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## Comparison of Coronavirus Anxiety, Sleep Quality and Quality of Life in Pregnant Women with Healthy Controls

### Gebelerde Koronavirüs Anksiyetesi, Uyku Kalitesi ve Yaşam Kalitesinin Sağlıklı Kontrollerle Karşılaştırılması

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#### ABSTRACT

**Objective:** In the pandemic, pregnant women are at the forefront of the disadvantaged groups and need special needs related to more mental problems. This study aims to evaluate the pandemic anxiety of pregnant women and how their sleep and quality of life are affected.

**Materials and Methods:** 200 pregnant and 200 control patients were included in the study. Informed consent was obtained from the participants. They were asked to fill out the sociodemographic data form, The Coronavirus Anxiety Scale (CAS), the Pittsburgh sleep quality index (PSQI), and the 12-Item Short Form Survey (SF-12) Quality of Life scale.

**Results:** No statistically significant difference was found in the CAS between pregnant and healthy controls ( $p=0.093$ ). While the physical score subscale of the SF-12 Quality of Life Scale (SF12-PCS) scored statistically significantly higher in pregnant women compared to the healthy controls, the mental score subscale (SF12-MCS) scored significantly lower (respectively:  $p<0.001$ ;  $p=0.009$ ).

A statistically weak correlation was found between coronavirus anxiety and sleep quality ( $r:0.222$ ;  $p=0.002$ ).

**Conclusion:** The pandemic process affects pregnant women's sleep quality and mental quality of life terribly. Clinicians should take care to evaluate the sleep quality of pregnant women in this process.

**Keywords:** Anxiety, coronavirus, pregnancy, quality of life, sleep quality

#### ÖZ

**Amaç:** Covid-19 pandemi süreci, insanların büyük çoğunluğunu ruhsal ve fiziksel olarak etkileyen önemli bir toplumsal durumdur. Bu süreçte dezavantajlı olan ve daha fazla düşünülmesi gereken grupların başında gebeler gelmektedir. Bu çalışmanın amacı gebelerin pandemi kaygısını, uyku ve yaşam kalitelerinin nasıl etkilendiği değerlendirmektir.

**Materyal ve Metot:** Çalışmaya 200 gebe ve 200 kontrol hastası dahil edilmiştir. Katılımcıların aydınlatılmış onamları alınmış ve sosyo demografik veri formu, Koronavirüs Anksiyetesi Ölçeği (CAS), Pittsburgh Uyku Kalitesi ölçeği (PSQI), Yaşam Kalitesi Ölçeğinin Kısa Form-12 (SF-12) yaşam kalitesi ölçeği doldurmaları istenmiştir.

**Bulgular:** Gebe ve sağlıklı kontroller arasında Koronavirüs Anksiyetesi Ölçeği puanları arasında istatistiksel olarak anlamlı fark bulunamamıştır ( $p=0,93$ ). Gebe ve sağlıklı kontroller arasında uyku kalitesi açısından istatistiksel olarak anlamlı fark bulunmuştur ( $p=0,02$ ). Gebelerde sağlıklı kontrollere göre Yaşam Kalitesi Ölçeğinin Kısa Form-12 (SF-12) fiziksel puan alt ölçeği istatistiksel olarak anlamlı daha yüksek puan almışken, mental puan alt ölçeği istatistiksel olarak anlamlı düşük puan almıştır (sırasıyla:  $p<0,001$ ;  $p=0,009$ ).

Koronavirüs anksiyetesi ile uyku kalitesindeki bozulma arasında istatistiksel olarak anlamlı pozitif yönde zayıf korelasyon bulunmuştur ( $r:0,222$ ;  $p=0,002$ ).

**Sonuç:** Pandemi süreci gebelerdeki uyku kalitesini ve mental olarak yaşama kalitelerini oldukça kötü yönde etkilenmektedir. Klinisyenler bu süreçte gebelerin uyku kalitelerini değerlendirmeye özen göstermelidirler.

**Anahtar Kelimeler:** Anksiyete, gebelik, koronavirüs, uyku kalitesi, yaşam kalitesi

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## INTRODUCTION

The COVID-19 pandemic has been in our lives for about 1.5 years; unfortunately, we have not been able to remove my halo from our lives altogether. In this process, while the COVID-19 pandemic continues to affect human health in many ways, our information about specific groups (pregnant women, senior population, children, etc.) is still limited. More psychological problems have started to be seen in the covid-19 pandemic process with pregnant women in the particular group.<sup>1-3</sup> The essential psychological symptom in this group is stress.<sup>4</sup> It is thought that the anxiety levels of pregnant women generally increase during the pandemic process, they are more depressed, and they experience more insomnia.<sup>2,5,6</sup> In a meta-analysis evaluating 19 recent studies, the prevalence of anxiety in lactating and pregnant women was 33%, depression 27%, and insomnia 34%.<sup>4</sup> Sleep physiology is highly affected during pregnancy, but most pregnant women reported poor sleep quality during the COVID-19 epidemic.<sup>2</sup> In the studies conducted before the pandemic, pregnant women's sleep and life quality were primarily evaluated in the last trimester. It is emphasised that it is vital to examine pregnant women during this period.<sup>7</sup> No study has been found to evaluate both sleep and quality of life together during the pandemic. During the COVID-19 pandemic, mental disorders can affect pregnant women's quality of life and the baby's future life to be born.<sup>8,9</sup> In this study, it was aimed to determine how pregnant women, who are the special group that may be affected during the pandemic period, are affected. It is crucial to take special precautions for pregnant women and closely support their mental health in this process. In this study, anxiety due to the coronavirus pandemic, sleep quality, and quality of life of pregnant women were evaluated during pregnancy. Their relations with each other during the pandemic period were examined.

## MATERIALS AND METHODS

**Ethics Committee Approval:** Our study was approved by Düzce University Ethics Committee (Date:05/04/2021, decision no:2021/99). The study was carried out in accordance with the International WHO Declaration of Helsinki.

**The Type of Study:** The type of study is a prospective, descriptive and cross-sectional study. In the power analysis using the G-power program, the total sample size was calculated as 398 people, when the Cohen's d value was taken as 0.25, the relatively weak effect size was accepted as the alpha error value of 0.05 and the power as 0.80.

The study was completed with 200 patients who applied to the pregnant outpatient clinic, and the

patients accompanying the hospital in the same period without active complaints were included. The researchers explained the study to the patients, and consent was obtained from the patients who agreed to participate in the research and the control group.

### Data Collection Tools

**Sociodemographic Form:** The form consists of 17 questions such as age, gender, physical and mental illness history, history of COVID-19, etc.

**The Coronavirus Anxiety Scale (CAS):** The scale created by Lee<sup>10</sup> in 2020 consists of 5 items, and the increase in the score indicates that coronavirus anxiety has also increased. The Turkish validity and reliability study was performed by Evren et al.<sup>11</sup>

**Pittsburgh Sleep Quality Index (PSQI):** PSQI consists of 24 questions. Nineteen of these questions are filled by the scale owner, and the other five questions are supplied by the person with whom they share their room. PSQI has a sensitivity of 89.6% and a specificity of 86.5% to identify cases with sleep disorders. It has been translated into 48 languages and is widely used in clinical research. The cut-off score of the scale was specified as 5. Scores of 5 and above indicate poor sleep quality. The scale questions seven sub-domains: Subjective Sleep, Sleep Latency, Sleep Duration, Sleep Efficiency, Sleep Disorder, Sleep Medication, and Daytime Dysfunction. The Turkish validity and reliability study was performed by Ağargün et al.<sup>12,13</sup>

**12-Item Short Form Survey (SF-12):** It is a scale developed by Ware et al.<sup>14</sup> in 1996 from the SF-36 form. The scale consists of 12 questions, resulting in two sub-areas: physical score (SF12-PCS) and mental score (SF12-MCS). The Turkish validity and reliability study of the scale was performed by Soyulu. The internal consistency coefficients of the scale were found for the components  $\alpha=0.73$  and 0.72.<sup>15</sup>

**Statistics:** SPSS 26.0 package program was used to evaluate the data. In the presentation of descriptive data, mean, standard deviation, number, percentage, and median values are given. Whether the numerical values showed normal distribution or not was evaluated with the Kolmogorov-Smirnov test. Mann Whitney U test was used to compare two groups that did not show normal distribution. The Kruskal-Wallis test was used for multi-group comparisons that did not show normal distribution. Correlations between non-normally distributed numerical data were evaluated with the Spearman correlation test. Statistical significance was accepted as  $p < 0.05$ .

## RESULTS

A total of 400 people, 200 pregnant and 200 control group members, participated in the study. The mean age of the pregnant group was  $27.6 \pm 4.3$ , and the



mean week of gestation was 25.5±9.3. The mean age in the control group was found to be 26.91±7.4 years; a statistically significant difference was found between the two groups (Z:-3.635; p=0.0001). Although the pregnant group had higher scores regarding coronavirus anxiety, there was no statistically significant difference between the groups (Z:-1.679 p=0.093). Sleep quality total score was statistically

significantly higher in the pregnant group than in the control group (Z:-3.138; p=0.002). The physical quality of life score was statistically significantly higher in the pregnant group (Z:-5.039; p=0.0001). The control group's psychological quality of life was statistically significantly higher (Z:-2.628; p=0.009). Scale scores are summarised in Table 1.

**Table 1.** Pregnant and control age comparison according to scale scores.

	Pregnant Group (n:200) Mean±SD	Control Group (n:200) Mean±SD	TOTAL	Z	p*
Age (min-max)	27.6±4.3	26.91±7.4	27.25±6.09	-3.635	<b>0.0001</b>
Pregnancy Week (min-max)	25.5±9.3				
CAS	2.06±2.83	1.5±2.3	1.8±2.6	-1.679	0.093
PSQI	8.08±3.4	6.09±3.4	7.5±3.2	-3.138	<b>0.002</b>
SF12-PCS	43.59±6.73	40.43±5.9	42.01±6.5	-5.039	<b>0.0001</b>
SF12-MCS	34.02±7.4	35.4±6.1	34.7±6.8	-2.628	<b>0.009</b>

\*: Mann Whitney U test; CAS: The Coronavirus Anxiety Scale; PSQI: Pittsburgh sleep quality index; SF12-PCS: Physical Score; SF12-MCS: Mental Score.

The correlations of the scales with each other in the pregnant group were examined in Table 2. A statistically weak correlation was found between CAS and PSQI scale (r:0.222, p=0.002). A statistically significant correlation was found, and the correlation level was found to be very weak CAS and SF12-PCS (r:0.156, p=0.027); no correlation was found between CAS and SF12-MCS (r:-0.39, p=0.582). A statistically significant correlation was found, and the correlation level was found to be very weak

PSQI and SF12-PCS (r:0.155, p=0.029); no correlation was found between PSQI and SF12-MCS (r:-0.055, p=0.438).

While 151 people in the pregnant group reported poor sleep quality, 130 in the control group said they had poor sleep quality. (Table 3). Pregnant women were found to have worse sleep quality, which was statistically significant between the two groups (x<sup>2</sup>:5.257; p=0.02).

**Table 2.** Examination of the correlations of the scales with each other in the pregnant group.

	CAS	PSQI	SF12-PCS	SF12-MCS
CAS	1			
PSQI	r 0.222** p 0.002	1		
SF12-PCS	r 0.156* p 0.027	0.155* 0.029	1	
SF12-MCS	r -0.039 p 0.582	-0.055 0.438	-0.556** 0.001	1

\*: Spearman test, p<0.05 (2-tailed); \*\*: Spearman test, p<0.01; CAS: The Coronavirus Anxiety Scale; PSQI: Pittsburgh sleep quality index; SF12-PCS: Physical Score; SF12-MCS: Mental Score.

**Table 3.** Comparison of sleep quality in pregnant and control groups.

	PSQI	GOOD SLEEP QUALITY	POOR SLEEP QUALITY	TOTAL	X <sup>2</sup>	p*
Pregnant Group		49	151	200	5.275	0.02
Control Group		70	130	200		
TOTAL		119	281	400		

\*: The Chi-Square Test; PSQI: Pittsburgh sleep quality index.

There was no difference between the periods when sleep quality was evaluated according to pregnancy trimesters (Table 4) ( $\chi^2:1.479$ ;  $p=0.477$ ). The pregnant and control groups were evaluated in Table 5 according to sleep quality subscales. Sleep latency, efficiency, and disorder scores were statisti-

cally significantly higher in the pregnant group (respectively,  $Z:-1.988$ ,  $p=0.047$ ;  $Z:-5.009$ ,  $p=0.0001$ ;  $Z:-5.230$ ,  $p=0.001$ ). The use of sleeping medication was statistically significantly higher in the control group ( $Z:-2.187$ ,  $p=0.029$ ).

