAIL) induces apoptosis in malignant tumor cells as an endogenous cytokine (35). In a study, it was shown for the first time that *Lactobacillus* started TNFAIL production in human peripheral blood mononuclear cells (PBMC) and induced TNFAIL production on the surface of PBMC and in culture medium. Treatment with *Lactobacillus* facilitated the natural killer activity of PBMC against prostate cancer. According to the results of the study, *Lactobacillus* facilitated the natural killer activity by producing TNFAIL and there was a possibility that a new TNFAIL-based treatment strategy might emerge against malignant tumors.

**Skin Cancer**

A study examined the prophylactic effect of probiotics and their metabolites against skin cancer (36). Hairless mice were orally administered lipoteichoic acids obtained from *Lactobacillus rhamnosus GG*. According to the results of the study, it was observed that the T cells of the treated subjects produced more interferon-γ, TH and CTL cells. In addition, a delay in tumor appearance was also observed. In addition, the immune-enhancing effect of lipoteichoic acids was emphasized. In another study, the effects of kefir on skin cancer were examined and a significant decrease was observed in intracellular reactive oxygen species, while suppressing the morphological changes caused by UVC irradiation (37). It was also observed that it suppressed apoptosis, prevented the formation of thymine dimer, and did not cause HMV-1 cell death caused by UVC irradiation.

**Head and Neck Cancer**

One study examined the effects of *Lactobacillus acidophilus* on tongue cancer (38). Cancer cells were incubated with probiotics for forty-eight hours, and as a result, it was observed that the proliferation of cancerous cells was greatly inhibited. It is thought that free radicals and Ca2+ increase in cells may cause this.

**Breast Cancer**

Surfactin produced from the *Bacillus subtilis* probiotic has been found to have an anticancer effect against breast cancer cells (39). It has been stated that this effect of surfactin is dose dependent and it inhibits cell growth by approximately 10 μg/mL in 24 hours. Another study examined the effect of *Lactobacillus casei shirota* on breast cancer in Japanese women (40). Regular consumption of *Lactobacillus* and isoflavones since puberty has been shown to be inversely proportional to the incidence of breast cancer. Although the interaction of *Lactobacillus* with isoflavones is not statistically significant, it is thought to be a biological interaction. In a study on mice, the effect of orally ingestion of *Lactobacillus acidophilus* on mammary tumors was investigated (41). According to the results of the study, it was observed that the treated group had more interleukin 12 production and less transforming growth factor production. A decrease in tumor growth rate was also observed. Another experiment on mice examined the immunomodulatory effects of *Lactobacillus acidophilus* (42). Administration of probiotics together with a chemotherapeutic agent (cyclophosphamide) for 15 days significantly regressed the tumor, increased lymphocyte proliferation and caused a change in cytokine expression pattern.

**Leukemia**

In a study, the apoptotic effect of kefir grain product (*Lactobacillus*) on multidrug resistant (MDR) leukemia cells was investigated by probiotic fermentation technology (PFT) (43). PFT was shown to increase apoptosis in cancer cells in a dose-dependent manner. The obtained data showed that treatment of cancer cells with PFT caused a remarkable reduction in mitochondrial polarization compared with untreated cells. The results indicated that PFT might be a potential therapy for the treatment of MDR leukemia. Kefir consumption is recommended for those with adult lymphoblastic leukemia based on its pro-apoptotic effect (36). In addition, kefir consumption causes decreased cell proliferation and increased apoptosis in leukemia (44,45). Chiu described bacterial soluble factors secreted by *Lactobacillus casei* rhamnosus which were shown to increase apoptosis of the human monocytic leukemia cell line (46).

A two-year-old child diagnosed as having leukemia and treated for it developed severe neutropenia and increased inflammation (47). Looking at the laboratory test results, *Bifidobacterium breve* was found. However, *Bifidobacterium breve* was not found when the child's food was examined. *Bifidobacterium* spp. sometimes

cause serious diseases and infections. *B. breve* septicemia was also found in another neonate treated with probiotics (48). A case of *B. breve* sepsis who had acute B-cell lymphoblastic leukemia was also reported (49). Therefore, it is not recommended to use probiotics as therapeutics due to their invasiveness. It has also been thought that the gut microbiota may regulate host immunity and homeostasis (50). However, it has been stated that these positive effects are strain and/or species specific.

## Conclusion

It is supported by studies that the microbiota, which is accepted as an organ on its own, has an important place in the diagnosis and treatment of diseases. In this context, probiotics continue to gain importance. Cancer is one of the diseases in which the mechanisms of action of probiotics are being investigated. There are many genetic and environmental causes that cause the formation of cancer, which is among the top causes of death in the world. In addition to the traditional methods used for cancer treatment, innovative research still continues. Although there are studies investigating the importance of probiotics in the diagnosis and treatment of cancer, their mechanism of action has not yet been fully explained. However, it is seen that most of the researches are for a limited number of cancer types, and more researches covering all cancer types are needed. While the strongest evidence for the anticancer effects of probiotics comes from animal studies, the evidence from human studies (epidemiology and experimental) appears to be still limited. Carefully designed human clinical trials to validate the wealth of experimental studies should be an important target for the future. In many studies, it is reported that the positive effects of probiotics vary greatly according to the type and strain of bacteria. In this direction, the effects of different probiotic strains on cancer formation and its mechanism should be determined, so that strains with positive effects should be identified. In addition, it should be observed whether the combination of probiotics with prebiotics or with each other is effective on cancer types. As a result, it is necessary to conduct many comprehensive and multidisciplinary studies to investigate the effects of probiotics on cancer types.

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Authorship Contributions

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## References

1. Pandey KR, Naik SR, Vakil BV. Probiotics, prebiotics and synbiotics-a review. J Food Sci Technol 2015;52:7577-87.
2. Aureli P, Capurso L, Castellazzi AM, Clerici M, Giovannini M, Morelli L, et al. Probiotics and health: an evidence-based review. Pharmacol Res 2011;63:366-76.
3. Butel MJ. Probiotics, gut microbiota and health. Med Mal Infect 2014;44:1-8.
4. Williams NT. Probiotics. Am J Health Syst Pharm 2010;67:449-58.
5. Tripathi MK, Giri SK. Probiotic Functional Foods: Survival of Probiotics During Processing and Storage. Journal of Functional Foods 2014;9:225-41.
6. Baykara O. Current Modalities in Treatment of Cancer. Balıkesir Health Sciences Journal 2016;5:154-65.
7. Kahraman M, Karahan AG. Tumor Suppresor Effects of Probiotics. Türk Hij Den Biyol Derg 2018;75:421-42.
8. Tüfekçi Alphan ME. Hastalıklarda Beslenme Tedavisi. Hatiboğlu Yayınları; 2018.
9. Górska A, Przystupski D, Niemczura MJ, Kulbacka J. Probiotic Bacteria: A Promising Tool in Cancer Prevention and Therapy. Curr Microbiol 2019;76:939-49.
10. Chandel D, Sharma M, Chawla V, Sachdeva N, Shukla G. Isolation, characterization and identification of antigenotoxic and anticancerous indigenous probiotics and their prophylactic potential in experimental colon carcinogenesis. Sci Rep 2019;9:14769.
11. Liong MT. Probiotics: a critical review of their potential role as antihypertensives, immune modulators, hypocholesterolemics, and perimenopausal treatments. Nutr Rev 2007;65:316-28.
12. Valeriano VD, Parungao-Balolong MM, Kang DK. In Vitro Evaluation of the Mucin-Adhesion Ability and Probiotic Potential of Lactobacillus mucosae LM1. Journal of Applied Microbiology 2014;117:485–97.
13. Sanders ME, Akkermans LM, Haller D, Hammerman C, Heimbach J, Hörmannsperger G, et al. Safety assessment of probiotics for human use. Gut Microbes 2010;1:164-85.
14. Haukioja A. Probiotics and oral health. Eur J Dent 2010;4:348-55.
15. Serban DE. Gastrointestinal cancers: influence of gut microbiota, probiotics and prebiotics. Cancer Lett 2014;345:258-70.
16. Javanmard A, Ashtari S, Sabet B, Davoodi SH, Rostami-Nejad M, Esmaeil Akbari M, et al. Probiotics and their role in gastrointestinal cancers prevention and treatment; an overview. Gastroenterol Hepatol Bed Bench 2018;11:284-95.
17. Orlando A, Refolo MG, Messa C, Amati L, Lavermicocca P, Guerra V, et al. Antiproliferative and proapoptotic effects of viable or heat-killed Lactobacillus paracasei IMPC2.1 and Lactobacillus rhamnosus GG in HGC-27 gastric and DLD-1 colon cell lines. Nutr Cancer 2012;64:1103-11.
18. So SS, Wan ML, El-Nezami H. Probiotics-mediated suppression of cancer. Curr Opin Oncol 2017;29:62-72.
19. Chong ES. A potential role of probiotics in colorectal cancer prevention: review of possible mechanisms of action. World J Microbiol Biotechnol 2014;30:351-74.
20. Kotzampassi K, Stavrou G, Damoraki G, Georgitsi M, Basdanis G, Tsaousi G, et al. A Four-Probiotics Regimen Reduces Postoperative Complications After Colorectal Surgery: A Randomized, Double-Blind, Placebo-Controlled Study. World J Surg 2015;39:2776-83.