**Table 4.** Examination of sleep quality according to pregnancy trimesters.

		Good Sleep	Poor Sleep	Total	$\chi^2$	$p^*$
Pregnancy trimester	1.	11	25	36	1.479	0.477
	2.	15	59	74		
	3	23	67	90		
<b>Total</b>		49	151	200		

\*: The Chi-Square Test; PSQI: Pittsburgh sleep quality index.

**Table 5.** Evaluation of sleep quality and subscales in the pregnant and control groups.

PSQI	Pregnant Group Median (IQR)	Control Group Median (IQR)	Z	$p^*$
Subjective sleep quality	1.0 (1.0)	1.0 (1.0)	-1.859	0.063
Sleep latency	2.0 (1.75)	2.0 (1.0)	-1.988	<b>0.047</b>
Sleep duration	1.0 (1.0)	0.0 (1.0)	-1.758	0.079
Sleep efficiency	1.0 (2.0)	0.0 (1.0)	-5.009	<b>0.0001</b>
Sleep disorder	2.0 (1.0)	1.0 (1.0)	-5.230	<b>0.0001</b>
Sleeping medication	0.0 (0.0)	0.0 (0.0)	-2.187	<b>0.029</b>
Daytime dysfunction	1.0 (2.0)	1.0 (2.0)	-1.242	0.214
<b>PSQI Total Score</b>	8.0 (4.0)	7.0 (5.0)	-3.138	<b>0.002</b>

\*: Mann Whitney U test; PSQI: Pittsburgh sleep quality index.

**DISCUSSION AND CONCLUSION**

Sleep is a physiological need that covers approximately one-third of our lives, necessary for our physical and mental health. Due to the importance of this period, many studies investigate the various effects of sleep affecting our lives and the reasons for these effects. It has been observed that sleep quality deteriorates and is affected by many parameters, especially in studies conducted with pregnant women. In addition, sleep quality is closely related to perceived stress. It is known that with the physical and mental changes that occur in pregnant women, night sleep also affects the quality of life in pregnant women.<sup>16,17</sup> In this study, we aimed to evaluate pregnant women's anxiety, sleep quality, and quality of life during the pandemic period we lived in. We wanted to contribute to the literature with this study. During the pandemic period, it was determined that the most common symptoms of depression, anxiety, post-traumatic stress disorder, and sleep disorders were found after the infection, especially in people infected with the coronavirus.<sup>18</sup> In studies conducted with pregnant women, there was an increase in anxiety and depressive symptoms during this period.<sup>19</sup> During the pandemic, the inability to be with family members at birth, the fear of virus transmission, and

the daily coronavirus (the number of cases and deaths) are among the reasons pregnant women create anxiety and depressive symptoms.<sup>5</sup> However, the study of Zhou et al., which reported that pregnant women were less affected by depression, anxiety, and sleep disorders during the COVID-19 period, published an investigation contrary to our findings and claimed that pregnant women were more resistant to anxiety disorders, depression and sleep disorders.<sup>6</sup> In our study, there was no difference between the two groups regarding coronavirus anxiety. In addition, no significant difference was found between coronavirus anxiety and the sociodemographic characteristics of our participants. One of the most important reasons for this may be that the healthy and pregnant groups are intensely concerned about the coronavirus. Anxiety and depression symptoms that may develop due to hormonal fluctuations and environmental effects during pregnancy and breastfeeding lead to various physiological and psychological effects during this period.<sup>20</sup> Especially sleep disorders have been the subject of research in this period. In addition to studies reporting that poor sleep quality is associated with depression and anxiety symptoms, it has been reported that pregnancy anxiety may be

related to poor sleep quality and premature birth.<sup>21</sup> In a study evaluating sleep quality in pregnant women during the pandemic, 88% reported poor sleep quality.<sup>2</sup> In our study, 75% of pregnant women reported poor sleep quality and claimed significantly worse sleep than the control group. When studies evaluating sleep quality in pregnant women before the pandemic are examined, lower rates are observed.<sup>22</sup>

During the pandemic, the sleep quality of pregnant women was impaired compared to the healthy group, and the rate of those whose sleep quality was impaired compared to previous studies increased. No studies were found comparing sleep quality before and after the pandemic during pregnancy. The pandemic may have many factors in the disruption of sleep, pregnant women at home may have isolated themselves more during this process, and their bed arrangements may have been disturbed. In addition, increased stress levels in pregnant women may also have adversely affected their sleep.

In a study evaluating the quality of life of pregnant women in which 37 studies conducted before pregnancy were assessed, it was found that while the physical component of quality of life decreased during pregnancy, the mental part remained stable and even improved during pregnancy.<sup>23</sup> Social isolation with curfews and restrictions during the pandemic period, feeling the threat of not being able to reach nutritional needs, security concerns, experiencing financial losses, misinformation about the disease, risky groups such as healthcare professionals or people with a history of infection with the Covid-19 virus in their family members' feeling lonely and its stigmatisation affected the quality of life.<sup>24</sup> In addition, it was found that the quality of life was below the moderate level in studies conducted during pregnancy.<sup>25</sup>

In our study, The Quality of Life SF12-PCS was higher in pregnant women, but the SF12-MCS was lower than in healthy controls. It may show that pregnant women feel worse mentally during this pandemic process. We think that staying at home, being physically removed from business life, and working remotely from the office improve the physical quality of life. However, unfortunately, mental overwork related to the pandemic seems to have adversely affected the mental quality of life in pregnant women.

In longitudinal studies comparing sleep quality between trimesters of pregnancy, it was found that the worst sleep quality was in the third trimester, and sleep quality decreased from the second trimester to the third trimester.<sup>26</sup> In addition, studies have found that sleep quality is associated with sociodemographic characteristics. It has been found that living in a crowded family with a high number of children

worsens sleep quality.<sup>27</sup> We did not see any difference between trimesters regarding sleep quality in pregnant women who participated in our study. In addition, there was no significant relationship between total PUKI score and age, gestational week, number of pregnancies, and number of children. The most common sleep disorders in pregnancy are caused by frequent urination at night, baby movements, back and waist pain, cramps, and weight gain.<sup>28</sup> These symptoms usually occur in the third trimester of pregnancy. In addition, it was observed that there was an increase in daytime sleepiness in the first trimester of pregnancy. Generally, sleep quality decreases during pregnancy.<sup>29</sup> The physical and mental changes in pregnant women during all three trimesters of pregnancy may have caused the similarity in the sleep quality we obtained in our study. Our research thought that different results could be obtained by transforming the cross-sectional evaluation into a follow-up study.

When the sleep quality scale sub-parameters were evaluated, a significant difference was found between the pregnant women and the control group in terms of sleep latency, sleep efficiency, sleep disorder, and sleep medication subscale scores (respectively  $p=0.047$ ,  $p=0.0001$ ,  $p=0.0001$ ,  $p=0.029$ ). No significant difference was found between the groups regarding subjective sleep quality, duration, and daytime dysfunction from other subscales. A study conducted on pregnant women observed that the rates of poor sleep quality varied between 46-89.3%.<sup>24</sup> The difference in the sub-parameter of sleeping medication may be related to avoiding drug use in pregnant women. Other observed differences may also be associated with physiological and psychological changes during pregnancy.

Another critical issue in our study is examining the correlation between CAS, quality of life, and sleep. Recently, the number of studies investigating sleep quality on quality of life has increased.<sup>30</sup> A study conducted on pregnant women showed that a decrease in sleep quality decreases the quality of life.<sup>30</sup> In our research, our correlations between sleep quality and two sub-parameters of quality of life during the pandemic were very weak. This does not coincide with the hypothesis we established at the beginning of this study. This may be because the quality of life is affected by very different conditions (restriction, stress, etc.) during the pandemic. Coronavirus anxiety also negatively affected the quality of life.

In conclusion, the study's limitations are the cross-sectional evaluation of pregnant women rather than a follow-up study. The collected cases are limited to the state hospital in the province, and the sleep assessment with subjective scales, not in the sleep laboratory. The relatively sufficient number of cases

participating in our study, the fact that pregnant women and healthy controls were not selected from complicated issues, and the fact that it is one of the rare studies evaluating both the quality of life and sleep quality of pregnant women during the pandemic are the features that may make our research meaningful. Sleep and mental stress impair the quality of life of pregnant women and pose a risk for their unborn children. As a result, the pandemic horribly affects pregnant women's sleep quality and mental quality of life. Clinicians should take care to evaluate the sleep quality of pregnant women in this process. In addition, providing sleep-oriented psychological support to pregnant women can reduce the long-term adverse effects of this pandemic.

**Ethics Committee Approval:** The study was approved by the Duzce University, Non-Interventional Clinical Research Ethics Committee (Date:05/04/2021, decision no:2021/99).

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

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

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## The Relationship between Tolerance, Forgiveness, and Depression Levels in Patients Diagnosed with Depression

### Depresyon Tanısı Alan Hastalarda Hoşgörü, Affetme ve Depresyon Düzeyleri Arasındaki İlişki

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#### ABSTRACT

**Objective:** This study aimed to determine the relationship between the level of tolerance, forgiveness, and depression in patients diagnosed with depression.

**Materials and Methods:** It was conducted with 80 patients in the outpatient psychiatry clinic of a hospital in Turkey. Data was collected with Beck Depression Inventory, Tolerance Scale and Heartland Forgiveness Scale. Data were evaluated using SPSS (21.0) statistical program.

**Results:** In this study, while it was determined that there was a statistically significant negative and moderately relationship between the mean Beck Depression Inventory and Tolerance Scale scores, a weak negative relationship was found between the mean Beck Depression Inventory and Heartland Forgiveness Scale scores. Also, it was determined that tolerance and forgiveness predicted depression negatively.

**Conclusion:** The results of this study can be used for interventions that include tolerance and forgiveness in reducing depression.

**Keywords:** Depression, tolerance, forgiveness

#### ÖZ

**Amaç:** Bu çalışmada, depresyon tanısı alan hastalarda hoşgörü, affetme ve depresyon düzeyleri arasındaki ilişkinin belirlenmesi amaçlanmıştır.

**Materyal ve Metot:** Bu çalışma, Türkiye’de bir hastanenin psikiyatri polikliniğinde 80 hasta ile yapılmıştır. Verilerin toplanmasında, Beck Depresyon Envanteri, Hoşgörü Ölçeği ve Heartland Affetme Ölçeği kullanılmıştır. Veriler, SPSS (21.0) istatistik programı kullanılarak değerlendirilmiştir.

**Bulgular:** Bu çalışmada Beck Depresyon Envanteri ve Hoşgörü Ölçeği puan ortalamaları arasında istatistiksel olarak orta düzeyde anlamlı negatif bir ilişki olduğu belirlenirken, Beck Depresyon Envanteri ve Heartland Affetme Ölçeği puan ortalamaları arasında negatif yönde zayıf bir ilişki bulunmuştur. Ayrıca hoşgörü ve affetmenin depresyonu negatif yönde yordadığı belirlenmiştir.

**Sonuç:** Depresyonun düzeyinin azaltulmasında, hoşgörü ve affetmeyi içeren müdahaleler için bu çalışmanın sonuçlarından yararlanılabilir.

**Anahtar Kelimeler:** Depresyon, hoşgörü, affetme

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## INTRODUCTION

Depression is a mood disorder in which the individual feels unhappy and intense pessimism prevails.<sup>1,2</sup> If life difficulties and problems in interpersonal relationships are long-lasting and the problem is not truly resolved, this may increase the individual's stress level and cause changes in neurotransmitters such as serotonin and dopamine, eventually leading to depression.<sup>2-4</sup> Therefore, interventions and methods to reduce the stress levels of individuals are recommended. Thus, the development of depression is tried to be prevented, and its level is tried to be reduced. Tolerance and forgiveness may be an important factor that reduces the stress levels of individuals and, therefore, depression. Increasing tolerance and forgiveness of individuals can prevent the deterioration of neuro-biochemical mechanisms by triggering the thought and behavior axis necessary to reduce their stress levels.<sup>2-7</sup> Because tolerance and forgiveness can reduce burden and stress by making a positive contribution to the interpersonal relationships of individuals. Tolerance is a concept that is important in interpersonal relations and is also called cognitive flexibility, which is called being flexible towards the feelings, thoughts, behaviors, beliefs and practices of other individuals, groups and other societies, and being able to give them various rights and privileges.<sup>6-9</sup> Thus, as the level of tolerance increases, the ability of individuals to make adaptive problem-solving decisions in new situations also increases.<sup>10</sup> Palm and Follette<sup>11</sup> stated that a positive relationship exists between cognitive flexibility and coping with psychological stress. Therefore, increased tolerance or cognitive flexibility may reduce the occurrence of psychiatric disorders.