21. Aisu N, Tanimura SHU, Yamashita Y, Yamashita K, Maki K, Yoshida, et al. Impact of Perioperative Probiotic Treatment For Surgical Site Infections in Patients with Colorectal Cancer. Experimental and Therapeutic Medicine 2015;10:966-72.
22. Gianotti L, Morelli L, Galbiati F, Rocchetti S, Coppola S, Beneduce A, et al. A randomized double-blind trial on perioperative administration of probiotics in colorectal cancer patients. World J Gastroenterol 2010;16:167-75.
23. Liu ZH, Huang MJ, Zhang XW, Wang L, Huang NQ, Peng H, et al. The Effects of Perioperative Probiotic Treatment on Serum Zonulin Concentration and Subsequent Postoperative Infectious Complications After Colorectal Cancer Surgery: A Double-Center and Double-Blind Randomized Clinical Trial. The American Journal Of Clinical Nutrition 2012;97:117-26.
24. Liu Z, Li C, Huang M, Tong C, Zhang X, Wang L, et al. Positive Regulatory Effects of Perioperative Probiotic Treatment on Postoperative Liver Complications After Colorectal Liver Metastases Surgery: A Double-Center and Double-Blind Randomized Clinical Trial. BMC Gastroenterol 2015;15:34.
25. Pala V, Sieri S, Berrino F, Vineis P, Sacerdote C, Palli D, et al. Yogurt consumption and risk of colorectal cancer in the Italian European prospective investigation into cancer and nutrition cohort. Int J Cancer 2011;129:2712-9.
26. Gao C, Ganesh BP, Shi Z, Shah RR, Fultz R, Major A, et al. Gut Microbe-Mediated Suppression of Inflammation-Associated Colon Carcinogenesis by Luminal Histamine Production. Am J Pathol 2017;187:2323-36.
27. Ambalam P, Raman M, Purama RK, Doble M. Probiotics, prebiotics and colorectal cancer prevention. Best Pract Res Clin Gastroenterol 2016;30:119-31.
28. Xie H, Lu Q, Wang H, Zhu X, Guan Z. Effects of probiotics combined with enteral nutrition on immune function and inflammatory response in postoperative patients with gastric cancer. J BUON 2018;23:678-83.
29. Zhao R, Wang Y, Huang Y, Cui Y, Xia L, Rao Z, et al. Effects of Fiber and Probiotics on Diarrhea Associated with Enteral Nutrition in Gastric Cancer Patients: A Prospective Randomized and Controlled Trial. Medicine 2017;96:e8418.
30. Zhu XY, Liu F. Probiotics as an adjuvant treatment in Helicobacter pylori eradication therapy. J Dig Dis 2017;18:195-202.
31. Han YM, Park JM, Lee D, Oh JY, Hahm KB. Korean Probiotic Kimchi Prevented Helicobacter pylori-Associated Gastric Cancer in Mice and Human. The FASEB Journal 2017;31:1067-71.
32. Li J, Sung CY, Lee N, Ni Y, Pihlajamäki J, Panagiotou G, et al. Probiotics modulated gut microbiota suppresses hepatocellular carcinoma growth in mice. Proc Natl Acad Sci U S A 2016;113:E1306-15.
33. Seow SW, Cai S, Rahmat JN, Bay BH, Lee YK, Chan YH, et al. Lactobacillus rhamnosus GG induces tumor regression in mice bearing orthotopic bladder tumors. Cancer Sci 2010;101:751-8.
34. Feyisetan O, Tracey C, Hellawell GO. Probiotics, dendritic cells and bladder cancer. BJU Int 2012;109:1594-7.
35. Horinaka M, Yoshida T, Kishi A, Akatani K, Yasuda T, Kouhara J, et al. Lactobacillus strains induce TRAIL production and facilitate natural killer activity against cancer cells. FEBS Lett 2010;584:577-82.
36. Weill FS, Cela EM, Paz ML, Ferrari A, Leoni J, González Maglio DH. Lipoteichoic acid from Lactobacillus rhamnosus GG as an oral photoprotective agent against UV-induced carcinogenesis. Br J Nutr 2013;109:457-66.
37. Patel S, Goyal A. Evolving Roles of Probiotics in Cancer Prophylaxis and Therapy. Probiotics Antimicrob Proteins 2013;5:59-67.
38. Shi X, Chen J, Che T, Bai D, He X. [A study on human tongue cancer cells' proliferation affected by Lactobacillus acidophilus]. Hua Xi Kou Qiang Yi Xue Za Zhi 2012;30:87-92.
39. Lee JH, Nam SH, Seo WT, Yun HD, Hong SY, Kim MK, et al. The Production of Surfactin During the Fermentation of cheonggukjang by Potential Probiotic Bacillus subtilis CSY191 and the Resultant Growth Suppression of MCF-7 Human Breast Cancer Cells. Food Chemistry 2012;131:1347-54.
40. Toi M, Hirota S, Tomotaki A, Sato N, Hozumi Y, Anan K, et al. Probiotic Beverage with Soy Isoflavone Consumption for Breast Cancer Prevention: A Case-control Study. Current Nutrition&Food Science 2013;9:194-200.
41. Yazdi MH, Soltan Dallal MM, Hassan ZM, Holakuyee M, Agha Amiri S, Abolhassani M, et al. Oral administration of Lactobacillus acidophilus induces IL-12 production in spleen cell culture of BALB/c mice bearing transplanted breast tumour. Br J Nutr 2010;104:227-32.
42. Maroof H, Hassan ZM, Mobarez AM, Mohamadabadi MA. Lactobacillus acidophilus could modulate the immune response against breast cancer in murine model. J Clin Immunol 2012;32:1353-9.
43. Ghoneum M, Gimzewski J. Apoptotic effect of a novel kefir product, PFT, on multidrug-resistant myeloid leukemia cells via a hole-piercing mechanism. Int J Oncol 2014;44:830-7.
44. Maalouf K, Baydoun E, Rizk S. Kefir induces cell-cycle arrest and apoptosis in HTLV-1-negative malignant T-lymphocytes. Cancer Manag Res 2011;3:39-47.
45. Jalali F, Sharifi M, Salehi R. Kefir induces apoptosis and inhibits cell proliferation in human acute erythroleukemia. Med Oncol 2016;33:7.
46. Chiu YH, Hsieh YJ, Liao KW, Peng KC. Preferential promotion of apoptosis of monocytes by Lactobacillus casei rhamnosus soluble factors. Clin Nutr 2010;29:131-40.
47. Bottacini F, Ventura M, van Sinderen D, O'Connell Motherway M. Diversity, ecology and intestinal function of bifidobacteria. Microb Cell Fact 2014;13(Suppl 1):S4.
48. Ohishi A, Takahashi S, Ito Y, Ohishi Y, Tsukamoto K, Nanba Y, et al. Bifidobacterium septicemia associated with postoperative probiotic therapy in a neonate with omphalocele. J Pediatr 2010;156:679-81.
49. Redman MG, Ward EJ, Phillips RS. The efficacy and safety of probiotics in people with cancer: a systematic review. Ann Oncol 2014;25:1919-29.
50. Bindels LB, Beck R, Schakman O, Martin JC, De Backer F, Sohet FM, et al. Restoring Specific Lactobacilli Levels Decreases Inflammation and Muscle Atrophy Markers in an Acute Leukemia Mouse Model. PloS One 2012;7:e37971.

Review

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# Difficulties for Mothers: Home Care of Babies Born Preterm

## Anneler için Zorluklar: Evde Prematüre Bebek Bakımı

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### ABSTRACT

Mothers who had preterm labor were expected to face difficulties with baby care during the postnatal period. This study aimed to review studies on difficulties experienced by mothers who had premature labor regarding childcare at home during the postnatal period. The literature review was carried out between 2000 and 2019 in databases of PubMed, Medline, CINAHL, Cochrane library, ULAKBIM, Google Scholar, and EMBASE. Mothers who had preterm labor experienced difficulties with diaper use, bathing, umbilical cord care, baby feeding, skin-to-skin contact, and recognition of newborn crying. Therefore, mothers need the support of health professionals for the health status of the newborn and their lack of self-confidence regarding baby care. However, the lack of home care guidelines leaves mothers helpless in meeting these needs. Mothers should be ready for the care of babies born preterm. For this reason, mothers who had preterm labor should be informed about the potential difficulties during their stay in the hospital. Mothers also need to be educated about the care of infants born preterm in the postnatal period. Thus, mothers can experience the home care process positively by becoming fully prepared to take the responsibility for home care. Developing clinical guidelines for postnatal care of babies born preterm can help reduce the concerns of mothers, shorten hospital stay, and reduce morbidity risks.

**Keywords:** Preterm labor, prematurity, baby care, difficulties

### ÖZ

Erken doğum yapan annelerin doğum sonu süreçte bebek bakımı konusunda güçlüklerle karşılaşmaktadırlar. Bu derlemede, erken doğum yapan annelerin doğum sonu dönemde bebeklerinin evde bakımı konusunda yaşadıkları güçlükleri incelemektir. Literatür taraması 2000-2019 yılları arasında PubMed, Medline, CINAHL, Cochrane kütüphanesi, ULAKBİM, Google Akademik ve Elseiver'in EMBASE veri tabanları kullanılarak yapılmıştır. Erken doğum yapan anneler, bebek bezi kullanma, banyo, göbek kordonu bakımı, bebek beslenmesi, ten tene temas, yenidoğan ağlamalarının tanınması konusunda zorluklar yaşamaktadırlar. Bu nedenle anneler, yenidoğanın sağlık durumu, bebeğin bakımında öz güven eksikliği ve sağlık profesyonellerine ihtiyaç duyma gibi konularda desteğe ihtiyaç duymaktadırlar. Ancak, evde bakım rehberlerinin olmaması annelerin bu ihtiyaçlarının karşılanamamasına neden olmaktadır. Prematüre bebeklerin bakımı için annelerin hazır olmaları gerekmektedir. Bu nedenle erken doğum tehdidi olan annelere hastanede kaldıkları süre içerisinde, yaşadıkları ya da daha sonra yaşayabilecekleri güçlüklere ilişkin eğitimler ve bilgilendirmeler yapılmalıdır. Annelerin prematür bebek bakımı ile ilgili doğum sonu dönemde de bilgilendirilmeye gereksinimleri vardır. Böylelikle anneler evde bakım sorumluluğunu tam olarak üstlenmeye hazır hale gelerek evde bakım sürecini olumlu yönde deneyimleyebilir. Prematüre bebeklerin doğum sonu bakımları ile ilgili klinik rehberlerinin geliştirilmesi, annelerin endişelerinin azaltılması, hastanede kalış süresinin kısaltılması ve morbidite risklerini azaltmada fayda sağlayabilir.

**Anahtar Sözcükler:** Erken doğum, prematürite, bebek bakımı, güçlükler

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## Introduction

A normal pregnancy lasts approximately 40 weeks, and infants born before the 37th gestational week are defined as "preterm" or "premature" (1,2). According to the World Health Organization (WHO), preterm babies are classified as extremely preterm (<28th gestational week), very preterm (28th-32th gestational week), and moderate to late preterm (32th-37th gestational week) (2).