Forgiveness is compassion and generosity towards the person who caused it when one's right is defeated, when anger and negative feelings are experienced.<sup>12</sup> It has been reported that there is a close relationship between forgiveness and empathy, altruistic behaviors, compassion, positive thinking, hopefulness, and psychological, spiritual and physical health.<sup>13,14</sup> Although the positive effects of tolerance and forgiveness on interpersonal relationships are known, no study has been found in the literature showing its relationship with depression.<sup>15-17</sup> Therefore, this study aimed to determine the relationship between depression, tolerance, and forgiveness.

## MATERIALS AND METHODS

**Study Setting and Procedure:** In this study, ethics committee approval was obtained from the University Ethics Committee (Date: 12.10.2018; decision no: 43/7), and it was carried out in accordance with the Declaration of Helsinki. This study is descriptive research. The data were obtained from 80 patients in

the outpatient psychiatry clinic of a hospital in Turkey between November 2018-October 2019. For the sample, at least 79 patients were needed with a 95% confidence interval, 5% error, 0.5 effect size, and 80% power analysis to represent the population. The study included patients diagnosed with depression for the first time by a psychiatrist who did not receive any psychiatric treatment for the past year. For the patients to participate in the study, the criteria were determined to be volunteers, be over 18 age, and have no communication problems. Patients completed the questionnaires in approximately 20-30 minutes.

**Data Collection and Instruments:** Data were collected using the Beck Depression Inventory, the Tolerance Scale, and the Heartland Forgiveness Scale. In addition, patients wrote their age, gender, marital status and income status on the forms.

**Beck Depression Inventory:** It is used to determine the level of depression in patients.<sup>18</sup> The Turkish validity and reliability of the inventory were performed by Hisli.<sup>19</sup> It is a 21-item and 4-Likert-type. The total score is between 0-63. The Cronbach alpha value of this study was determined as 0.86.

**Tolerance Scale:** This scale was developed by Demirci<sup>20</sup> and had 6 questions and 5- Likert-type. The total score is between 6-30. High scores indicate that individuals' tolerance is high. The Cronbach alpha of this study was determined as 0.83.

**The Heartland Forgiveness Scale:** This scale was developed by Thompson et al.,<sup>21</sup> and Turkish adaptation was conducted by Bugay and Demir.<sup>22</sup> It is an 18-item, 7-point Likert-type scale with three subscales. This scale has forgiveness of self (1, 2, 3, 4, 5, 6), forgiveness of others (7, 8, 9, 10, 11, 12) and forgiveness of situations (13, 14, 15, 16, 17, 18) subscales. The scores that can be obtained from the scale are between 18-126. While scoring the scale, some items (2, 4, 6, 7, 9, 11, 13, 15, 17) are inversely scored. The Cronbach alpha value was determined as 0.85 in this study.

**Statistical Analysis:** SPSS 21.00 was used, and the frequency, percentage, mean, and standard deviation values were calculated. The Kolmogorov-Smirnov test was used to analyse the normal distribution of the data in the study. It was determined that the scale scores showed a normal distribution. Therefore, Pearson's correlation analysis was used. The correlation values were evaluated as 0-0.2=very weak, 0.2-0.4=weak, 0.4-0.6=moderate and 0.6-0.8=strong. Also, regression analyses were carried out for further analysis.  $p < 0.05$  was accepted as the statistical significance.

**RESULTS**

Of the depression patients, 90% were women (N=72), 51.3% were single, and the mean age was 31.31 ± 10.80 (19-62). A total of 72.5% of the patients expressed their income status as a medium (Table 1).

**Table 1.** Participant characteristics.

Characteristic		n(%)
Gender	Female	72(90.0)
	Male	8(10.0)
Age	19-29	42(52.5)
	30≥	38(47.5)
Marital Status	Married	39(48.8)
	Single	41(51.3)
Income Status	Bad	13(16.3)
	Medium	58(72.5)
	Good	9(11.3)

**Table 2.** Participant scales scores.

Scales	X±SD	Min-Max	K-S Z
Beck Depression Inventory	22.61±11.03	0-63	0.073*
Tolerance Scale	20.77±5.98	6-30	0.097*
Heartland Forgiveness Scale	71.56±20.26	18-126	0.069*
Forgiveness of self	24.88±7.84	1-42	0.079*
Forgiveness of others	23.38±9.45	1-42	0.070*
Forgiveness of situations	24.40±9.84	1-42	0.085*

K-S Z: Kolmogorov-Smirnov Z; \*:p>0.05.

sion Inventory and Tolerance Scale (r=-.412; p<.05). In addition, a significant negative relationship was found between the mean the Beck Depression Inventory and the Heartland Forgiveness Scale total and forgiveness of self and forgiveness of situations sub-

Beck Depression Inventory, Tolerance Scale, and Heartland Forgiveness Scale scores of patients were 22.61±11.03, 20.77±5.98, and 71.56±20.26, respectively. The forgiveness of self, forgiveness of others, and forgiveness of situations sub-scales of the Heartland Forgiveness Scale scores were 24.88±7.84, 23.38±9.45, and 24.40±9.84, respectively (Table 2).

A positive and significant relationship was determined between the mean the Tolerance Scale and the Heartland Forgiveness Scale total and forgiveness of self, forgiveness of others, and forgiveness of situations sub-scales of the Heartland Forgiveness Scale scores (r=.488, r=0.295, r=0.474, r=0.523; p<.05). A significant negative relationship was determined between the mean the Beck Depres-

sion Inventory and Tolerance Scale (r=-.369, r=-0.386, r=-0.521; p<.05) (Table 3). According to the regression model, while the tolerance explains 18.6% (p<0.05) of depression, the forgiveness explains 13.6% (p<0.05) of depression (Table 4).

**Table 3.** Correlations among scales.

	Beck Depression Scale	Tolerance Scale	Heartland Forgiveness Scale	Forgiveness of self	Forgiveness of others	Forgiveness of situations
Beck Depression Scale	1					
Tolerance Scale	-0.412*	1				
Heartland Forgiveness Scale	-0.369*	0.488*	1			
Forgiveness of self	-0.386*	0.295*	0.777**	1		
Forgiveness of others	-0.085	0.474**	0.798**	0.332**	1	
Forgiveness of situations	-0.521**	0.523**	0.771**	0.595**	0.508**	1

\*\* : p<0.01; \* : p<0.05; Pearson's correlation test.

**Table 4.** Regression among scales.

Dependent Variable	Independent Variable	R <sup>2</sup>	F	β	p
Beck Depression Inventory	Heartland Forgiveness Scale	0.136	12.275	-0.369	0.001*
Beck Depression Inventory	Tolerance Scale	0.186	17.813	-0.431	0.000*
Tolerance Scale	Heartland Forgiveness Scale	0.238	24.350	0.488	0.000*

\*p<0.05.



## DISCUSSION AND CONCLUSION

Much research has been done on the causes and treatment of depression since Hippocrates claimed that bodily fluids affect mood.<sup>2,4</sup> In addition, psychological factors such as the individuals' personality, perspective, negative life events, and individuals' ability to cope with stress have been revealed in the development and prognosis of depression.<sup>3,23-25</sup> However, despite all these studies, neither the occurrence of depression has been prevented, nor the frequency of depression has decreased.<sup>1,3,26</sup>

According to the results obtained from this study, it can be said that the mean the Beck Depression Scale, the Tolerance Scale and the Heartland Forgiveness Scale total and forgiveness of self, forgiveness of others and forgiveness of situations subscales scores were moderate. In addition, this study determined that as the tolerance level of patients with depression increased, the level of forgiveness increased. As the level of tolerance and forgiveness of the patients improved, the level of depression decreased. According to the regression model, a 1-unit increase in the tolerance level decreases the depression level by 0.431 units ( $\beta = -0.431$ ;  $p < 0.05$ ). Also, it is determined that a 1-unit increase in the level of forgiveness decrease the depression level by 0.369 units ( $\beta = -0.369$ ;  $p < 0.05$ ). This result can be interpreted as tolerance and forgiveness having a positive effect on the mental health of individuals and reducing the level of depression. Tolerance and forgiveness mean ending an ongoing internal dialogue, whether litigation, justification, blame, clarification, or judgment of the other. When these dialogues cease, tolerance towards others and forgiveness take place.<sup>20-22</sup> Personality traits, teachings, cultures, and religious beliefs are important factors in individuals tolerating and forgiving others.<sup>20,21,27</sup>

These characteristics are the prerequisites that affect their tolerance and forgiveness. In particular, religious teachings attributed tolerance and forgiveness to God and stated that human behavior that is tolerant and able to forgive others reflects God's characteristics.<sup>27,28</sup> Ultimately, the results of tolerance and forgiveness can lead to a feeling of pleasantness to all who forgive and are forgiven. It can create a sense of happiness and satisfaction in individuals. This can be a factor that protects mental health.

Researchers reported that tolerance and forgiveness contribute positively to reducing anger and maintaining physical and psychological well-being.<sup>28,29</sup> Forgiveness is emotional, cognitive and behavioral, and it has a role in forgiveness because tolerance increases resilience.<sup>28,30</sup> It has been reported that individuals with low tolerance levels have less resilience and have high-stress levels.<sup>20,29,30</sup> Because many individuals can forgive after reconciliation is achieved, it is necessary for the individual to depend

on others to protect his health. There is no compromise between tolerance and forgiveness. There can be tolerance and forgiveness without reconciliation. What provides this results from the individual's feelings, thoughts and behaviors. Therefore, to protect and improve mental health, it can be recommended that individuals change their thoughts, feelings and behaviors instead of constantly waiting for the forgiveness and tolerance of others.

According to the data obtained from this study, mental health professionals need to know the relationship between the level of depression and the level of tolerance and forgiveness for the prevention and treatment of depression. Thus, physical, psychological, and social destructions can be prevented and reduced by reducing the individual and social negativities caused by depression.

In conclusion, it has been determined as an important issue to improve patients' tolerance and forgiveness skills to reduce the depression levels of patients diagnosed with depression. For this reason, it may be recommended to focus on tolerance and forgiveness skills in patients with depression.

This study has some limitations. The first limitation is that it was performed in a single hospital. The second limitation is that it was conducted with patients who agreed to participate in the study. Another limitation is the inability to control the individual, cultural and social variables of the patients with whom the study was conducted. Therefore, the results cannot be generalised.

**Ethics Committee Approval:** The ethical permission was obtained from the Bilecik Şeyh Edebali University Ethics Committee (Date: 12/10/2018, decision no: 43/7).

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

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## The Relationship between Treatment Adherence, Social Support and Recovery Status of Patients Receiving Psychiatric Treatment

### Psikiyatri Tedavisi Alan Hastaların Tedaviye Uyumluları ile Algıladıkları Sosyal Destek ve İyileşme Durumları Arasındaki İlişki

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#### ABSTRACT

**Objective:** This research was performed to determine the correlations and effective factors for treatment adherence with perceived social support and the recovery status of psychiatric patients receiving outpatient treatment.

**Materials and Methods:** This study was descriptive, cross-sectional, and relational. Data collection tools used were the 'Patient Information Form', 'Morisky Medication-taking Adherence Scale (MMAS-4)', 'Recovery Assessment Scale (RAS)', and the 'Multidimensional Scale of Perceived Social Support (MSPSS)'.

**Results:** Of the participants, 22.3% had low treatment adherence. There were statistically significant correlations between the treatment adherence scale with the RAS personal confidence and hope, RAS willingness to ask for help subscales, and RAS total points between all dimensions of the multidimensional perceived social support scale and all dimensions of the RAS ( $p<0.05$ ). The diagnosis was determined to affect treatment adherence points ( $F=5.041$ ,  $p<0.05$ ). RAS total points had a negative effect on treatment adherence ( $\beta= -0.011$ ;  $p<0.050$ ) but a positive effect on MSPSS points ( $\beta= 0.447$ ;  $p<0.001$ ).

**Conclusion:** In the study, it was found that as recovery status increased, the patient's adherence to treatment decreased, and as the perceived social support increased, the level of recovery (RAS) increased.

**Keywords:** Mental disease, perceived social support, recovery, treatment adherence

#### ÖZ

**Amaç:** Bu araştırma, ayaktan tedavi gören psikiyatri hastalarının iyileşme durumlarının algıladıkları sosyal destek ve tedaviye uyumluları ile ilişkisini ve etkileyen faktörleri belirlemek amacıyla yapılmıştır.

**Materyal ve Metot:** Bu çalışma, tanımlayıcı, kesitsel ve ilişkisel tipte bir araştırmadır. Veri toplamak için 'Hasta Bilgi Formu', 'Morisky İlaç Uyumu Ölçeği (MMAS-4)', 'İyileşme Değerlendirme Ölçeği (RAS)' ve 'Çok Boyutlu Algılanan Sosyal Destek Ölçeği (MSPSS)' kullanıldı.