According to the WHO, nearly 15 million babies are born preterm each year, and this number is increasing annually (2). Mothers hospitalized in maternity wards with a diagnosis of threatened preterm labor are most commonly anxious about infant care (3-6). Therefore, mothers expect support from nurses for pregnancy care and postnatal home care of the baby (7). Mothers diagnosed with preterm labor should be educated starting from the onset of gestation, including the neonatal intensive care unit (NICU) process if the baby requires intensive care after the birth, to the discharge process. Moreover, comprehensive home care plans are needed, support services should be determined, and continuity of care should be ensured and maintained (8,9). This raises the issue of the need for evidence-based care guidelines that will support parents and eliminate their anxieties so that home care of the baby born preterm can be maintained appropriately.

Guidelines for neonatal intensive care and discharge process are mostly related to the treatment and follow-up of infants (10-13). Appropriate guidelines, which involve the family, are needed to provide quality care to babies after discharge. The lack of home care guidelines may cause mothers who had premature births to have difficulty providing care due to the lack of information (14). Therefore, mothers who had premature birth should be informed accurately and adequately about how to care for their babies before discharge (15). Potential difficulties will be prevented when mothers are informed well before discharge.

Nurses have important roles in helping mothers who give premature birth adapt to the home care of the baby after discharge (16). These roles include assessment and direct care of the baby in the hospital and at home (17), training mothers on threatened preterm labor and preterm labor (18), assessment of the home environment, assessment of maternal health (19), and provision of support (17). However, the provision of adequate information about home care of preterm babies and extension of the appropriate care at home is not among the priority options of nurses.

This literature review aimed to reveal the difficulties experienced by mothers who had premature labor regarding infant care at home.

## Methods

The literature review was conducted between 2000 and 2019 in Turkish and English by scanning databases of PubMed, Medline, CINAHL, Cochrane library, ULAKBIM, Google Scholar, and EMBASE. The following keywords were used: "prematurity," "premature infant," "neonatal intensive care," "threatened preterm labor," "premature birth," "discharge from neonatal intensive care," "home care of premature neonatal," "baby care," "challenge," and "difficulty" and their Turkish translations. As a result of the screening, 36 articles that met the inclusion criteria were included in the review. Of these articles, five were about the psychological conditions experienced by mothers with babies in the NICU, six focused on the difficulties of mothers in the care of their babies in the NICU, seven investigated the psychological conditions experienced by mothers because of preterm birth, three reported about the difficulties experienced by healthcare professionals in adapting mothers to the NICU, and 15 presented home care challenges of premature newborns.

### Difficulties in Home Care of Preterm Infants

Mothers who have babies born preterm experience a mixture of happiness and sadness. The reason is the thought of being separated from the baby after birth (20) because the natural process expected to develop between the mother and baby may be disrupted during the treatment of babies born preterm in the NICU, and families may face difficulties related to baby care (21). During the NICU treatment, mothers who had a premature birth are reported to experience difficulties such as concerns about the health of the infant, loss of the maternal role, performing parenting roles for other children, limited visiting hours, transportation barriers, balancing other aspects of family life, and financial problems (22-24). Unclear medical explanations made during the NICU treatment, technological equipment used during the care, and changes in the physical appearance of the baby are quite stressful factors for parents (25). Hemati et al. (26) reported that mothers had difficulty in achieving the home care of the infant after discharge from the NICU, they felt a sense of incompetence regarding breastfeeding, they recognized dependence on the hospital and the nurse, and they felt stressed and anxious constantly. In another study, mothers who had their baby treated in the NICU were found to feel alienated toward their babies while caring for them, and this result suggested that, in addition to mothers' training regarding the treatment and care of the baby in the NICU, interventions for understanding mothers and preventing them from feeling alienated should be arranged (21). Nevertheless, several mothers report that their emotional state is not understood by NICU nurses and physicians (27). This may lead to new problems that need coping for mothers who have infants born preterm and who feel that they are not understood by healthcare workers.

The main difficulties experienced after discharge include feeding and breastfeeding the baby born preterm (28-30). Nutritional problems, sudden death, and hyperbiluribinemia risk are higher in infants discharged from the NICU than infants born at term (31,32). Difficulties such as the need for oxygen therapy as in the hospital, tube feeding, medication administration, and apnea follow-up increase the difficulties experienced by mothers after the baby's discharge from the NICU (14). All these practices bring about an uncertain and anxious process for mothers who had a preterm delivery (14,33). In a study conducted in our country, parents who have infants born preterm were expected to experience a mild level of anxiety. Their anxiety was found to increase especially while counting and assessing the baby's

breathing (34). These complications, which may occur after discharge, increase the risk of postpartum depression in mothers who had a premature delivery (35). By contrast, the depressed state of women during and after delivery may adversely affect the mental health of their spouses/partners and may disrupt family integrity (36). Moreover, the material losses that occur during the treatment at NICUs may affect family integrity (37,38). In addition to spiritual stress felt after the baby was discharged from the NICU, failure to continue working to care for the baby and failure to find alternative solutions for working conditions such as part-time employment also cause financial stress in families (37,38). Parents may experience psychosocial problems as a result of material and spiritual difficulties.

Recent research presented that the difficulties experienced by mothers are similar. Nurses should address any difficulties before discharge and explain potential problems systematically to mothers in a quiet environment without waiting for the day of discharge. If mothers are facing threatened preterm labor, they should be educated and informed about the expected difficulties during the hospital stay and later upon discharge. Thus, on the day of discharge, missed care services of mothers should be offered gradually without overloading them with information.

**Role of Healthcare Professionals in the Home Care of the Baby Born Preterm**

For mothers who had premature delivery, the discharge of the baby from the NICU means going back to their daily lives and making self-decisions about baby care. Mothers state that social (spouse, family, and friends) and professional support is an important factor in adapting to the transition from hospital to home (39). Aldirawi et al. (40) determined that nurses were the leading information sources of mothers after discharge. However, a standard guide on the care offered by nurses, who rank the first in terms of information sources, could not be found.

The qualitative study conducted by Raffray et al. (41) revealed that healthcare workers had difficulty in preparing the family about discharge from the NICU, diaper use, bathing the baby, umbilical cord care, feeding the baby, skin-to-skin contact, and recognition of normal and abnormal states of baby's crying. Batman and Şeker (42) used web-based education given by health personnel to prepare parents for discharge and found that the intervention increased the self-confidence and decreased the anxiety levels of parents with infants born preterm. Moreover, other studies have recommended that health professionals should develop programs that provide both education and support to mothers before discharge (18), nurses should arrange home visits and keep in contact with mothers (14), video conferences should be held so that mothers can contact the nurse when necessary (17), and a written control list should be made for customized training programs and home use as the birth weights of infants born preterm are different from each other and they make heterogeneous groups depending on birth weeks (9).

The recommendations of international associations and related studies are as follows**:**

• Infants born preterm and mothers should have skin-to-skin contact (43).

• The first home visit to the infant born preterm and the mother who had been discharged should be conducted within 72 h if possible (44).

• The infant born preterm should be re-visited 1 month after the first home visit, the mother should be followed for breastfeeding, and the infant should be assessed for feeding problems (45).

• The importance of breastfeeding the infant at least 10-12 times or feeding it with formula 8-10 times a day should be explained to the mother (46).

• Mothers should be informed that infants born preterm may be sleeping all the time and should be fed even if asleep (46).

## Conclusion

The NICU treatment of babies born preterm and the discharge period are complex processes due to potential complications. During this process, mothers experience physiological, psychological, and financial difficulties. Mothers' preparation is very important for baby care after discharge. For this reason, mothers should see their babies regularly during NICU treatment until discharge and to participate in the care of the baby so that sustainable home care can be achieved. Nurses should understand, empathize, and empower mothers and facilitate their participation in baby care. Nurses who care for infants born preterm are advised to train families, communicate with them regularly, and place the mother–infant relationship at the center of their care by considering the care needs of the baby and complications that may occur after discharge.

Concerns that mothers will have about baby care in the postnatal period will adversely affect their physiological changes, especially breastfeeding. The support of physicians and nurses for this area, which has some deficiencies, and preparation of guidelines for home care will be a highly valuable service for parents.

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## References

1. The American College of Obstetricians and Gynecologists (ACOG). Extremely Preterm Birth. August 2019 (cited 2019 December 10). Availablefrom: URL: https://www.acog.org/Patients/FAQs/Extremely-Preterm-Birth?IsMobileSet=false

2. World Health Organisation (WHO). PretermBirth. February 2018 (cited 2019 December 3). Availablefrom: URL: https://www.who.int/news-room/fact-sheets/detail/preterm-birth
3. Trumello C, Candelori C, Cofini M,Cimino S, Cerniglia L, Paciello M,et al. Mothers' depression, anxiety, and mental representations after preterm birth: A study during the ınfant's hospitalization in a neonatal ıntensive care unit. Front Public Health 2018;6:359.
4. Henderson J, Carson C, Redshaw M. Impact of preterm birth on maternal well-being and women's perceptions of their baby: a population-based survey. BMJ Open 2016;6:e012676.
5. Rodrigues PB, Zambaldi CF, Cantilino A, Sougey EB. Special features of high-risk pregnancies as factors in development of mental distress: a review. Trends Psychiatry Psychother 2016;38:136-40.
6. Oliveira DC, Mandu ENT. Women with high-risk pregnancy: Experiences and perceptions of needs and care. Escola Anna Nery 2015;19:93-101.
7. Guillaume S, Michelin N, Amrani E, Benier B, Durrmeyer X, Lescure S, et al. Parents' expectations of staff in the early bonding process with their premature babies in the intensive care setting: a qualitative multicenter study with 60 parents. BMC Pediatr 2013;13:18.
8. González MPO, Espitia EC. Caring for a premature child at home: From fear and doubt to trust.Text Context Nursing, Florianópolis 2014;23:828-35.
9. American Academy of Pediatrics Committee on Fetus and Newborn. Hospital discharge of the high-risk neonate. Pediatrics 2008;122:1119-26.
10. Turkish Society of Neonatology. Premature and sicktermın fant nutrition guide. April 2018 (cited 2019 December 3).Availablefrom: URL: http://www.neonatology.org.tr/wp-content/uploads/2016/12/premature_rehber_2018.pdf
11. Tschudy MM, Raphael JL, Nehal US, O'Connor KG, Kowalkowski M, Stille CJ. Barriers to Care Coordination and Medical Home Implementation. Pediatrics 2016;138:e20153458.
12. American Academy of Pediatrics Committee on Fetus and Newborn. Hospital discharge of the high-risk neonate. Pediatrics 2008;122:1119-26.
13. McCourt MF, Griffin CM. Comprehensive primary care follow-up for premature infants. J Pediatr Health Care 2000;14:270-9.
14. Lopez GL, Anderson KH, Feutchinger J. Transition of premature infants from hospital to home life. Neonatal Netw 2012;31:207-14.
15. Collins CT, Makrides M, McPhee AJ. Early discharge with home support of gavage feeding for stable preterm infants who have not established full oral feeds. Cochrane Database Syst Rev 2003;(4):CD003743.
16. Broedsgaard A, Wagner L. How to facilitate parents and their premature infant for the transition home. Int Nurs Rev 2005;52:196–203.
17. Lindberg B, Axelsson K, Öhrling K. Taking care of their baby at home but with nursing staff as support: the use of video conferencing in providing neonatal support to parents of preterm infants. J Neonatal Nurs 2009;15:47–55.
18. Willis V. Parenting preemies: a unique program for family support and education after NICU discharge. Adv Neonatal Care 2008;8:221-30.
19. Glazebrook C, Marlow N, Israel C, Croudace T, Johnson S, White IR, et al. Randomised trial of a parenting intervention during neonatal intensive care. Arch Dis Child Fetal Neonatal Ed 2007;92:F438-43.
20. Osorio Galeano SP, Ochoa Marín SC, Semenic S. Preparing for post-discharge care of premature infants: Experiences of parents. Invest Educ Enferm 2017;35:100-6.
21. Williams KG, Patel KT, Stausmire JM, Bridges C, Mathis MW, Barkin JL. The neonatal ıntensive care unit: Environmental stressors and supports. Int J Environ Res Public Health 2018;15:60.
22. Hall S, Hynan N, Phillips R, Press J, Kenner C, Ryan DJ. Development of program standards for psychosocial support of parents of infants admitted to a neonatal intensive care unit: A national interdisciplinary consensus model. Newborn Infant Nurs Rev 2015;15:24-7.
23. Alkozei A, McMahon E, Lahav A. Stress levels and depressive symptoms in NICU mothers in the early postpartum period. J Matern Fetal Neonatal Med 2014;27:1738-43.
24. Lee HC, Martin-Anderson S, Dudley RA. Clinician perspectives on barriersto and opportunitiesfor skin-to-skin contact forprematureinfants in neonatalintensivecareunits. Breast feed Med 2012;7:79–84.
25. Lefkowitz DS, Baxt C, Evans JR. Prevalence and correlates of posttraumatic stress and postpartum depression in parents of infants in the Neonatal Intensive Care Unit (NICU). J Clin Psychol Med Settings 2010;17:230-7.
26. Hemati Z, Namnabati M, Taleghani F, Sadeghnia A. Mothers' challenges after infants' discharge from neonatal intensive care unit: A qualitative study. Iranian Journal of Neonatology 2017;8:31-6.
27. Mackley AB, Locke RG, Spear ML, Joseph R. Forgotten parent: NICU paternal emotional response. Adv Neonatal Care 2010;10:200-3.
28. Phillips-Pula L, Pickler R, McGrath JM, Brown LF, Dusing SC. Caring for a preterm ınfant at home: a mother's perspective. J Perinat Neonatal Nurs 2013;27:335-44.
29. Hutchinson SW, Spillett MA, Cronin M. Parent's experiences during their infant's transition from neonatal intensive care unit to home: A qualitative study. Qual Rep 2012;17:1-20.
30. Murdoch MR, Franck LS. Gaining confidence and perspective: A phenomenological study of mothers' lived experiences caring for infants at home after neonatal unit discharge. J Adv Nurs 2011;68:2008-20.
31. Engle WA, Tomashek KM, Wallman C; Committee on Fetus and Newborn, American Academy of Pediatrics. "Late-preterm" infants: a population at risk. Pediatrics 2007;120:1390-401.
32. Blair PS, Platt MW, Smith IJ, Fleming PJ; CESDI SUDI Research Group. Sudden infant death syndrome and sleeping position in pre-term and low birth weight infants: an opportunity for targeted intervention. Arch Dis Child 2006;91:101-6.
33. Hill A. Mothers' Perceptions of child vulnerability in previous pretermin fants. ABNF Journal2015;26:11–6.
34. Çelen R, Taş Arslan F. The anxiety levels of the parents of premature infants and related factors. J Pediatr Res 2017;4:68-74.
35. Hergüner S, Annagür A, Çiçek E, Altunhan H, Örs R. Postpartum depression in mothers of infants with very low birth weight. Nöropsikiyatri Arşivi 2013;50:30-3.

36. Bradley R, Slade P. A review of mental health problems in fathers following the birth of a child. J Reprod Infant Psychol 2011;29:19-42.

37. Wharam JF, Graves AJ, Kozhimannil KB. Navigating the rise of high-deductible health insurance: childbirth in the bronze age. JAMA 2015;313:245-6.

38. Committee on Understanding Premature Birthand Assuring Healthy Outcomes. Pretermbirth: Causes, consequences, andprevention. 2007 (cited 2019 December 12). Availablefrom: URL: http://www.nap.edu/catalog/11622.html

39. Breivold K, Hjaelmhult E, Sjöström-Strand A, Hallström IK. Mothers' experiences after coming home from the hospital with a moderately to late preterm infant - a qualitative study. Scand J Caring Sci 2019;33:632-40.

40. Aldirawi A, El-Khateeb A, Mustafa AA, Abuzerr S. Mothers' knowledge of health caring for premature infants after discharge from neonatal intensive care units in the Gaza Strip, Palestine. Open Journal of Pediatrics 2019;9:239-52.

41. Raffray M, Semenic S, Osorio Galeano S, Ochoa Marín SC. Barriers and facilitators to preparing families with premature infants for discharge home from the neonatal unit. Perceptions of health care providers. Invest Educ Enferm 2014;32:379-92.

42. Batman D, Seker S. Effect of web basededucation which has been applied to parents of premature infants to anxiety and self-confidence (dissertation). Adnan Menderes University. 2014.

43. Reymundo MG, Suazoa JAH, AguilarMJC, Faura FJS, Galiana GG, Peinador YM, et al. Follow-upre commendations for the latepretermin fant. An Pediatr (Barc) 2019;90:318.e1-318.e8.

44. Kuo DZ, Lyle RE, Casey PH, Stille CJ. Care System Redesign for Preterm Children After Discharge From the NICU. Pediatrics 2017;139:e20162969.

45. Noble LM, Okogbule-Wonodi AC, Young MA. ABM clinical protocol #12: Transitioning the breastfeeding preterm ınfant from the neonatal ıntensive care unit to home, revised 2018. Breast feed Med 2018;13:230-6.

46. Méio MDBB, Villela LD, GomesJúnior SCDS, Tovar CM, Moreira MEL. Breast feeding of preterm newborn infants following hospital discharge: follow-up during the first year of life. Cien Saude Colet 2018;23:2403-2412.

Review

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# Transcranial Magnetic Stimulation (TMS) Applications in Alzheimer's Disease: A Systematic Review

## Alzheimer Hastalığında Traskraniyal Manyetik Stimülasyon (TMS) Uygulamaları Üzerine Sistematik Bir Derleme

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**ABSTRACT**

Alzheimer's disease (AD), is characterized by its progressive feature and loss of cognitive functions, is common among dementia types. There is no curative treatment of the disease today. In recent years, transcranial magnetic stimulation (TMS) techniques together with drug therapy have been explored by experts considering that they will produce beneficial results. Repetetive TMS (rTMS) can modulate cortical excitability and prevent long-term neuroplastic changes. The aim of this study is an updated and comprehensive systematic review of studies using TMS/rTMS in AD patients. Our study was designed as a systematic review prepared according to the PRISMA guideline. In this study, English and Turkish AD-TMS articles that entered the literature published between 2002 and 2017 were included. Randomized and non-randomized controlled clinical studies on humans evaluating the effectiveness of rTMS applications at different concentrations, durations and different regions in AD have been reviewed. The databases we used were Pubmed®, MEDLINE®, Webofscience®, EMBASE®, Türkiye Atif Dizini®. Keywords were "TMS, rTMS, Alzheimers Disease" used in our search, 116 artticles complied with the determined protocol were identified and 14 were included in our study. The studies presented in this review, show the therapeutic potential of rTMS in

**ÖZ**

İlerleyici özelliği ve bilişsel fonksiyonların kaybı ile karakterize olan Alzheimer hastalığı (AH), demans türleri arasında sık karşılaşılanıdır. Hastalığının günümüzde küratif bir tedavisinin yoktur. Son yıllarda ilaç tedavisinin yanında transkraniyal manyetik stimülasyon (TMS) tekniklerinin, uzmanlar tarafından faydalı sonuçlar oluşturacağı düşünülerek araştırılmaktadır. Tekrarlı TMS (rTMS) kortikal uyarılabilirliği modüle edebilir ve uzun süreli nöroplastik değişiklikleri önleyebilir. Bu çalışmanın amacı, AH hastalarında TMS/rTMS kullanan çalışmaların güncellenmiş ve kapsamlı bir sistematik derlemesini oluşturmaktadır. Çalışmamız PRISMA kılavuzuna göre hazırlanmış bir sistematik derleme olarak tasarlanmıştır. Araştırmamızda 2002-2017 tarihleri arasında literatüre girmiş İngilizce ve Türkçe AH-TMS araştırmaları taranmıştır. Farklı yoğunluklarda, sürelerde ve farklı bölgelere yapılan rTMS uygulamalarının AH'de etkinliğini değerlendiren randomize ve non-randomize kontrollü klinik çalışmalar gözden geçirilmiştir. Taramadan kullandığımız veri tabanları Pubmed®, Medline®, Webofscience®, EMBASE®, Türkiye Atıf Dizini®'dir. Taramamızda anahtar kelime olarak "TMS, rTMS, AH" kullanılmıştır. Hayvanlar ve deney modellerinde yapılan çalışmalar taramamız kapsamında dışlanmıştır. Belirlenen protokole uygunluğu bulunan 116 makale belirlenmiş ve 14'ü çalışmamıza dahil edilmiştir. Bu derlemede sunulan çalışmalar, AH'den etkilenen bilişsel alanlardan bazılarına fayda sağlayan, demansı iyileştiren ve işlevsellikte daha iyi performansa neden olan etkileri gözlemleyerek AD hastalarında

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AD patients. Benefits of rTMS were to communicate with patients and especially caregivers in their daily activities, thereby improving their QoL. The possibility of using TMS to increase neuroplasticity is promising not only to improve our understanding of brain plasticity mechanisms, but also to design new neurorehabilitation strategies.