**Bulgular:** Katılımcıların %22,3'ünün tedavi uyumu düşüktü. Tedaviye uyum ölçeği ile RAS kişisel güven ve umut, RAS yardım isteme istekliliği ve RAS toplam puanları arasında; çok boyutlu algılanan sosyal destek ölçeğinin tüm boyutları ile RAS'ın tüm alt boyutları arasında istatistiksel olarak anlamlı ilişkiler bulundu ( $p<0,05$ ) ve tanının tedaviye uyum puanlarını etkilediği belirlendi ( $F=5,041$ ,  $p<0,05$ ). RAS toplam puanlarının tedaviye uyum üzerinde olumsuz bir etkisi vardı ( $\beta= -0,011$ ;  $p<0,050$ ). RAS toplam puanları MSPSS puanları üzerinde olumlu bir etkiye sahipti ( $\beta= 0,447$ ;  $p<0,001$ ).

**Sonuç:** Çalışmada, iyileşme durumu arttıkça hastaların tedaviye uyumunun azaldığı ve algılanan sosyal destek arttıkça iyileşme düzeyinin arttığı bulunmuştur.

**Anahtar Kelimeler:** Algılanan sosyal destek, iyileşme, ruhsal hastalık, tedaviye uyum

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## INTRODUCTION

Non-adherence to drug treatment, a common problem in medicine, directly affects cognitive functions in psychiatric patients,<sup>1,2</sup> lack of insight into psychiatric disease, stigma, concomitant substance abuse, and social isolation.<sup>3</sup> It was shown that at least one-third of psychiatric patients with treatment-resistant profiles have poor treatment adherence, and the drug level in the blood is at subtherapeutic levels.<sup>4,5</sup> Non-adherence to both antipsychotic and antidepressant medication use causes increased hospital admission rates with recurrence (increased 5.2 times for bipolar disorder), worsening of symptoms, higher rates of suicide, negative economic/social/health outcomes, and increased care costs.<sup>6,7</sup> After patients begin treatment, the rate of missed appointments is reported to be 12-60%. In the group not adhering to treatment, 28% applied to the emergency service, which was determined to cost the health sector 100 billion dollars.<sup>6</sup> Studies show that 1/3 of psychiatric patients have at least one readmission during the follow-up period (within 90 days after discharge).<sup>8,9</sup>

The traditional understanding of psychiatry has been approaching mental illness by reducing the importance of patient experiences. However, patient experiences embody the disease, explain the patient's reality and coping routes, and ensure disease control.<sup>10,11</sup>

Recovery does not just involve assessing reduced symptoms, recurrence, or hospitalisation rates. It also includes defining the patient's perspective and subjective experiences related to the disease.<sup>12,13</sup> In recent years, recovery-focused practices have shaped mental health services.<sup>14</sup> Pharmacological treatment, which is an important factor contributing to the recovery of psychiatric patients, can lead to treatment non-adherence, poor treatment outcomes, and poor care outcomes if not considered together with other effective factors. However, techniques used to identify factors affecting adherence and improve treatment adherence remain at the level of pragmatic recommendations for clinical practice.<sup>15</sup> The number of studies focusing on patient-related and subjective factors affecting the adherence of psychiatric patients to treatment is quite limited.

Therefore, this study aimed to investigate the relationship between perceived social support, recovery levels, and treatment adherence of psychiatric patients.

## MATERIALS AND METHODS

**Ethical Approval:** In this study, before starting the study, institutional permission was obtained from Tokat Gaziosmanpaşa University Faculty of Medicine Dean's Office (Date: 28.08.2018, Decision No:18-KAEK-192), and ethical approval for the

study was obtained from the Ethics Committee of Tokat Gaziosmanpaşa University Ethics Committee (Date: 05.12.2018, Decision No: 18-KAEK-192/626).

**Design:** This research had a descriptive, cross-sectional, and correlational design.

**Setting and Sample:** The research universe comprised 58.814 patients attending Tokat Dr Cevdet Aykan Mental Health and Diseases Hospital psychiatry outpatient clinic between 22 November 2017 and 22 November 2018. The sample of the research comprised patients attending Tokat Dr Cevdet Aykan Mental Health and Diseases Hospital psychiatry outpatient clinic between 22 November 2018 and 10 May 2019. The study sample consisted of 139 patients who applied to the outpatient psychiatry clinic of this mental health hospital between these dates. Post-hoc power analysis determined that with a 0.05 significance level and 95% confidence interval, the power of the study should be 0.80 (correlation  $H1=0.238$ , lower critical  $r=-0.159$ , upper critical  $r=0.159$ , power 0.80). The sample ( $n=139$ ) was determined to be adequate for this value.

**Inclusion Criteria for the Research:** Receiving outpatient psychiatric treatment for at least three weeks or more, not being in the acute period of the disease, being conscious, having no problems with speech and comprehension, being 18 years or older, having no developmental intellectual disorder, dementia, amnesia or other cognitive disorder, and accepting participation in the research.

**Data Collection Tools:** Data were collected during face-to-face interviews between the researcher and the patient. Preliminary interviews were held with identified patients. Patients abiding by the inclusion criteria were given information about the study and provided consent. Collection of data used the 'Patient Information Form', 'Morisky Medication-taking Adherence Scale (MMAS-4)', 'Recovery Assessment Scale (RAS)' and the 'Multidimensional Scale of Perceived Social Support (MSPSS)'.

**Patient Information Form:** This was prepared by the researchers in line with the literature and comprised 10 questions about socio-demographic information and 9 questions about clinical information.<sup>6,7</sup>

**Morisky Medication-taking Adherence Scale (MMAS-4):** The validity and reliability study of this scale, which was created by Morisky, Levine, and Green in 1986 (Cronbach  $\alpha=0.61$ ), was conducted by Yılmaz in 2004 in Turkey, and the Cronbach alpha reliability coefficient was found to be 0.52.<sup>16</sup> Permission was obtained from the author to use the scale.

**Recovery Assessment Scale (RAS):** The Recovery Assessment Scale was developed containing 41

items and was revised by Corrigan et al.<sup>17</sup> to include 24 items in 5 subscales. The Turkish validity was performed by Güler.<sup>18</sup> The dimensions of the scale were identified to have Cronbach alpha values from 0.74 to 0.87. The subdimensions are ‘personal confidence and hope’, ‘willingness to ask for help’, ‘goal and success orientation’, ‘dependency on others, and ‘no domination by symptoms.’ In this study, the Cronbach alpha values for the subscales varied from 0.76 to 0.89, with a total Cronbach alpha value of 0.94. Permission was obtained from the author for the use of the scale.

**The Multidimensional Scale of Perceived Social Support (MSPSS):** This was developed by Zimet et al. in 1988 and adapted to Turkish by Eker and Arkar.<sup>19</sup> It is a diverse scale that individuals with low educational levels can understand. The scale comprises 3 subdimensions and has a 7-point Likert style. Eker et al. found that the total Cronbach alpha coefficient for the perceived social support scale was 0.89, with Cronbach alpha coefficients for the subscales varying from 0.85 to 0.92. In this study, the Cronbach  $\alpha$  reliability coefficients for the subscales were 0.88-0.90, while the Cronbach  $\alpha$  reliability coefficient for the whole scale was 0.91. Permission

was obtained from the author to use the scale.

**Statistical Analysis:** Data were analysed with IBM SPSS V23. Conformity to normal distribution was evaluated by Kolmogorov-Smirnov and Shapiro-Wilk tests. Parametric tests were used if the data fit the normal distribution, and non-parametric tests were used if the data did not fit the normal distribution. Spearman's rho correlation coefficient was used to examine the relationship between non-normally distributed scale scores. One-way MANOVA was used to investigate the factors affecting total scale scores, and the Bonferroni test was used for multiple comparisons. One-way analysis of variance was used to compare the MSPSS and ISS total scores according to treatment adherence classes. Analysis results are presented as mean  $\pm$  standard deviation. The significance level was taken as  $p < 0.05$ .

## RESULTS

Among participants, 63.3% were male, 43.9% were single, 55.4% were primary education graduates, and 80.6% did not work. Of the participants, 56.1% had a mood disorder diagnosis, and 22.3% had low treatment adherence (MMAS-4) (Table 1).

**Table 1.** Frequency distribution of categorical variables.

Demographic Information	n (%)	
Sex	Female	51 (36.7)
	Male	88 (63.3)
Marital status	Married	44 (31.7)
	Single	61 (43.9)
	Divorced	34 (24.4)
	Widowed	14 (10.1)
Education status	Literate	77 (55.3)
	Primary Education	34 (24.5)
	High School	14 (10.1)
	University	14 (10.1)
Working situation	Working	27 (19.4)
	Not working	112 (80.6)
Social security	Yes	104 (74.8)
	No	35 (25.2)
Taking medication	Taking without help	94 (67.6)
	Taking with help	40 (28.8)
	Not taking medications	5 (3.6)
	Attending follow-ups regularly	20 (14.5)
Time to go to follow-ups	When s/he feels bad	71 (50.7)
	When s/he is guided by the family	26 (18.9)
	Other	22 (15.9)
Adherence class (MMAS-4)	High adherence to treatment	43 (30.9)
	Moderate adherence to treatment	65 (46.8)
	Low adherence to treatment	31 (22.3)
Additional disease	Yes	47 (33.8)
	No	92 (66.2)
Diagnostic class	Psychotic disorder	78 (56.1)
	Mood Disorder	46 (33.1)
	Anxiety disorder	7 (5.0)
	Substance abuse	5 (3.6)
	Personality Disorder	3 (2.2)
Income status	Income is less than expenses	50 (36.2)
	Income is equal to expenses	76 (55.1)
	Income is more than expenses	13 (8.7)

Table 1. Continue.

<b>How many times a day does she/he take medication</b>	3 and less	41 (29.5)
	4 and above	98 (70.5)
<b>Demographic information and scales</b>		<b>Mean±SD</b>
	Age	41.9±13.2
	Number of children	2.8±2.2
	MSPSS	53.4±21.5
	RAS	85.2±20.8
	MMAS-4	1.5±1.3

The mean points for adherence to treatment (MMAS-4), MPSS, and RAS according to sociodemographic features and multivariate analysis results related to scale points are given in Table 2.

Table 2. Multivariate analysis results for MMAS-4, MSPSS, and RAS scores according to sociodemographic characteristics.

<b>Demographic Information</b>		<b>Treatment adherence (MMAS-4)</b>	<b>MSPSS total</b>	<b>RAS total</b>
<b>Sex</b>	Female (n=51)	1.49 ± 1.29	58.12 ± 20.76	91.73 ± 17.51
	Male (n=88)	1.44 ± 1.27	50.70 ± 21.55	81.45 ± 21.64
	<b>F; p</b>	F=0.416; p=0.520	F=2.101; p=0.150	F=7.333; p=0.008
	<b>Partial eta squared</b>	0.003	0.017	0.057
<b>Marital status</b>	Married (n=44)	1.20 ± 1.23	59.39 ± 20.61	90.20 ± 18.26
	Single (n=61)	1.57 ± 1.22	50.54 ± 20.54	83.66 ± 22.39
	Divorced (n=34)	1.59 ± 1.40	50.88 ± 23.25	81.59 ± 20.12
	<b>F; p</b>	F=1.692; p=0.189	F=1.089; p=0.340	F=2.034; p=0.135
	<b>Partial eta squared</b>	0.027	0.018	0.033
<b>Education status</b>	Literate (n=14)	2.14 ± 1.29	52.50 ± 14.98	81.71 ± 17.67
	Primary Education (n=77)	1.53 ± 1.27	54.83 ± 22.39	86.14 ± 19.83
	High School (n=34)	1.09 ± 1.19	52.59 ± 19.75	84.15 ± 23.87
	University (n=14)	1.29 ± 1.20	48.64 ± 26.79	86.29 ± 22.24
	<b>F; p</b>	F= 2.844; p=0.041	F=0.114; p=0.952	F= 0.864; p=0.462
	<b>Partial eta squared</b>	0.066	0.003	0.021
<b>Time to go to follow-ups</b>	Attending follow-ups regularly (n=20)	1.70 ± 1.17	42.15 ± 23.90	88.10 ± 17.02
	When s/he feels bad (n=70)	1.49 ± 1.22	53.86 ± 18.92	84.01 ± 21.63
	When guided by the family (n=26)	1.27 ± 1.28	58.65 ± 24.14	87.58 ± 22.04
	Other (n=22)	1.45 ± 1.50	56.55 ± 21.84	84.91 ± 19.97
	<b>F; p</b>	F=0.247; p=0.864	F=1.685; p=0.174	F=1.130; p=0.340
	<b>Partial eta squared</b>	0.006	0.040	0.027
<b>Income status</b>	Income is less than expenses (n=50)	1.48 ± 1.30	50.52 ± 21.40	84.54 ± 21.12
	Income is equal to expenses (n=76)	1.45 ± 1.28	56.22 ± 20.94	85.34 ± 21.36
	Income is more than expenses (n=12)	1.42 ± 1.24	50.67 ± 23.56	89.25 ± 15.51
	<b>F; p</b>	F= 0.056; p=0.946	F=0.736; p=0.481	F=0.012; p=0.988
	<b>Partial eta squared</b>	0.001	0.012	0.000
<b>Additional disease</b>	Yes (n=47)	1.51 ± 1.38	51.36 ± 23.30	84.74 ± 20.40
	No (n=92)	1.43 ± 1.22	54.48 ± 20.55	85.47 ± 21.05
	<b>F; p</b>	F=0.104; p=0.748	F=1.048; p=0.308	F= 0.126; p=0.723
	<b>Partial eta squared</b>	0.001	0.009	0.001
<b>How many times a day does s/he take medication</b>	3 and less (n=41)	1.44 ± 1.29	54.02 ± 21.61	87.71 ± 19.52
	4 and above (n=98)	1.47 ± 1.27	53.17 ± 21.54	84.18 ± 21.27
	<b>F; p</b>	F=0.045; p=0.832	F=0.185; p=0.668	F=0.205; p=0.652
	<b>Partial eta squared</b>	0.000	0.002	0.002
<b>Diagnostic class</b>	Psychotic disorder (n=78)	1.26 ± 1.20 <sup>a</sup>	50.88 ± 21.85	82.05 ± 20.09
	Mood disorder (n=46)	1.52 ± 1.31 <sup>ab</sup>	55.41 ± 20.64	91.22 ± 19.67
	Other (n=15)	2.33 ± 1.18 <sup>b</sup>	60.53 ± 21.31	83.33 ± 24.64
	<b>F; p</b>	F=5.041; p=0.008	F=0.808; p=0.448	F=1.125; p=0.328
	<b>Partial eta squared</b>	0.077	0.013	0.018