**Keywords:** Alzheimer's disease, dementia, rTMS

rTMS'nin terapötik potansiyelini göstermektedir. rTMS'nin spesifik faydaları, günlük aktivitelerinde hastalar için, özellikle de bakıcı ve hastalıkla ilişkili davranışla iletişim kurma yetenekleri, böylece yaşam kalitelerini iyileştirme ve hatta erken koşullar için tıbbi hizmetlerin kullanımını sınırlandırma ve kurumsallaşma. Beyin stimülasyonunu nöroplastisiteyi artırmak için bir araç olarak kullanma olasılığı, sadece beyin plastisite mekanizmaları hakkındaki anlayışımızı geliştirmek için değil, aynı zamanda yeni nörorehabilitasyon stratejileri tasarlamak için de umut vericidir.

**Anahtar Sözcükler:** Alzheimer hastalığı, demans, rTMS

## Introduction

Alzheimer's disease (AD) is the most common type of dementia, characterized by progressive loss of cognitive functions. The disease is often accompanied by loss of memory functions, decreased orientation ability, and motor dysfunctions. In addition to the symptoms such as aphasia, agnosia, and apraxia the main symptom in AD is memory dysfunction. AD is associated with synaptic dysfunction at the cellular level, with amyloid beta and tau protein accumulation (1). Loss of cognitive and motor function as a result of the progressive nature of the disease ultimately leads to death.

Today, the absence of a curative alternative in the treatment of AD obliges healthcare professionals to find treatments aimed at slowing the course of the disease and reducing cognitive damage. These treatment approaches are mostly carried out through pharmacological agents. However, pharmacological agents cannot produce an effective solution to the course of AD and they bring other problems with them due to their high side-effect profile. Therefore, scientists have turned to research different methods other than pharmacological agents for the treatment of this disease.

Transcranial Magnetic Stimulation (TMS), which has been used in the treatment of depression for a long time with successful results, is also used as a promising alternative treatment in neurodegenerative diseases (2). TMS is a non-invasive method that aims to stimulate or inhibit certain parts of the brain as a result of applying the magnetic field created outside the body on the scalp. TMS treatment seems to be advantageous in some respects compared to the pharmacological approach. Easy to apply, low side-effect profile as well as positive behavioral and cognitive results suggest that TMS can be preferred over pharmacological agents.

The dorsolateral prefrontal cortex (DLPFC) is mostly preferred as the target area to stimulate in the treatment of AD with TMS (3). In general, although this treatment protocol has led to improvements in executive functions, attention and behavioral functions in individuals with AD, completely satisfactory results could not be obtained in memory functions. Therefore, different protocols are being investigated and studies are continuing to obtain more effective results with TMS treatment.

In addition to the pharmacological alternatives used in AD, repetetive Transcranial Magnetic Stimulation (rTMS) applications with promising results in the treatment will be examined in our study. Randomized and non-randomized controlled clinical studies evaluating the effectiveness of TMS applications at different intensities and in different regions in AD were reviewed in this study.

## Methods

This study, designed as a systematic review, English and Turkish AD-TMS studies between 2002-2017 were screened. The evaluation of the studies were made according to application area of TMS [Broca, Wernicke, right-left DLPFC, right-left parietal somato-sensory association cortex (PSAC)], frequency (1-20 Hz), online-offline applications, and duration (from 1 session to 6 weeks). During our literature search, randomized and non-randomized controlled clinical studies and human studies were searched with the keywords "TMS, rTMS and Alzheimers Disease" in Pubmed®, Medline®, Webofscience®, EMBASE®, and Turkey Citation Index search engines. Animal studies and experimental models were excluded. The last screening was made on 31 December 2017.

Analysis method and inclusion criteria were predetermined and documented in Figure 1. Randomized and non-randomized controlled studies evaluating the effectiveness of rTMS applications of different intensities and different regions in AD were reviewed. The reliability of the reviewed articles was evaluated in terms of evidence levels and some were eliminated after evaluated in terms of insufficiency of control group, randomization, bias, and small sample size. The number of articles included is given in Figure 1.

Data gathered from each included study were as follows; (1) characteristics of study participants (age, presence of AD type dementia, disease severity); (2) the type, dose, duration, and frequency of intervention (duration, intensity, and site of rTMS administration), current treatment versus placebo or another treatment; (3) type of outcome measure (improved cognitive function, improved quality of life, increased daily activities).

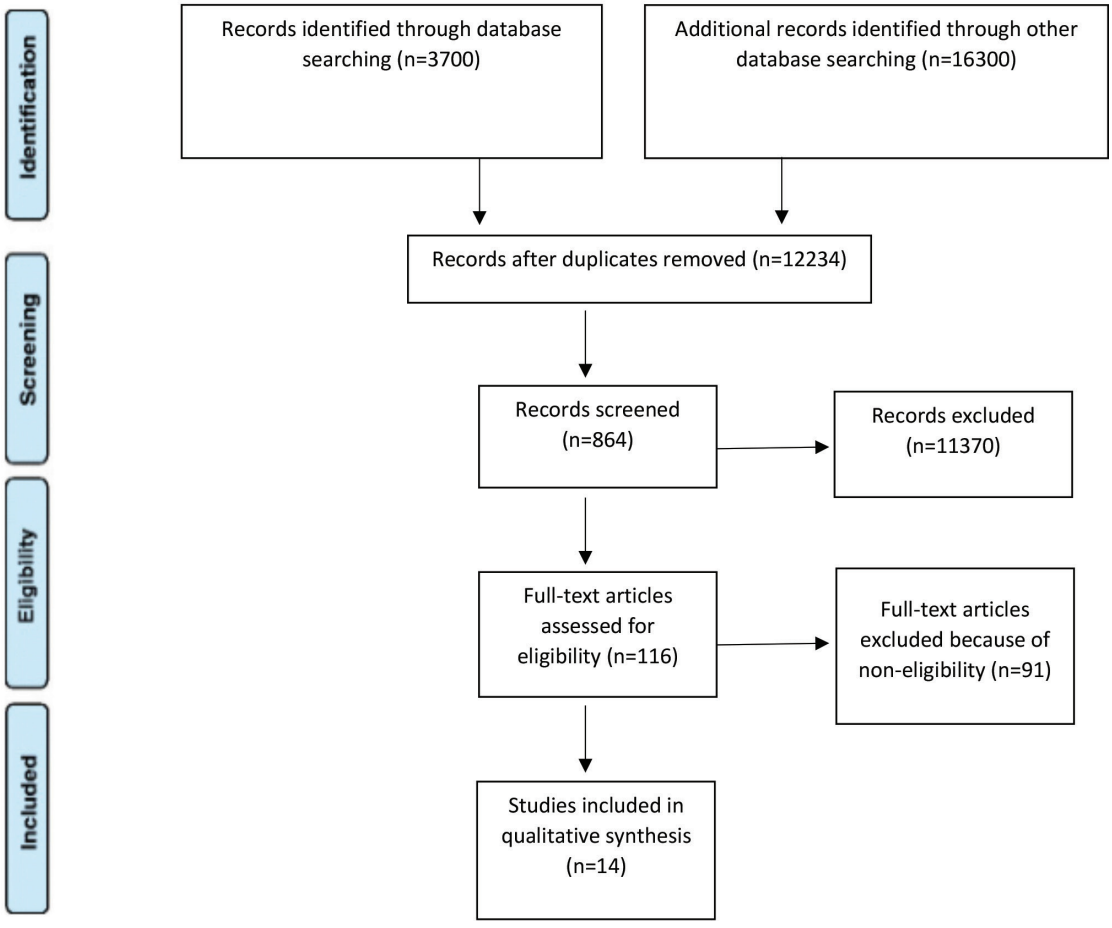


**Figure 1.** Flow diagram according to PRISMA study protocol (41)

## Discussion

The magnetic field principle, discovered by Faraday in the 19th century, constitutes the basic working system of TMS (4). According to this system, the electric current passing in a wire coil causes magnetic flux in another conductor nearby, which can create an electric field in another conductor in the immediate vicinity. Similarly, a high density and faster than 1 ms electrical current produced in the TMS device is passed through the coil and a magnetic field of 2.5 tesla is obtained. When this magnetic field is directed perpendicular to the skull, it can create an electrical current in nerve cells (5). The magnetic field created by TMS is not a constant magnetic field, but a magnetic field characterized by intermittant pulses. Thus, it becomes possible to stimulate brain cells with magnetic pulses created one after another. The induced magnetic field, which passes through the skull and reaches the cortical areas, causes depolarization in the cells and creates neurophysiological responses (6).

Considering the density of the scalp, skull and cerebrospinal fluid, the effectiveness of TMS is limited to a distance 2 cm from the scalp. Because of this limited area of action, it is difficult for TMS stimulation to reach subcortical regions (7). With the developing technology, the area of influence of TMS can extend to deeper regions. However, new systems cause more stimulation of the regions in the cortex during the stimulation of the subcortical regions (8).

TMS has been an important tool in the investigation of various neurological and psychiatric disorders since it was first developed (9). The use of TMS in the treatment of drug-resistant major depression was approved by the American Food and Drug Administration (FDA) in 2008 (10). Following this approval, the FDA's approval of the use of TMS in the treatment of drug-resistant migraine caused it to be used in many clinics around the world (11).

As a specialized TMS protocol, a long-term modulating effect on brain activity can be achieved with rTMS. rTMS makes it possible for all of the stimulating magnetic pulses to be given together in order to create an effect in the cortical area in one stimulation period (12). Due to its long effect profile, rTMS is

considered as a promising treatment option in diseases such as major depression, chronic pain and epilepsy (13).

Drugs developed in AD type dementia have been used for more than 20 years, but researchers have turned to new treatment approaches because these drugs do not have the desired level of efficacy and cannot slow the prognosis of the disease sufficiently (14). In this respect, rTMS has an important place among the new treatment approaches considered in the treatment of AD. Being noninvasive, painless and reliable are the prominent advantages of rTMS (15). Nevertheless, a curative treatment is not obtained with TMS and TMS does not restore atrophied tissues. However, it is thought that the course of the disease may improve as a result of slowing the progression and increasing the synaptic connectivity between neurons with this treatment (16).

As a result of magnetic stimulation treatment, cognitive functions such as mood, executive functions, learning, memory and attention were increased. In randomized controlled studies, it has been determined that rTMS applied to the right DLPFC may cause an increase in episodic memory functions (17-19). Although the DLPFC is frequently targeted in AD, there are studies in the literature in which TMS is applied to Broca, Wernicke, PSAC, inferior temporal gyrus, inferior frontal gyrus (IFG), and superior temporal gyrus (STG) areas (20). On the other hand, rTMS applications to different regions have been shown to affect different cognitive and behavioral functions. It has been shown that magnetic stimulation to the motor cortex for improving motor functions and TMS applications to the prefrontal cortex found beneficial for mood, depression, and cognitive functions. It has also been reported to improve cognitive functions in patients with mild to moderate AD (21). In addition to frequency differences, the regions where TMS application is made also vary. Different application methods (application area, frequency, duration of application, etc.) have been developed for to modulate behavioral and motor symptoms such as mood, cognition, anxiety, memory, executive functions (22). High frequency (>5 Hz) is preferred in TMS protocols when stimulation is aimed. On the other hand low frequency (1 Hz) is preferred in protocols for inhibition (23, 24). Also in some protocols, TMS and pharmacological treatment can be used together. Another method to increase the effectiveness is online-TMS protocols. In this protocols cognitive tasks related to the function of the application area apply to patients during TMS application.

The Alzheimer-TMS studies published in the last 15 years and the results of the changes in patients are listed in Table 1.

In 2006 Cotelli et al. (25) performed a single session of 20 Hz TMS on the right and left DLPFC of 15 patients. In the study, the Object-Action Picture-Naming test results of the TMS applied group and the sham control group were compared. They reported that the action naming capacity of the TMS group was increased compared to the sham control (25).

Again, Cotelli et al. (3) applied 20 Hz single session TMS to the right and left DLPFC in their randomized controlled study in 2008. In the study, which included 12 patients with mild AD and 12 patients with moderate-severe AD, patients with mild AD type dementia showed an increase in object and action naming capacity compared to the sham group. On the other hand, both action and object naming skills were improved in patients with moderate-to-severe AD (3).

In another study conducted by Cotelli et al. (26) in 2011, rTMS was applied in 10 patients with AD only to the left DLPFC and an increase in the cognitive functions of the patients was reported. They applied 20Hz rTMS for 4 weeks to the first of the two patient groups, and placebo TMS for 2 weeks and rTMS for 2 weeks to the second group. Mini Mental State Exemination (MMSE), Activities of Daily Living (ADL), The Lawton Instrumental ADL (IADL), Picture Naming Test, and Battery for Analysis of Aphasic Deficits (SC-BADA) were used as evaluation criteria. In the obtained results, a significant difference was observed only in one of the subtests of SC-BADA, and it was observed that TMS stimulation caused an increase in the perception of the heard sentences (26).

Bentwich et al. (27) investigated the effects of long-term TMS treatment protocol in 7 patients with AD. Bentwich et al. (27) targeted Broca, Wernicke, the right-left DLPFC and right-left PSAC as the application sites and applied 10 Hz TMS to the patients 5 days a week for 6 weeks and 2 days a week for the following 3 months. In this online-TMS protocol study, The Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) scores were evaluated together with cognitive assessments, and statistically significant improvements were observed (27).

Ahmed et al. (24) divided 45 patients with AD (13 severe dementia and 32 mild dementia) into 20 Hz, 1 Hz and sham groups. rTMS was applied to the right and left DLPFC for 5 days, and the cognitive assessment was repeated at the end of 1 and 3 months after TMS application. Compared to the sham control, significant improvements were noted in the IADL score in the 1 Hz treatment group. On the other hand, an increase was observed in all MMSE, Geriatric Depression Scale (GDS) and IADL scores in the 20 Hz group (24).

Haffen et al. (28) shared the results of 10 sessions of 10 Hz TMS application on 1 patient in 2012. In the study, the patient was subjected to cognitive evaluation 3 times, 4 months before the treatment and 1 month and 5 months after the treatment. In the second and third cognitive evaluations, significant improvements were noted in episodic memory and rapid processing skills compared to baseline. However, as a result of the comparison of the third evaluation with the second, the patient's cognitive functions returned back, in other words, worsened. As a result of their study, Haffen et al. (28) concluded that the effect of TMS application decreased over time.

In an online TMS study, Rabey et al. (29) combined stimulation protocol with cognitive assessments, and applied 54 sessions of 10 Hz TMS to the right-left DLPFC, right-left PSAC, Broca and Wernicke areas 5 days a week for 6 weeks and 2 days a week for the following 3 months in 15 patients with AD. When the

**Table 1.** Literature on rTMS applications in Alzheimer's disease, 2002-2017

| Number of Patients | Localization of application | Application duration and Hz | Improved function | Reference |
|---|---|---|---|---|
| 15 AD | Right-left DLPFC | One session 20 Hz | Improvement in Object Naming test compared to Sham | Cotelli et al. 2006 |
| 12 mild AD (1)<br>12 moderate AD (2) | Right-left DLPFC<br>Right-left DLPFC | One session 20 Hz | (1) Improvement in Action Naming test compared to Sham<br>(2) Improvement in Action-Object Naming test compared to Sham | Cotelli et al. 2008 |
| 5 AD (1)<br>5 AD (2) | Left DLPFC<br>Left DLPFC | 4 weeks 20 Hz<br>2 weeks 20 hz + 2 weeks Placebo | (1, 2) Improved perception of heard sentences<br>MRI used for localization determination for TMS application | Cotelli et al. 2011 |
| 7 AD | Broca, Wernicke, right-left DLPFC, right-left PSAC | 6 weeks 10 Hz+3 months, 2 days a week 10 Hz | ADCS-ADL | Bentwich et al. 2011 |
| 15 AD (1)<br>15 AD (2)<br>15 AD (3) | Right-left DLPFC<br>Right-left DLPFC<br>Sham | 5 days 20 Hz<br>5 days 1 Hz<br>Sham | (1) MMSE, GDS<br>(2) IADL | Ahmed et al. 2012 |
| 1 AD | Left DLPFC | 2 weeks 10 Hz | Assessment 4 months before, 1 and 5 months after TMS, Increase in episodic memory and rapid processing, decrease in the third assessment compared to the second | Haffen et al. 2012 |
| 15 AD | Broca, Wernicke, right-left DLPFC, right-left PSAC | Online TMS, 6 weeks 10 Hz + 3 months 2 days a week 10 Hz | ADAS-Cog, CGIC<br>MRI used for localization determination for TMS application | Rabey et al. 2013 |
| 10 mild AD ve MCI | IFG | 10 Hz for 3 days at 1 day intervals | Attention and Psychomotor speed | Eliasova et al. 2014 |
| 6 AD (1)<br>6 AD (2) | Right-left DLPFC<br>Right-left DLPFC | 4 sessions in 2 weeks, 10 Hz<br>4 sessions in 2 weeks, 15 Hz | (1,2) Verbal fluency, nonverbal fluency<br>4 weeks after TMS<br>fMRI study | Devi et al. 2014 |
| 4 AD<br>6 AD | Right-left DLPFC<br>Right-left DLPFC | 4 weeks sham x 4 weeks treatment with 20 Hz<br>4 weeks treatment with 20 Hz x 4 weeks sham | MoCA, ADAS-Cog | Rutherford et al. 2015 |
| 26 AD (1)<br>26 AD (2) | Left DLPFC + Antipsychotic (1 mg risperidone)<br>Sham+ Antipsychotic (1 mg risperidone) | 4 weeks 20 Hz | BEHAVE-AD, ADAS-Cog | Wu et al. 2015 |
| 30 AD | Broca, Wernicke, right-left DLPFC, right-left PSAC | Online TMS, 6 weeks 10 Hz | ADAS-Cog, MMSE | Rabey et al. 2016 |
| 18 AD (1)<br>18 AD (2) | Broca, Wernicke, right-left DLPFC, right-left PSAC<br>Sham | Online TMS, 6 weeks 10 Hz | ADAS-Cog, CGIC | Lee et al. 2016 |
| 17mild+ moderate AD | Parietal P3/P4, posterior temporal T5/T6 | 6 weeks 20 Hz | Cognitive functions, language and memory | Zhao et al. 2017 |

AD: Alzheimer's disease, MCI: Mild cognitive impairment, TMS: Transcranial magnetic stimulation, fMRI: Functional magnetic resonance imaging, DLPFC: Dorsolateral prefrontal cortex, PSAC: Parietal somato-sensory association cortex, IFG: Inferior frontal gyrus, ADCS-ADL: Alzheimer's Disease Cooperative Study- Activities of Daily Living, MMSE: Mini-mental state examination, IADL: The lawton instrumental activities of daily living, SC-BADA: The Battery for Analysis of Aphasic Deficits, ADAS-Cog: Alzheimer's disease assessment scale-cognitive subscale, GDS: Geriatric depression scale, CGIC: Clinical global ımpression of change, MoCA: Montreal cognitive assessment, BEHAVE-AD: Behavioral pathology in Alzheimer's disease rating scale

patients included in the study were evaluated cognitively at 6 weeks and 4.5 months later, increases in ADAS-Cog and Clinical Global Impression of Change (CGIC) scores were observed (29).

In the study of Eliasova et al. (30) published in 2014, 10 Hz rTMS was applied to the IFG of 10 individuals with mild cognitive impairment (MCI) and mild AD, 3 times within 6 days, with an interval of one day. Improvements in attention and psychomotor speed were observed in patients whose results were evaluated with the trail making test (30).