a-b: There is no difference between groups with the same letter; \*: multiple comparisons were made with the Bonferroni test. 1R<sup>2</sup>: 0.156; Adjusted R<sup>2</sup> = 0.051; 2 R<sup>2</sup>: 0.134; Adjusted; R<sup>2</sup>: 0.026. 3R<sup>2</sup>: 0.140; Adjusted R<sup>2</sup>: 0.033; F1: One-way analysis of variance test statistic.

Correlations related to the MMAS-4, RAS, and MSPSS scales are given in Table 3. Data investigating the mediating role of MSPSS total points in the effect of RAS total points on treatment adherence points (MMAS-4) are given in Ta-

ble 4. RAS total points had a negative effect on treatment adherence (MMAS-4 ( $\beta = -0.011$ ;  $p < 0.050$ ). The path coefficient between MSPSS points and treatment adherence (MMAS-4) was not found to be significant ( $p > 0.050$ ).

**Table 3.** Relationships between scale scores.

		Multidimensional Perceived Social Support Scale (MSPSS)					Recovery Assessment Scale (RAS)				
		MMAS-4	Family <sup>1</sup>	Friend <sup>1</sup>	Special friend <sup>1</sup>	Total	Orienta-tion toward goal and success <sup>2</sup>	Confidence and hope <sup>2</sup>	Trust the people around <sup>2</sup>	Coping with symp-toms <sup>2</sup>	Seeking help <sup>2</sup>
MSPSS family	r	-0.158	-	-	-	-	-	-	-	-	-
	p	0.063	-	-	-	-	-	-	-	-	-
MSPSS friend	r	-0.121	0.450**	-	-	-	-	-	-	-	-
	p	0.156	0.000	-	-	-	-	-	-	-	-
MSPSS special person	r	0.031*	0.425**	0.621**	-	-	-	-	-	-	-
	p	0.718	0.000	0.000	-	-	-	-	-	-	-
MSPSS total	r	-0.085	0.700**	0.856**	0.863**	-	-	-	-	-	-
	p	0.319	0.000	0.000	0.000	-	-	-	-	-	-
RAS Orientation toward goal and success	r	-0.066	0.249*	0.249*	0.333**	0.331**	-	-	-	-	-
	p	0.441	0.003	0.003	0.000	0.000	-	-	-	-	-
RAS Confidence and hope	r	-0.238*	0.354**	0.406**	0.421**	0.474**	0.658**	-	-	-	-
	p	0.087	0.000	0.000	0.000	0.000	0.000	-	-	-	-
RAS Trust the people around	r	-0.146	0.362**	0.488**	0.381**	0.493**	0.543**	0.730**	-	-	-
	p	0.087	0.000	0.000	0.000	0.000	0.000	0.000	-	-	-
RAS Coping with symptoms	r	-0.130	0.251*	0.311**	0.326**	0.351**	0.452**	0.639**	0.537**	-	-
	p	0.128	0.003	0.000	0.000	0.000	0.000	0.000	0.000	-	-
RAS Seek help	r	-0.171*	0.243*	0.314**	0.217*	0.297**	0.472**	0.584**	0.635**	0.458**	-
	p	0.045	0.004	0.000	0.010	0.000	0.000	0.000	0.000	0.000	-
RAS total	r	-0.186*	0.379**	0.465**	0.450**	0.517**	0.770**	0.932**	0.838**	0.717**	0.705**
	p	0.028	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

r: Spearman's rho correlation coefficient; 1: sub-dimensions of the multidimensional perceived social support scale; 2: sub-dimensions of the recovery and evaluation scale; \*\*: <0.001, \* <0.05.

**Table 4.** Investigation of the mediating role of MSPSS total score in the effect of RAS total score on MMAS-4 score.

	MMAS-4		RAS total score	
	$\beta$	SH	$\beta$	SH
<b>RAS total</b>	-0.011**	0.005	0.447*	0.079
<b>R<sup>2</sup></b>	0.033	-	0.187	-
<b>RAS total score</b>	-0.010***	0.006	-	-
<b>MSPSS total score</b>	-0.002***	0.005	-	-
<b>R<sup>2</sup></b>	0.034	-	-	-
<b>Indirect effect</b>	-0.001 (-0.006; 0.005)***	-	-	-

\*: <0,001; \*\*: p<0,05; \*\*\*: p>0,050; Prediction (%95CI).

Data investigating the mediating role of RAS total points in the effect of MSPSS total points on treatment adherence points (MMAS-4) are given in Table 5. MSPSS total points positively affected RAS total points ( $\beta = 0.418$ ;  $p < 0.001$ ). When RAS total

points are investigated as mediating variables, the direct effect of MSPSS total points on treatment adherence points (MMAS-4) did not reach statistical significance ( $p > 0.050$ ), but its indirect effect was significant ( $p < 0.05$ ).



**Table 5.** Examination of the mediating role of RAS total score in the effect of MSPSS total score on treatment adherence score.

	MMAS-4		RAS total score	
	$\beta$	SH	$\beta$	SH
MSPSS total score	-0.006***	0.005	0.418*	0.074
R <sup>2</sup>	0.010	-	0.187	-
MSPSS total score	-0.002***	0.005	-	-
RAS total score	-0.010***	0.006	-	-
R <sup>2</sup>	0.034	-	-	-
Indirect effect	-0.004 (-0.011; 0.001)**		-	-

\*:  $p < 0,001$ ; \*\*:  $p < 0,05$ ; \*\*\*:  $p > 0,050$ ; Guess (%95CI).

## DISCUSSION AND CONCLUSION

The findings obtained because of the research were discussed considering the literature data. In this study, 5 diagnosis groups (psychotic disorder, mood disorder, anxiety disorder, substance abuse, personality disorder) were examined. Advanced analyses determined significant differences in adherence to treatment (MMAS-4) based on diagnosis and recovery level (RAS) based on sex ( $p < 0.05$ ). Similarly, in a study conducted with schizophrenia patients on the same subject, it was reported that individuals with high cognitive insight had low drug adherence.<sup>20</sup> Again, in a study in which 332 patients from 6 diagnostic categories (substance abuse disorders, schizophrenia, bipolar disorders, depressive disorders, anxiety disorders, and personality disorders) were followed, a significant negative relationship was found between self-stigma and adherence to treatment. It was determined that self-stigmatization was also positively related to the severity of the disorders and negatively related to adherence to treatment.<sup>21</sup> However, some studies in the literature found the opposite results. In a study conducted to examine the relationship between treatment adherence and hope levels of forensic psychiatry patients with violent behaviour, a highly significant positive relationship was found between the score and adherence to treatment for the sub-dimensions of the Herth hope scale “positive readiness and expectation”, “the bond between themselves and those around them” subscales, and total score ( $p < 0.001$ ).<sup>22</sup> Findings from this study and findings from studies in the literature show that treatment adherence may differ according to the severity of symptoms, diagnosis, and sex in participating patients.

In this study, 69.1% of psychiatric patients did not adhere to treatment (in varying numbers/levels (MMAS-4)). In a study, 50% of major depression patients stopped taking the prescribed antidepressants within 3 months. It was determined that 33% of schizophrenia patients were non-adherent, and the other third did not use any medication. In patients with bipolar disorder, adherence was measured as low as 35%.<sup>23</sup> In a study conducted to evaluate the

drug adherence rate in a group of schizophrenia patients, 68.8% of the patients were non-adherent to antipsychotic drugs, while 31.2% of them were adherent.<sup>1</sup> In a study conducted with patients with bipolar disorder, drug non-adherence rates ranged from 20% to 60%.<sup>7</sup> Contrary to these findings, for long-term psychiatric illnesses, individuals were found to take only about 50% of the prescribed drugs.<sup>24</sup> This study and studies in the literature show that most psychiatric patients have low adherence to treatment.

In this study, advanced analyses determined that perceived social support (MSPSS) affected treatment adherence (MMAS-4) indirectly ( $p < 0.05$ ). A study on the topic determined that only 21.5% of patients had good medication adherence, and there was a statistically significant correlation between perceived social support and medication adherence.<sup>6</sup> A study on the same topic found that the perceived social support of those complying with treatment significantly differed from those who did not comply with treatment ( $p < 0.05$ ). Those adhering to treatment took lower numbers of medications by a significant degree, remembered more efficiently, and experienced fewer psychiatric symptoms ( $p < 0.01$ ).<sup>1</sup> Again, in the literature, coping with disease and control beliefs related to health and social support were reported as positive indicators in schizophrenia patients.<sup>25</sup> A study conducted with 324 psychiatric patients found a significant positive correlation between MSPSS and treatment adherence ( $p < 0.05$ ).<sup>26</sup> These findings indicate that directly or indirectly perceived support measured with MSPSS affects treatment adherence.

In this study, the recovery levels (RAS) of patients were above average ( $85.2 \pm 20.8$ ), with the highest points for the ‘personal confidence and hope’ ( $31.7 \pm 8.5$ ) subdimension and lowest points for the ‘coping with symptoms’ ( $9.9 \pm 3.3$ ) subdimension. Most patients ( $n=70$ ) went to doctor’s appointments when they felt bad, and there was a significant negative correlation between RAS (recovery level) and treatment adherence (MMAS-4) ( $p < 0.05$ ). Advanced analyses found a negative effect of RAS total

points on treatment adherence ( $\beta=-0.011$ ;  $p<0.050$ ). A study using MMAS-4 determined that 39.35% of patients did not adhere to treatment, 42.3% of the patients not complying with treatment did not take medications at the correct dose and correct time, 35.3% did not pay attention, 29.3% stopped medication when they recovered, and 17.3% stopped medication when the disease worsened.<sup>5</sup> These findings show that the results of this study contrast with some studies in the literature.

An advanced degree of significant correlation was found between recovery level (RAS) and social support received from family and friends in MSPSS ( $p<0.01$ ). Advanced analyses found a positive effect of RAS total points on MSPSS points. A study performed over 12 months with psychiatric patients in Zurich investigated the possible effects of perceived social support on rehospitalisation rates and psychopathology and determined that lack of social support increased psychopathologic disorder and repeated hospitalisation ( $p<0.05$ ).<sup>27</sup> In a study conducted to determine the drug adherence of patients hospitalised in a psychiatry clinic and their relationship with social support, there was a statistically significant positive and weak relationship between friend support and drug adherence ( $p<0.001$ ).<sup>28</sup> Again, in a study conducted with 176 schizophrenic patients, both perceived social support subscales and total scores had statistically significant ( $\leq 0.001$ ) relationships with recovery.<sup>29</sup> These findings show that perceived social support is effective in the emotional recovery of patients.

In conclusion, personal confidence, hope, and willingness to ask for help were correlated with patients' treatment adherence (MMAS-4) and recovery level (RAS) was correlated with perceived social support, and each affected the other. Recovery was found to be affected by sex, while treatment adherence (MMAS-4) was affected by the diagnosis. Recovery level had a negative effect on treatment adherence, while perceived social support had a positive impact on recovery. In addition, the results of this study cannot be generalised since it was conducted only in a public hospital and was done by self-report, and these are the study's limitations.

**Ethics Committee Approval:** Before starting the study, institutional permission was obtained from Tokat Gaziosmanpaşa University, Faculty of Medicine, Dean's Office (Date: 28.08.2018, Decision No: 18-KAEK-192) and ethical approval for the study was obtained from the Ethics Committee of Tokat Gaziosmanpaşa University, Ethics Committee (Date: 05.12.2018, Decision No: 18-KAEK-192/626). The study was conducted following the Declaration of Helsinki.

**Conflict of Interest:** No conflict of interest was de-

clared by the authors.

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

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## Evaluation of Sleep Hygiene According to the Sociodemographic Characteristics of the Nurses

### Hemşirelerin Sosyodemografik Özelliklerine Göre Uyku Hijyeninin Değerlendirilmesi

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#### ABSTRACT

**Objective:** This study was conducted to determine the evaluation of sleep hygiene according to the sociodemographic characteristics of nurses.

**Materials and Methods:** This is a descriptive study. Permission was obtained from Hakkari University Scientific Research and Publication Ethics Committee for research permission. It was collected by 243 nurses who voluntarily participated in the study, using the online questionnaire method, sociodemographic data collection form and sleep hygiene index (SHI). The SPSS 26.0 data analysis program was used for the t-test and one-way analysis of variance (ANOVA).

**Results:** According to the sociodemographic characteristics of the nurses participating in the study, the average of the total sleep hygiene index scores in the evaluation of sleep hygiene was 34.68; When the averages of the 4th, 9th, 10th and 11th items were examined, it was determined that the results were generally "low level" and the averages of the other items were "medium".

**Conclusion:** It was determined that the sleep hygiene index scores of the nurses were "moderate". Organising training programs for nurses to increase sleep hygiene and quality (emphasising its physiological and spiritual importance) will help improve sleep hygiene and quality.

**Keywords:** Assessment, nurses, sociodemographic characteristics, sleep hygiene

#### ÖZ

**Amaç:** Bu çalışma, hemşirelerin sosyodemografik özelliklerine göre uyku hijyeninin değerlendirilmesini belirlemek amacıyla yapılmıştır.

**Materyal ve Metot:** Bu tanımlayıcı bir çalışmadır. Araştırma izni için Hakkari Üniversitesi Bilimsel Araştırma ve Yayın Etiği Kurulu'ndan izin alınmıştır. Araştırmaya gönüllü olarak katılan 243 hemşire tarafından online anket yöntemi, sosyodemografik veri toplama formu ve uyku hijyeni indeksi (SHI) kullanılarak toplanmıştır. İstatistiksel analizlerde SPSS 26.0 veri analiz programı ile t testi ve tek yönlü varyans analizi (ANOVA) kullanılmıştır.

**Bulgular:** Çalışmaya katılan hemşirelerin sosyodemografik özelliklerine göre uyku hijyeni değerlendirmesinde toplam uyku hijyeni indeksi puanlarının ortalaması 34,68; 4., 9., 10. ve 11. maddelerin ortalamaları incelendiğinde sonuçların genel olarak "düşük düzeyde", diğer maddelerin ortalamalarının ise "orta" olduğu belirlenmiştir.

**Sonuç:** Hemşirelerin uyku hijyen indeksi puanlarının "orta" olduğu belirlendi. Hemşirelere yönelik uyku hijyeni ve kalitesini artırmaya yönelik (fizyolojik ve ruhsal önemi vurgulayan) eğitim programları düzenlenmesi uyku hijyeni ve kalitesinin artmasına yardımcı olacaktır.

**Anahtar Kelimeler:** Değerlendirme, hemşireler, sosyodemografik özellikler, uyku hijyeni

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## INTRODUCTION

Sleep, one of the most fundamental needs of human beings, is at the bottom of the pyramid table called "Maslow's Hierarchy of Basic Needs."<sup>1</sup> Sleep affects the quality of life of all organisms, especially humans; It is an important basic need that affects physiological, psychological and social.<sup>2</sup> Sleep hygiene is important in ensuring sleep quality.<sup>3,4</sup> Sleep hygiene is the principles that increase the quality of sleep.<sup>5</sup> Sleep quality, on the other hand, is the practices and habits created for a good sleep regularly that support better sleep. The need for sleep hygiene and quality is affected by sociodemographic characteristics (education status and institution of employment) and environmental factors such as age, gender, illness, physical activity, emotional state, drugs, environment, alcohol, and other stimulants.<sup>6</sup> In the study of sleep quality according to sociodemographic characteristics (gender, marital status) conducted with nurses, it was shown that there was a positive relationship between sleep quality, hygiene and age and that single nurses had significant differences in sleep quality according to marital status, and showed better quality sleep compared to divorced or separated nurses.<sup>7</sup> Psychological status and sleep quality of nursing interns during the outbreak of COVID-19; It was stated that variables such as age and marital status level negatively affected the sleep quality of nurses and reflected on their quality of life. It was generally determined that nurses had problems such as waking up frequently during sleep, having nightmares, and turning over in bed.<sup>8</sup> Associations between the timing and nutritional characteristics of bedtime meals and sleep quality for nurses after a rotating night shift: a cross-sectional analysis study found a significant relationship between nurses' results regarding age, gender, marital status, educational status, and having a child, and their sleep quality.<sup>9</sup>

Is there a relationship between nurses' sociodemographic characteristics and sleep hygiene? Supported by research on the hypothesis. In the study of Siva et al.,<sup>10</sup> It was concluded that there is a relationship between sociodemographic information and sleep hygiene. Pathways between multiple sclerosis, sleep disorders, and cognitive function by Braley et al., longitudinal findings from The Nurses' Health Study reveal that employees generally sleep less than 8 hours and wake up frequently at night.<sup>11</sup> In the study of Simonetti et al., it was concluded that the nurses could not sleep due to their shifts and slept intermittently while on leave.<sup>12</sup>

This study aimed to evaluate the sleep hygiene of nurses according to their sociodemographic characteristics.

## MATERIALS AND METHODS

**Ethical Considerations:** The study was carried out by the Helsinki Declaration and approved by Hakkari University Scientific Research and Publication Ethics Committee (Date: 25.04.2022, decision no: IRB:2022/40-1), and written consent was obtained.

**Study Design:** The study was conducted as a descriptive study to evaluate nurses' sleep hygiene according to their sociodemographic characteristics.

**Research Questions:** Is there a significant difference in sleep hygiene of nurses according to sociodemographic characteristics (age, gender, marital status, education level, health institution)

**Place and Time of the Study:** It was collected between 25 April 2022 and 20 June 2022 on nurses who voluntarily participated in Hakkari and filled out the informed consent form using an online questionnaire (Google Form). A sociodemographic data form, sleep hygiene index, and an informed consent form created online in Google form were added, and the nurses participating in the study accepted and marked the informed consent form and their consent was obtained. It took an average of 5 minutes for the nurses participating in the study to answer the questions.

**Sample:** The research population was planned to be composed of nurses in Türkiye who voluntarily participated in the study between 25 April 2022 and 20 June 2022 and filled out the informed consent form. However, since it is nearly impossible to reach all nurses in Türkiye, the study was created online. An online survey (Google Forms) has been tried to be achieved through social networks and social media. The sample size in the study was calculated based on the number of variables used in multivariate data analysis. Since there were 13 statements in the questionnaire, it was aimed to reach 250 people. In this context, the research sample was selected from nurses working in Hakkari province, in the eastern region of Türkiye. The convenience sampling method included 243 nurses who participated voluntarily and met the conditions of participation.

### Variables of the Study

**Research Inclusion Criteria:** - Nurses who agreed to participate in the study voluntarily and nurses who filled out the informed consent form.

**Research Exclusion Criteria:** - Nurses who did not agree to participate in the study voluntarily and nurses who filled out the informed consent form.

**Data Collection Tools:** Research data were collected with the following data collection forms: 1- Sociodemographic data collection form; 2- Sleep Hygiene Index (SHI) was used.

**Sociodemographic Data Collection Form:** This form, which nurses will fill, consists of 5 questions

regarding gender, age, marital status, educational status, and the institution they work for.

**Sleep Hygiene Index (SHI):** UHI was developed as its Turkish validity and reliability performed by Güzel Özdemir et al. The questionnaire consists of 13 questions. The questions are on a 5-point Likert scale (none: 1, rarely: 2, sometimes: 3, often: 4, and always: 5). The scale enables the evaluation of sleep behaviours that constitute the sleep hygiene of the participants. Scores ranged from 13 to 65, with higher scores indicating poorer sleep hygiene in the participants. The Cronbach Alpha value of SHI was calculated as 0.70, which was valid and reliable.<sup>13</sup> In our study, the Cronbach Alpha value was 0.73.

**Statistical Analysis:** SPSS (Statistical Package for Social Sciences) 26.0 package program was used to analyse the data. T-test and one-way analysis of variance (ANOVA) was used in the study of sleep hygiene according to the sociodemographic characteristics of the nurses ( $p < 0,05$ ).

**RESULTS**

Regarding sociodemographic characteristics, of the nurses participating in the study, 56.8% were wom-

en. 58% are married. When the nurses are analysed according to age groups, 33.7% are 26-30 years old age group. Educational status is examined; 71.2% of them are undergraduates. When the data are analysed according to the health institutions they work in, 58% work in public hospitals (Table 1).

Mean Scores and Results of the Items in the Sleep Hygiene Index: In the sleep hygiene index of the study, the 2nd item, "The hours I go to bed changes from day to day" ( $\bar{x}=3.36\pm\sigma=1.04$ ), the 3rd item, "The time I get out of bed changes from day to day" ( $\bar{x}=2.95\pm\sigma=1.107$ ) and item 7 "Before bedtime, I do something that increases my alertness. (e.g., playing video games, using the internet or cleaning)" ( $\bar{x}=2.84\pm\sigma=1.223$ ) and the 4th item, which is the behaviour that nurses do most frequently and affects sleep hygiene the most, is "1 hour before going to bed. When the averages of the 4th, 9th, 10th and 11th items in the sleep hygiene index were examined, the results were found to be "low level" in general, and the averages of the other items and the average of the total sleep hygiene index scores were found to be "moderate" (Tablo 2).

**Table 1.** Findings related to sociodemographic characteristics.

		n (%)
<b>Gender</b>	Male	105 (43.2)
	Female	138 (56.8)
<b>Marital status</b>	Single	141 (58.0)
	Married	102 (42.0)
<b>Age Group</b>	20-25 age	29 (11.9)
	26-30 age	82 (33.7)
	31-35 age	51 (21.0)
	36-40 age	40 (16.5)
	41-45 age	30 (12.3)
	46-50 age	11 (4.6)
<b>Level of Education</b>	Undergraduate	173 (71.2)
	Associate degree	23 (9.5)
	Health High School	13 (5.3)
	Master's degree and above	34 (14.0)
<b>Employed Institution</b>	Public Hospital	141 (58.0)
	Private Hospital	60 (24.7)
	Other (family medicine etc.)	42 (17.3)
<b>Total</b>		243 (100.0)

**Table 2.** Mean scores and results of the items in the sleep hygiene index.

	Mean±SD	Result
1. I take a nap for two hours or more during the day.	2.67±1.167	Intermediate
2. The hours I go to bed vary from day to day.	3.36±1.04	Intermediate
3. The time I get out of bed varies from day to day.	2.95±1.107	Intermediate
4. Within 1 hour before going to bed, I exercise until I sweat.	2.1±1.079	Low level
5. I stay in bed longer than I should two or three times a week.	2.65±1.166	Intermediate
6. I use alcohol, tobacco or caffeine in the 4 hours before or after going to bed.	2.65±1.301	Intermediate
7. Before bedtime, I do something that increases my alertness. (e.g. playing video games, using the internet, or cleaning)	2.84±1.223	Intermediate
8. I get stressed, angry, sad, or nervous when I go to bed.	2.63±1.136	Intermediate
9. I use my bed for other things besides sleeping (for example, watching TV, reading, eating or studying)	2.6±1.176	Low level
10. I sleep in an uncomfortable bed. (For example, I have a bad mattress or pillow, too thick or thin duvet)	2.37±1.23	Low level

**Table 2.** Continue.

<b>11.I sleep in an uncomfortable bedroom (For example, it gets too much light, too stuffy, too hot, too cold, or too noisy)</b>	2.35±1.278	Low level
<b>12.Before I go to bed, I do important things that need my attention. (For example, paying bills, programming or working)</b>	2.65±1.15	Intermediate
<b>13.I think, plan, or worry while in bed.</b>	2.81±1.18	Intermediate
<b>Total Sleep Hygiene Index Scores</b>	34.63±7.81	Intermediate

Findings related to the evaluation of sleep hygiene according to the age variable, because of the analysis, it was found that there was a statistically significant difference between the averages of sleep hy-

giene index items 1, 4, 5, 10, 11, and 13 according to age groups ( $p < 0.05$ ). It was found that there was no difference between the means of the 2nd, 3rd, 6th, 7th, 8th, 9th, and 12th items ( $p > 0.05$ ) (Table 3).