Devi et al. (19) applied 4 sessions of 10 and 15 Hz rTMS with two-day intervals for two weeks in 2 groups of patients with AD, including 6 patients in each group. Boston Diagnostic Aphasia Evaluation Test, Category Fluency Test and MMSE were used in the cognitive evaluation performed 2 weeks before and after the TMS application and 4 weeks after the last day of the application. Verbal agility score performed immediately after the application and non-verbal agility score after the test performed 4 weeks after TMS showed a statistically significant improvement compared to baseline. On the other hand, functional magnetic resonance imaging (fMRI) with cognitive tasks measuring motor and language functions was applied to 8 patients who were compatible with MRI before, immediately after and 4 weeks after rTMS application. According to fMRI results after magnetic stimulation, an increase in activity was observed in some patients, especially in Broca's area, but this increase was not statistically significant (19).

In the study by Rutherford et al. (31) in which the placebo effect was evaluated crossover, 10 patients with AD were divided into two groups as the sham-treatment group consisting of 4 patients and the treatment-sham group consisting of 6 patients. Twenty Hz rTMS application to the right-left DLPFC region was divided into two 4-week periods. In the first period, rTMS was applied to the treatment group, but not to the sham group. The cognitive status of the patients was measured with ADAS-Cog and Montreal Cognitive Assessment (MoCA) tests at the beginning and end of the treatment, and with the MoCA test at the end of each week. The second 4-week period was planned one month later for the TMS effects to cease, and the groups were crossed and the same protocol was applied as the previous one. At the end of the study, the test scores of the treatment group were significantly higher than those of the sham group. In the second arm of the study, 10 sessions of rTMS were applied to 6 patients in 3 months with the same protocol. Extensive evaluations were made before and after the treatment, and the MoCA test was repeated every week for partial evaluation. According to the neuropsychological evaluation results of the patients in the treatment-sham group, cognitive improvement was observed after rTMS applications (31).

Fifty two patients with AD, consisting of 26 sham controls and 26 patients receiving treatment, were included in the study in which the effects of rTMS combined with antipsychotic drugs on behavioral and psychological functions were examined. Wu et al. (32) applied 20 Hz stimulation to the left DLPFC region of patients using 1 mg of risperidone for 20 sessions for 4 weeks. The Behavioral Pathology in AD Rating Scale (BEHAVE-AD) and ADAS-Cog test scores were obtained before and 4 weeks after treatment. It was reported that both test results improved significantly in the rTMS group (32).

In an online TMS study, conducted by Rabey et al. (30), left IFG (Broca's area), left STG (Wernicke's area), right-left DLPFC and right-left PSAC regions were targeted. During a 6-week period, 10 Hz pulses were applied for 5 days a week, for a total of 30 sessions. Anatomical MR images were obtained from the patients for neuronavigational use. rTMS was applied to 3 determined localizations (the other 3 localizations in the following days), and during this time, the patient was given homework related to the stimulated region (syntax and grammar tasks for Broca's area, dictionary meaning and categorization tasks for Wernicke's area, action-object naming tasks and spatial memory tasks for right-left DLPFC, and spatial attention tasks for right-left PSAC. High significance values were obtained in ADAS-Cog and MMSE scores in pre- and post-treatment comparisons. Seven months after the end of the treatment, 5 more patients were included in the study and a second treatment was performed with the same protocol. As a result, Rabey et al. (33) reported that ADAS-Cog scores improved compared to pre-treatment.

Lee et al. (22) divided the patients into two groups as the treatment group consisting of 18 patients 8 sham controls in the study in which they included 26 patients with AD. In this online study, in which rTMS application was performed simultaneously with cognitive tasks, stimulation was applied to Broca, Wernicke, right-left DLPFC and right-left PSAC regions. Syntax and grammar tasks for Broca's area, dictionary meaning and categorization tasks for Wernicke, action-object naming tasks and spatial memory tasks of shapes, colors, words for right-left DLPFC, and spatial attention tasks of shapes and words were given for PSAC. Ten Hz frequency online rTMS protocol which was applied 5 days a week and 30 sessions for 6 weeks, Broca, Wernicke and right DLPFC areas were stimulated on the 1$^{st}$, 3$^{rd}$ and 5$^{th}$ days of the week, while the left DLPFC and the right-left PSAC areas were stimulated on the 2$^{nd}$ and 4$^{th}$ days of the week, and it was aimed to stimulate only three brain regions in one session. Evaluation tests were performed 2 weeks before, at the end of treatment, and 6 weeks after treatment. ADAS-Cog scores in the treatment group differed significantly compared to the sham control. While no significant difference was observed in the first cognitive test comparisons, only the tests performed at 6 weeks after treatment in patients with mild AD showed significance. The GDS scores after treatment in the Sham group showed significant differences. In the CGIC applied immediately after the treatment, there was significant change in the treatment group compared to the sham control, but there was no significant difference between groups after 6 weeks (22).

Zhao et al. (34) divided 30 patients with mild and moderate AD into two groups as rTMS group consisting of 17 patients and sham control group consisting of 13 patients, and determined the magnetic field application area as parietal P3/P4 and posterior temporal T5/T6 regions according to the 10-20 electroencephalography system. Twenty Hz stimulations were

applied 30 times for 6 weeks to the patients who underwent TMS application. Patients did 20-40 second off-line tasks after 10-minute sessions. MMSE, MoCA, and Auditory Verbal Learning Test (AVLT) were performed 2 weeks before, immediately after, and 6 weeks after treatment. It was reported that improvements in memory, language and cognitive functions were detected in especially patients with mild AD in the treatment group compared to all patients in the sham control group (34).

With the developments in neuromodulation and neuroimaging methods, it has become possible, in a way, to monitor how an intervention like TMS causes a functional change in the brain (35). Cognitive disorders that occur in patients with stroke with focal brain damage are generally not primarily related to the center of the injury (36). Disruption of functional neural network integrity can be associated with neurological or psychological diseases such as depression, obsessive compulsive disorder and schizophrenia. In this group of patients, in order to repair impaired neural association, non-invasive methods such as TMS or transcranial direct current stimulation (tDCS) can be aimed at stimulating neural plasticity and restoring lost cognitive abilities (35).

Brain is highly active even during resting-state phase, and therefore, active areas of brian produce signals depending to blood oxygen levels (BOLD). Analysis of the changes in these signals provides insight into brain connectivity. Therefore, during an fMRI in which resting state activity is measured, the functional activity of the brain can be manipulated with TMS application and it can be observed how TMS makes a change in the brain network (37). In addition to the use of TMS for therapeutic purposes, the effect of TMS on brain connectivity can be confirmed with fMRI so that data can be analyzed more accurately. By using MR and TMS devices together, resting state functional connectivity can be measured. This measurement can be obtained as a result of fMRI analyzes simultaneously with TMS stimulation (39). Apart from that, TMS can provide more precise data on how different localizations of the brain function by being used as a mapping tool (40).

Neuroimaging is the most appropriate option to determine the localization of non-invasive brain stimuli, to elucidate the mechanism, and to identify regions where cognitive functions were increased or decreased after TMS.

Currently, AD is the most common cause of dementia with no known cure. Cognitive decline increases as the disease progresses, and current therapeutic approaches are not effective in improving cognitive deficits or functional limitations. TMS appears to be a promising tool for this purpose, given its ability to modulate cortical excitability and neural network activity.

When we look at the studies in the literature, it is observed that beneficial results are obtained by stimulating the DLPFC area of the brain in patients with AD. In addition, it is observed that the treatment perspective is tried to be expanded by stimulating other different areas such as Broca, Wernicke, PSAC, posterior parietal region.

We can briefly list the factors affecting the success of treatment in TMS application as follows. Age and disease progression seem to be the most important factors in the potential to benefit from TMS. The response of younger patients with AD to TMS treatment is remarkably high. In addition, TMS applications, especially in individuals with MCI, have given more beneficial results than those with AD. Because there is not much atrophy in patients with MCI, the cell stimulation mechanism can be activated more easily with TMS and thus the cognitive and behavioral losses can be compensated. However, since the progression continues faster and the atrophic process is at a more advanced level in AD, beneficial results are not always obtained.

Another factor affecting the treatment process is the duration of TMS treatment. There is no consensus on the number of TMS sessions. However, studies show that as the number of sessions increases, the effectiveness of treatment also increases. In many centers, 10 sessions of TMS are applied for neurodegenerative and depressive patients. Statistically more significant results were determined in the treatment course of the patients in studies in which 20 sessions were applied or 54 sessions were applied at intervals.

Another issue regarding the efficacy of treatment is the application site. Studies have shown that bilateral DLPFC is used as the most stimulating region, especially in patients AD. However, when this region is stimulated, although improvements are observed in behavioral and executive functions, sufficient progress is not achieved in memory functions. In the formation of this situation, it is possible that the memory uses many brain networks in a combined way, and in case of incomplete functioning of one of these networks, the memory also suffers a loss of function. Therefore, many researchers aim to improve memory and some other cognitive functions by stimulating different localizations and stimulating these localizations consecutively or in combination.

Online TMS paradigm is another factor that contributes to the effectiveness of treatment. Having the patient do a cognitive task while performing TMS actually makes it possible to perform two-way brain stimulation. For example, let's consider a patient with AD in whom DLPFC region is stimulated to correct executive dysfunction. While performing TMS, having this patient perform a cognitive task or test on executive functions will increase the power of effect. This can actually be thought of as a method to shorten the long-term progress of brain plasticity. Many studies available in the literature show that online TMS protocols provide more effective results.

## Conclusion

As a result, although research in this area has increased significantly in recent years, there is still very little and the most effective stimulation parameters in terms of frequency, intensity, localization and stimulation duration are unknown. In addition, it is necessary to include functional and structural neuroimaging measures to reveal the neural mechanisms underlying the beneficial effects of TMS. Although the studies available in

the literature have revealed the beneficial effects of TMS in the treatment of AD, more in-depth and comprehensive studies are needed for TMS to be used as a routine treatment option in AD. In addition, our knowledge of how TMS works is very limited. Although we observe the effect it has on behavioral and cognitive functions of patients, we almost have no idea about what kind of interventions on which parameters cause this effect. The mechanism of action of TMS can be examined in more detail, for example, by evaluating neurotropic, anti-inflammatory and antioxidant mechanisms. This will pave the way for the TMS method to be used more widely as a treatment option and for many patients to benefit from this method.

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## References

1. Husain M, Schott JM, editors. Oxford Textbook of Cognitive Neurology and Dementia [Internet]. Oxford University Press; 2016 [cited 2018 Nov 13]. Available from: http://oxfordmedicine.com/view/10.1093/med/9780199655946.001.0001/med-9780199655946
2. Kobayashi M, Pascual-Leone A. Transcranial magnetic stimulation in neurology. Lancet Neurol 2003;2:145-56.
3. Cotelli M, Manenti R, Cappa SF, Zanetti O, Miniussi C. Transcranial magnetic stimulation improves naming in Alzheimer disease patients at different stages of cognitive decline. Eur J Neurol 2008;15:1286-92.
4. Wagner T, Valero-Cabre A, Pascual-Leone A. Noninvasive Human Brain Stimulation. Annu Rev Biomed Eng 2007;9:527–65.
5. Hallett M. Transcranial magnetic stimulation and the human brain. Nature 2000;406:147-50.
6. Wagner T, Rushmore J, Eden U, Valero-Cabre A. Biophysical foundations underlying TMS: setting the stage for an effective use of neurostimulation in the cognitive neurosciences. Cortex 2009;45:1025-34.
7. Deng ZD, Lisanby SH, Peterchev AV. Electric field depth-focality tradeoff in transcranial magnetic stimulation: simulation comparison of 50 coil designs. Brain Stimul 2013;6:1-13.
8. Wagner TA, Zahn M, Grodzinsky AJ, Pascual-Leone A. Three-dimensional head model simulation of transcranial magnetic stimulation. IEEE Trans Biomed Eng 2004;51:1586-98.
9. Barker AT, Jalinous R, Freeston IL. Non-invasive magnetic stimulation of human motor cortex. Lancet. 1985;1(8437):1106-7.
10. Rotenberg A, Horvath JC, Pascual-Leone A. The Transcranial Magnetic Stimulation (TMS) Device and Foundational Techniques. In Humana Press, New York, NY; 2014 [cited 2018 Nov 13]. p. 3-13. Available from: http://link.springer.com/10.1007/978-1-4939-0879-0_1
11. Davis NJ, Gold E, Pascual-Leone A, Bracewell RM. Challenges of proper placebo control for non-invasive brain stimulation in clinical and experimental applications. Eur J Neurosci 2013;38:2373-7.
12. Fitzgerald PB, Fountain S, Daskalakis ZJ. A comprehensive review of the effects of rTMS on motor cortical excitability and inhibition. Clin Neurophysiol 2006;117:2584-96.
13. Najib U, Bashir S, Edwards D, Rotenberg A, Pascual-Leone A. Transcranial brain stimulation: clinical applications and future directions. Neurosurg Clin N Am 2011;22:233-51.
14. Fargo KN, Aisen P, Albert M, Au R, Corrada MM, DeKosky S, et al. 2014 Report on the Milestones for the US National Plan to Address Alzheimer's Disease. Alzheimer's Dement 2014;10:S430–52.
15. Freitas C, Mondragón-Llorca H, Pascual-Leone A. Noninvasive brain stimulation in Alzheimer's disease: systematic review and perspectives for the future. Exp Gerontol 2011;46:611-27.
16. Cantone M, Di Pino G, Capone F, Piombo M, Chiarello D, Cheeran B, et al. The contribution of transcranial magnetic stimulation in the diagnosis and in the management of dementia. Clin Neurophysiol 2014;125:1509-32.
17. Innocenti I, Giovannelli F, Cincotta M, Feurra M, Polizzotto NR, Bianco G, et al. Event-related rTMS at encoding affects differently deep and shallow memory traces. Neuroimage 2010;53:325-30.
18. Manenti R, Cotelli M, Robertson IH, Miniussi C. Transcranial brain stimulation studies of episodic memory in young adults, elderly adults and individuals with memory dysfunction: a review. Brain Stimul 2012;5:103-9.
19. Devi G, Voss HU, Levine D, Abrassart D, Heier L, Halper J, et al. Open-label, short-term, repetitive transcranial magnetic stimulation in patients with Alzheimer's disease with functional imaging correlates and literature review. Am J Alzheimers Dis Other Demen 2014;29:248-55.
20. Liao X, Li G, Wang A, Liu T, Feng S, Guo Z, et al. Repetitive Transcranial Magnetic Stimulation as an Alternative Therapy for Cognitive Impairment in Alzheimer's Disease: A Meta-Analysis. J Alzheimers Dis 2015;48:463-72.
21. Sasaki N, Kakuda W, Abo M. Bilateral high- and low-frequency rTMS in acute stroke patients with hemiparesis: a comparative study with unilateral high-frequency rTMS. Brain Inj 2014;28:1682-6.
22. Lee J, Choi BH, Oh E, Sohn EH, Lee AY. Treatment of Alzheimer's Disease with Repetitive Transcranial Magnetic Stimulation Combined with Cognitive Training: A Prospective, Randomized, Double-Blind, Placebo-Controlled Study. J Clin Neurol 2016;12:57-64.
23. Turriziani P, Smirni D, Zappalà G, Mangano GR, Oliveri M, Cipolotti L. Enhancing memory performance with rTMS in healthy subjects and individuals with Mild Cognitive Impairment: the role of the right dorsolateral prefrontal cortex. Front Hum Neurosci 2012;6:62.

24. Ahmed MA, Darwish ES, Khedr EM, El Serogy YM, Ali AM. Effects of low versus high frequencies of repetitive transcranial magnetic stimulation on cognitive function and cortical excitability in Alzheimer's dementia. J Neurol 2012;259:83-92.

25. Cotelli M, Manenti R, Cappa SF, Geroldi C, Zanetti O, Rossini PM, et al. Effect of transcranial magnetic stimulation on action naming in patients with Alzheimer disease. Arch Neurol 2006;63:1602-4.

26. Cotelli M, Calabria M, Manenti R, Rosini S, Zanetti O, Cappa SF, et al. Improved language performance in Alzheimer disease following brain stimulation. J Neurol Neurosurg Psychiatry 2011;82:794-7.

27. Bentwich J, Dobronevsky E, Aichenbaum S, Shorer R, Peretz R, Khaigrekht M, et al. Beneficial effect of repetitive transcranial magnetic stimulation combined with cognitive training for the treatment of Alzheimer's disease: a proof of concept study. J Neural Transm (Vienna) 2011;118:463-71.

28. Haffen E, Chopard G, Pretalli JB, Magnin E, Nicolier M, Monnin J, et al. A case report of daily left prefrontal repetitive transcranial magnetic stimulation (rTMS) as an adjunctive treatment for Alzheimer disease. Brain Stimul 2012;5:264-6.

29. Rabey JM, Dobronevsky E, Aichenbaum S, Gonen O, Marton RG, Khaigrekht M. Repetitive transcranial magnetic stimulation combined with cognitive training is a safe and effective modality for the treatment of Alzheimer ' s disease : a randomized , double-blind study. J Neural Transm 2013;120:813-9.

30. Eliasova I, Anderkova L, Marecek R, Rektorova I. Non-invasive brain stimulation of the right inferior frontal gyrus may improve attention in early Alzheimer's disease: A pilot study. J Neurol Sci 2014;346:318-22.

31. Rutherford G, Lithgow B, Moussavi Z. Short and Long-term Effects of rTMS Treatment on Alzheimer's Disease at Different Stages: A Pilot Study. J Exp Neurosci 2015;9:43-51.

32. Wu Y, Xu W, Liu X, Xu Q, Tang L, Wu S. Adjunctive treatment with high frequency repetitive transcranial magnetic stimulation for the behavioral and psychological symptoms of patients with Alzheimer's disease a randomized, double-blind, sham-controlled. Shanghai archives of psychiatry Oct 2015. p. 280–8.

33. Rabey JM, Dobronevsky E. Repetitive transcranial magnetic stimulation (rTMS) combined with cognitive training is a safe and effective modality for the treatment of Alzheimer's disease: clinical experience. J Neural Transm (Vienna) 2016;123:1449-55.

34. Zhao J, Li Z, Cong Y, Zhang J, Tan M, Zhang H, et al. Repetitive transcranial magnetic stimulation improves cognitive function of Alzheimer's disease patients. Oncotarget 2017;8:33864-71.

35. Sale M V., Mattingley JB, Zalesky A, Cocchi L. Imaging human brain networks to improve the clinical efficacy of non-invasive brain stimulation. Neurosci Biobehav Rev 2015;57:187-98.

36. Verdon V, Schwartz S, Lovblad K-O, Hauert C-A, Vuilleumier P. Neuroanatomy of hemispatial neglect and its functional components: a study using voxel-based lesion-symptom mapping. Brain 2010;133:880–94.

37. Caparelli EC, Backus W, Telang F, Wang GJ, Maloney T, Goldstein RZ, et al. Simultaneous TMS-fMRI of the Visual Cortex Reveals Functional Network, Even in Absence of Phosphene Sensation. Open Neuroimag J 2010;4:100-10.

38. Fox MD, Buckner RL, Liu H, Chakravarty MM, Lozano AM, Pascual-Leone A. Resting-state networks link invasive and noninvasive brain stimulation across diverse psychiatric and neurological diseases. Proc Natl Acad Sci 2018;111:E4367–75.

39. Fox MD, Halko MA, Eldaief MC, Pascual-Leone A. Measuring and manipulating brain connectivity with resting state functional connectivity magnetic resonance imaging (fcMRI) and transcranial magnetic stimulation (TMS). Neuroimage 2012;62:2232-43.

40. van de Ruit M, Perenboom MJ, Grey MJ. TMS brain mapping in less than two minutes. Brain Stimul 2015;8:231-9.

41. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339:b2700.

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Aygül Yanık
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Burcu Yeşilkaya
Çağla Kızılarslan Hançer
Cevper Ersöz
Ceyda Uzun Şahin
Cumali Karatoprak
Demet Dinçel
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Deniz Çelik
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Eda Becer
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Elif Dönmez
Emin Köse
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Emine Geçkil
Emine Karaman
Emine Koç
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Erdal Tekarslan
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Ertan Sönmez
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Esra Atılgan
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Fevzi Sağlam
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Figen Yardımcı
Gökhan Polat
Gülay Okay
Gülis Durmuşoğlu Kavadar
Güven Çetin
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Hakan Abdullah Özgül
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# 2021 Referee Index

# 2021 Author Index

# 2021 Author Index

# 2021 Author Index

# 2021 Subject Index

# 2021 Subject Index

# 2021 Subject Index

# 2021 Subject Index