**Table 3.** Findings regarding the evaluation of sleep hygiene by age variable.

Substances	n	Mean±SD	F	df	p	Difference	
<b>SHI-1</b>	20-25 age	29	2.07±1.25	3.338	5	0.006	20-25 years to 31-35 years old
	26-30 age	82	2.71±1.05				
	31-35 age	51	3.06±1.08				
	36-40 age	40	2.8±1.16				
	41-45 age	30	2.43±1.22				
	46-50 age	11	2.36±1.43				
	<b>Total</b>	243	2.67±1.17				
<b>SHI-2</b>	20-25 age	29	3.38±1.35	0.452	5	0.812	None
	26-30 age	82	3.35±1.02				
	31-35 age	51	3.39±1				
	36-40 age	40	3.38±0.95				
	41-45 age	30	3.43±1.01				
	46-50 age	11	2.91±0.94				
	<b>Total</b>	243	3.36±1.04				
<b>SHI-3</b>	20-25 age	29	3.07±1.19	1.889	5	0.097	None
	26-30 age	82	3.18±1.02				
	31-35 age	51	2.86±1.06				
	36-40 age	40	2.85±1.14				
	41-45 age	30	2.63±1.22				
	46-50 age	11	2.45±1.04				
	<b>Total</b>	243	2.95±1.11				
<b>SHI-4</b>	20-25 age	29	1.76±0.99	2.572	5	0.027	31 years. 36-40 years and 46-50 years
	26-30 age	82	2.05±1.06				
	31-35 age	51	2.41±1.17				
	36-40 age	40	2.28±1.09				
	41-45 age	30	2.03±1.03				
	46-50 age	11	1.45±0.52				
	<b>Total</b>	243	2.1±1.08				
<b>SHI-5</b>	20-25 age	29	3.17±1.54	2.653	5	0.023	20-25 years old. 36-40 years old. 41-45 years old and 46-50 years old
	26-30 age	82	2.72±1.13				
	31-35 age	51	2.75±1.13				
	36-40 age	40	2.33±1.07				
	41-45 age	30	2.47±0.97				
	46-50 age	11	2.09±0.83				
	<b>Total</b>	243	2.65±1.17				
<b>SHI-6</b>	20-25 age	29	2.86±1.51	0.884	5	0.492	None
	26-30 age	82	2.68±1.28				
	31-35 age	51	2.8±1.33				
	36-40 age	40	2.33±1.16				
	41-45 age	30	2.5±1.25				
	46-50 age	11	2.64±1.43				
	<b>Total</b>	243	2.65±1.3				

Table 3. Continue.

<b>SHI-7</b>	20-25 age	29	2.97±1.4	0.604	5	0.697	None
	26-30 age	82	2.96±1.16				
	31-35 age	51	2.84±1.24				
	36-40 age	40	2.78±1.25				
	41-45 age	30	2.6±1.07				
	46-50 age	11	2.55±1.51				
<b>Total</b>	243	2.84±1.22					
<b>SHI-8</b>	20-25 age	29	2.66±1.08	1.309	5	0.261	None
	26-30 age	82	2.79±1.18				
	31-35 age	51	2.67±1.26				
	36-40 age	40	2.65±0.89				
	41-45 age	30	2.23±1.01				
	46-50 age	11	2.27±1.35				
<b>Total</b>	243	2.63±1.14					
<b>SHI-9</b>	20-25 age	29	2.93±1.28	1.569	5	0.170	None
	26-30 age	82	2.73±1.16				
	31-35 age	51	2.59±1.12				
	36-40 age	40	2.45±1.32				
	41-45 age	30	2.23±0.97				
	46-50 age	11	2.27±1.1				
<b>Total</b>	243	2.6±1.18					
<b>SHI-10</b>	20-25 age	29	1.55±0.69	3.883	5	0.002	20-25 years old. 26.30 years old. 31-35 years old. 36-40 years old
	26-30 age	82	2.45±1.27				
	31-35 age	51	2.67±1.18				
	36-40 age	40	2.53±1.24				
	41-45 age	30	2.37±1.27				
	46-50 age	11	1.91±1.38				
<b>Total</b>	243	2.37±1.23					
<b>SHI-11</b>	20-25 age	29	1.79±0.98	4.212	5	0.001	20-25 years old. 31-35 years old. 36-40 years old
	26-30 age	82	2.27±1.19				
	31-35 age	51	2.59±1.25				
	36-40 age	40	2.73±1.41				
	41-45 age	30	2.57±1.45				
	46-50 age	11	1.27±0.65				
<b>Total</b>	243	2.35±1.28					
<b>SHI-12</b>	20-25 age	29	2.62±1.42	1.019	5	0.407	None
	26-30 age	82	2.62±1.06				
	31-35 age	51	2.84±1.17				
	36-40 age	40	2.65±1.19				
	41-45 age	30	2.7±1.06				
	46-50 age	11	2±0.89				
<b>Total</b>	243	2.65±1.15					
<b>SHI-13</b>	20-25 age	29	3.17±1.23	2.391	5	0.039	20-25 years. 36-40 years. 46-50 years
	26-30 age	82	2.89±1.18				
	31-35 age	51	2.84±1.24				
	36-40 age	40	2.4±0.84				
	41-45 age	30	2.97±1.35				
	46-50 age	11	2.18±0.98				
<b>Total</b>	243	2.81±1.18					

F: One-way ANOVA test ( $p < 0.05$ ); SHI: Sleep Hygiene Index.

Findings related to the evaluation of sleep hygiene according to the gender and marital status variable, as a result of the analysis of the sleep hygiene index scores according to the gender of the nurses, it was determined that there was no statistically significant difference between the averages of the 1st, 2nd, 3rd, 5th, 6th, 7th, 8th, 12th, and 13th items according to the gender ( $p > 0.05$ ). It was found that men's sleep hygiene scores were higher in items 4, 9, 10, and 11 according to their gender, and their averages differed

( $p < 0.05$ ); item 4, "I exercise until I sweat within 1 hour before I go to bed" ( $t = 2.879$ ;  $p < 0.05$ ). As a result of the analysis, there was no statistically significant difference between the averages of the 1st, 2nd, 3rd, 4th, 5th, 7th, 8th, 10th, 11th, 12th, and 13th items according to marital status ( $p > 0.05$ ). It was found that singles had high sleep hygiene scores, and their averages were different ( $t = 2.001$ ;  $p < 0.05$ ;  $t = 2.672$ ;  $p < 0.05$ ) (Table 4).



**Table 4.** Findings related to the evaluation of sleep hygiene according to the gender and marital status variable.

Substances		n	Mean±SD	F	df	p
SHI-1	Male	105	2.79±1.14	1.397	241	0.164
	Female	138	2.58±1.18			
SHI-2	Male	105	3.33±1.06	-0.322	241	0.748
	Female	138	3.38±1.03			
SHI-3	Male	105	2.98±1.14	0.423	241	0.673
	Female	138	2.92±1.08			
SHI-4	Male	105	2.32±1.01	2.879	241	0.004
	Female	138	1.93±1.1			
SHI-5	Male	105	2.6±1.22	-0.633	241	0.528
	Female	138	2.7±1.12			
SHI-6	Male	105	2.79±1.32	1.513	241	0.132
	Female	138	2.54±1.28			
SHI-7	Male	105	2.96±1.17	1.317	241	0.189
	Female	138	2.75±1.26			
SHI-8	Male	105	2.71±1.26	0.964	241	0.336
	Female	138	2.57±1.03			
SHI-9	Male	105	2.83±1.22	2.717	241	0.007
	Female	138	2.42±1.11			
SHI-10	Male	105	2.58±1.27	2.396	241	0.017
	Female	138	2.2±1.18			
SHI-11	Male	105	2.57±1.3	2.427	241	0.016
	Female	138	2.17±1.24			
SHI-12	Male	105	2.63±1.11	-0.304	241	0.761
	Female	138	2.67±1.18			
SHI-13	Male	105	2.66±1.14	-1.776	241	0.077
	Female	138	2.93±1.2			
SHI-1	Single	141	2.76±1.121	1.386	241	0.167
	Married	102	2.55±1.224			
SHI-2	Single	141	3.2±1.057	2.850	241	0.005
	Married	102	3.58±0.979			
SHI-3.	Single	141	2.93±1.033	0.288	241	0.774
	Married	102	2.97±1.206			
SHI-4	Single	141	2.19±1.028	1.580	241	0.115
	Married	102	1.97±1.138			
SHI-5	Single	141	2.71±1.192	0.863	241	0.389
	Married	102	2.58±1.13			
SHI-6	Single	141	2.79±1.292	2.001	241	0.047
	Married	102	2.45±1.295			
SHI-7	Single	141	2.82±1.249	0.313	241	0.755
	Married	102	2.87±1.191			
SHI-8	Single	141	2.7±1.157	1.104	241	0.271
	Married	102	2.54±1.105			
SHI-9.	Single	141	2.77±1.163	2.672	241	0.008
	Married	102	2.36±1.159			
SHI-10	Single	141	2.36±1.117	0.068	241	0.946
	Married	102	2.37±1.378			
SHI11.	Single	141	2.29±1.174	0.787	241	0.432
	Married	102	2.42±1.41			
SHI-12	Single	141	2.76±1.121	1.675	241	0.095
	Married	102	2.51±1.175			
SHI-13	Single	141	2.82±1.169	0.076	241	0.940
	Married	102	2.8±1.203			

F: Independent groups t-test (p&lt;0.05); SHI: Sleep Hygiene Index.

Findings on the evaluation of sleep hygiene according to the variable of educational status because of the analysis, it was found that there was a statistically significant difference between the averages of the 10th and 13th items of the sleep hygiene index according to the education level of the nurses ( $p < 0.05$ ). At the same time, there was no difference between the other items ( $p > 0.05$ ), Findings regarding the

evaluation of sleep hygiene according to the institution of employment variable. It was found that there was a statistically significant difference between the averages of sleep hygiene index items 10 and 11 according to the variable of the institution where the nurses worked ( $p < 0.05$ ). Still, there was no difference between the other items ( $p > 0.05$ ) (Table 5).

**Table 5.** Findings on the evaluation of sleep hygiene according to the variable of educational status and institution of employment.

Substances	n	Mean±SD	F	df	p	Difference	
<b>SHI-1</b>	Undergraduate	173	2.76±1.16	1.488	3	0.218	None
	Associate Degree	23	2.39±1.23				
	Health High School	13	2.77±1.24				
	Master and above	34	2.38±1.13				
	<b>Total</b>	243	2.67±1.17				
<b>SHI-2</b>	Undergraduate	173	3.42±1.02	0.943	3	0.420	None
	Associate Degree	23	3.13±1.06				
	Health High School	13	3.08±1.38				
	Master and above	34	3.29±1				
	<b>Total</b>	243	3.36±1.04				
<b>SHI-3</b>	Undergraduate	173	2.97±1.12	0.131	3	0.942	None
	Associate Degree	23	2.83±0.98				
	Health High School	13	2.92±1.26				
	Master and above	34	2.91±1.08				
	<b>Total</b>	243	2.95±1.11				
<b>SHI-4</b>	Undergraduate	173	2.1±1.12	1.978	3	0.118	None
	Associate Degree	23	2.52±1.08				
	Health High School	13	2±0.91				
	Master and above	34	1.82±0.87				
	<b>Total</b>	243	2.1±1.08				
<b>SHI-5</b>	Undergraduate	173	2.59±1.17	1.353	3	0.258	None
	Associate Degree	23	2.57±0.95				
	Health High School	13	3.15±1.21				
	Master and above	34	2.85±1.23				
	<b>Total</b>	243	2.65±1.17				
<b>SHI-6</b>	Undergraduate	173	2.64±1.3	0.446	3	0.720	None
	Associate Degree	23	2.48±1.2				
	Health High School	13	3±1.15				
	Master and above	34	2.65±1.43				
	<b>Total</b>	243	2.65±1.3				
<b>SHI-7</b>	Undergraduate	173	2.92±1.25	1.353	3	0.258	None
	Associate Degree	23	2.87±1.1				
	Health High School	13	2.31±0.95				
	Master and above	34	2.65±1.25				
	<b>Total</b>	243	2.84±1.22				
<b>SHI-8</b>	Undergraduate	173	2.7±1.16	0.768	3	0.513	None
	Associate Degree	23	2.48±0.99				
	Health High School	13	2.62±1.33				
	Master and above	34	2.41±1.05				
	<b>Total</b>	243	2.63±1.14				
<b>SHI-9</b>	Undergraduate	173	2.68±1.2	1.152	3	0.329	None
	Associate Degree	23	2.43±0.95				
	Health High School	13	2.23±1.09				
	Master and above	34	2.41±1.18				
	<b>Total</b>	243	2.6±1.18				
<b>SHI-10</b>	Undergraduate	173	2.45±1.24	2.985	3	0.032	Undergraduate and postgraduate and above
	Associate Degree	23	2.57±1.16				
	Health High School	13	2.46±1.05				
	Master and above	34	1.79±1.17				
	<b>Total</b>	243	2.37±1.23				
<b>SHI-11</b>	Undergraduate	173	2.4±1.31	1.201	3	0.310	None
	Associate Degree	23	2.35±1.19				
	Health High School	13	2.54±1.13				
	Master and above	34	1.97±1.19				
	<b>Total</b>	243	2.35±1.28				

Table 5. Continue.

<b>SHI-12</b>	Undergraduate	173	2.58±1.17	0.918	3	0.433	None
	Associate Degree	23	2.78±0.95				
	Health High School	13	2.85±1.07				
	Master and above	34	2.88±1.2				
	<b>Total</b>	243	2.65±1.15				
<b>SHI-13</b>	Undergraduate	173	2.73±1.16	3.084	3	0.028	Undergraduate and postgraduate and above
	Associate Degree	23	2.52±1.31				
	Health High School	13	3.15±1.21				
	Master and above	34	3.29±1.09				
	<b>Total</b>	243	2.81±1.18				
<b>SHI-1</b>	Public Hospital	141	2.68±1.17	1.109	2	0.331	None
	Other (family medicine etc.)	42	2.45±1.17				
	Private Hospital	60	2.8±1.15				
	<b>Total</b>	243	2.67±1.17				
	<b>SHI-2</b>	Public Hospital	141	3.4±1.07	0.432	2	0.650
Other (family medicine etc.)		42	3.38±0.99				
Private Hospital		60	3.25±1.02				
<b>Total</b>		243	3.36±1.04				
<b>SHI-3</b>		Public Hospital	141	3±1.08	0.919	2	0.400
	Other (family medicine etc.)	42	2.74±1.29				
	Private Hospital	60	2.97±1.02				
	<b>Total</b>	243	2.95±1.11				
	<b>SHI-4</b>	Public Hospital	141	1.97±1.07	11.27	2	0.000
Other (family medicine etc.)		42	1.76±0.98	6			
Private Hospital		60	2.63±0.99				
<b>Total</b>		243	2.1±1.08				
<b>SHI-5</b>		Public Hospital	141	2.69±1.16	0.142	2	0.868
	Other (family medicine etc.)	42	2.62±1.19				
	Private Hospital	60	2.6±1.18				
	<b>Total</b>	243	2.65±1.17				
	<b>SHI-6</b>	Public Hospital	141	2.6±1.33	0.565	2	0.569
Other (family medicine etc.)		42	2.57±1.4				
Private Hospital		60	2.8±1.16				
<b>Total</b>		243	2.65±1.3				
<b>SHI-7</b>		Public Hospital	141	2.82±1.25	0.228	2	0.797
	Other (family medicine etc.)	42	2.79±1.32				
	Private Hospital	60	2.93±1.1				
	<b>Total</b>	243	2.84±1.22				
	<b>SHI-8</b>	Public Hospital	141	2.6±1.1	0.718	2	0.489
Other (family medicine etc.)		42	2.55±1.29				
Private Hospital		60	2.78±1.12				
<b>Total</b>		243	2.63±1.14				
<b>SHI-9</b>		Public Hospital	141	2.52±1.19	1.399	2	0.249
	Other (family medicine etc.)	42	2.52±1.11				
	Private Hospital	60	2.82±1.17				
	<b>Total</b>	243	2.6±1.18				
	<b>SHI-10</b>	Public Hospital	141	2.3±1.25	4.372	2	0.014
Other (family medicine etc.)		42	2.05±1.21				
Private Hospital		60	2.73±1.13				Private Hospital
<b>Total</b>		243	2.37±1.23				
<b>SHI-11</b>		Public Hospital	141	2.16±1.26	4.593	2	0.011
	Other (family medicine etc.)	42	2.38±1.34				
	Private Hospital	60	2.75±1.19				
	<b>Total</b>	243	2.35±1.28				
	<b>SHI-12</b>	Public Hospital	141	2.52±1.17	2.936	2	0.055
Other (family medicine etc.)		42	2.67±1.18				
Private Hospital		60	2.95±1.03				
<b>Total</b>		243	2.65±1.15				
<b>SHI-13</b>		Public Hospital	141	2.8±1.11	2.271	2	0.105
	Other (family medicine etc.)	42	3.12±1.31				
	Private Hospital	60	2.62±1.22				
	<b>Total</b>	243	2.81±1.18				

F: Independent groups t-test (p<0.05); SHI: Sleep Hygiene Index.

## DISCUSSION AND CONCLUSION

Evaluation of sleep hygiene in nurses according to their sociodemographic characteristics (age, gender, marital status, educational status, health institution) is vital in terms of sleep quality. When the averages of our research findings and the total sleep hygiene index scores were examined, it was concluded that it was at a moderate level. When the literature is reviewed, it is seen that there are a limited number of studies examining the evaluation of sleep hygiene according to the sociodemographic characteristics (age, institution of employment and economical situation) of nurses. The results of the study titled The Effect of the stress response, physical activity, and sleep hygiene on sleep quality<sup>14</sup> of nurses working in Shifts and the study titled The Role of sleep hygiene in the Risk of Shift Work Disorder in Nurses are like our findings. In the study conducted by Sun et al. on sleep problems of nurses during work shifts, they stated that nurses were sleepless at work and their sleep quality was moderate or poor.<sup>15</sup> The effect of the nurse-oriented sleep hygiene protocol on sleep quality is in parallel with the total sleep hygiene result found in our research results, in which the effect of sleep problems was determined, and sleep hygiene was poor.<sup>16</sup>

Findings related to the evaluation of sleep hygiene according to the age variable of nurses Park et al. investigated the relationship between nurses' sleep quality and job performance, and it was determined that the nurses were in favour as their average age increased.<sup>17</sup> The results of the study conducted by Karakaş et al. on sleep problems and influential factors in nurses are similar.<sup>18</sup> The fact that sleep hygiene is better with increasing age may be related to the increase in the nurses' compliance as the working years increase or the fact that the nurses whose working years increase are removed from the night shift and work only during the day.

Results on the evaluation of sleep hygiene of nurses according to gender variable in the study of Çetinel and Özurmaz,<sup>19</sup> comparing the sleep-related characteristics of shift and non-shift nurses, it was determined that male nurses had higher sleep quality. In another study, Ferri et al.'s results on the psychological dimension of shift work on nurses, in which male nurses do active activities before bed and have a high sleep quality are compatible with our findings.<sup>20</sup> Findings related to sleep hygiene according to the marital status variable of nurses In the study conducted by Kaçan et al., examining the sleep quality of nurses is consistent with the results that single people have higher sleep quality.<sup>21</sup> In the study of Şentürk et al., investigating the relationship between the burnout levels of intensive care nurses and sleep quality, it was found that married people had sleep problems.<sup>22</sup> According to the marital status of the

nurses, it was concluded that single nurses had fewer sleep problems than married nurses.

Results on the evaluation of sleep hygiene according to the variable of education status of nurses The results of Toros's study on the working (Including 28 nurses working in 16- and 24-hour shifts) conditions of night nurses are similar.<sup>23</sup> A hospital cross-sectional study by Giorgi et al.<sup>24</sup> (It consisted of 315 nurses working in shifts in 39 hospital services) according to the results of Giorgi et al.'s study, it was concluded that the unique characteristics of nurses working in shifts could affect sleep quality and burn-out directly or indirectly on work performance.

In the study, it was determined that there was a difference between the sleeping levels in an uncomfortable bed between those working in other (family medicine, dispensaries, etc.) institutions compared to those working in private hospitals. Psychometric analysis of the Chinese version of the Sleep Hygiene Index in nursing students in China: in a cross-sectional study, volunteer student nurses stated that they were more tired and sleepless and had a higher workload in private hospitals.<sup>25</sup> According to the study titled The Relationships Between Cortisol, Sleep, Stress and Mood in Night Shift Nurses, nurses working in government institutions are more comfortable and have no sleep problems. Still, nurses working in private institutions are more tired.<sup>26</sup> Poor Sleep Quality in Nurses Working and Past Night Shift: A Cross-sectional Study Results revealed in our findings that those who have the most sleep hygiene problems are those who work in private hospitals, and those who have minor sleep hygiene problems are family medicine, dispensaries, etc. This is consistent with the results that employees in organisations provide health services.<sup>27</sup>

In conclusion, this study does not reflect the general nurses in our country and is limited to the nurses who participated in the study voluntarily. In this study, there is a relationship between the sociodemographic characteristics of nurses and sleep hygiene and quality; It was determined that more than half of the nurses had low sleep quality and sleep hygiene index scores were generally "moderate". These results show that nurses typically have problems with sleep hygiene. Studies on evaluating the sleep hygiene of nurses in Türkiye are insufficient. In this study, it is important to assess sleep hygiene in terms of the sociodemographic characteristics of nurses and will guide similar studies in the future. Organising training programs for nurses to increase sleep hygiene and quality, emphasising sleep's physiological and spiritual importance will help increase sleep hygiene and quality.

**Ethics Committee Approval:** The study was carried out by the Helsinki Declaration and approved by

Hakkari University Scientific Research and Publication Ethics Committee (Date: 25.04.2022, decision no: IRB:2022/40-1), and written consent was obtained.

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

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

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## Mental Health of COVID-19 Pandemic from Pregnancy to Postpartum Period: A Longitudinal Study

### COVID-19 Pandemisinde Gebelikten Doğum Sonrasına Ruh Sağlığı: Boylamsal Bir Çalışma

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#### ABSTRACT

**Objective:** This study aimed to determine the effect of stress levels of prenatally diagnosed or contacted pregnant women on anxiety and depression symptoms in the postpartum period and compare them with those who had a healthy pregnancy period.

**Materials and Methods:** This internet-based longitudinal study was conducted with pregnant women with COVID-19(+) (n=91), contact with COVID-19(+) (n=74), and healthy pregnant women (n=220).

**Results:** Severe anxiety was found in 51.4% of COVID-19(+) pregnant women, and depression was found in 28.7%. NuPDQ and BAI mean scores of positive pregnant women were higher than contact and healthy pregnant women. When the EPDS score averages were compared, it was determined that the postpartum period mean scores of those who were positive during pregnancy and were in contact were higher than those of healthy pregnant women. There is a positive correlation between the psychological effects of pregnant women from COVID-19 and social isolation and NuPDQ (r=0.316, r=0.279), BAI (r=0.337, r=0.293) and EPDS (r=0.333, r=0.311) respectively relationship was determined.

**Conclusion:** Our results point to the need to provide urgent psychosocial support in the postpartum period to women who were diagnosed and/or had contact with COVID-19 during pregnancy.

**Keywords:** Anxiety, COVID-19, depression, pregnancy, stress

#### ÖZ

**Amaç:** Bu çalışmanın amacı, prenatal dönemde COVID-19 tanısı konmuş veya temaslı gebelerin stres düzeylerinin postpartum dönemdeki anksiyete ve depresyon semptomlarına etkisini belirleyerek, gebelik sürecini sağlıklı geçirenlerle karşılaştırmaktır.

**Materyal ve Metot:** İnternet tabanlı longitudinal tipte olan bu çalışma, COVID-19 (+) gebeler (n=91), COVID-19 (+) ile temaslı gebeler (n=74) ve sağlıklı gebelerle (n=220) yürütüldü.

**Bulgular:** COVID-19 (+) gebelerin %51,4'ünde şiddetli düzeyde anksiyete, %28,7'sinde depresyon varlığı belirlendi. Pozitif gebelerin NuPDQ ve BAI puan ortalamalarının temaslı ve sağlıklı gebelerden daha yüksek olduğu saptandı. EPDS puan ortalamaları karşılaştırıldığında, gebeliğinde pozitif ve temaslı olanların postpartum dönem puan ortalamalarının sağlıklı gebelerden daha yüksek olduğu belirlendi. Gebelerin COVID-19'dan ve sosyal izolasyondan psikolojik etkilenimleri ile NuPDQ (sırasıyla r=0,316, r=0,279), BAI (sırasıyla r=0,337, r=0,293) ve EPDS (sırasıyla r=0,333, r=0,311) arasında pozitif yönde ilişki olduğu belirlendi.

**Sonuç:** Sonuçlarımız, gebelik süresince COVID-19 tanısı almış ve/veya temaslı olmuş kadınlara postpartum dönemde acil psikososyal destek sağlama ihtiyacına işaret ediyor.

**Anahtar Kelimeler:** Anksiyete, COVID-19, gebelik, depresyon, stres

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## INTRODUCTION

COVID-19 has negatively affected individuals all over the world. While its physical effects cause destructive consequences in humans, it can also cause severe problems in mental health.<sup>2,3</sup> However, studies mainly focus on the physical effects of the COVID-19 pandemic. Therefore, the data on its effects on mental health are insufficient.<sup>4</sup> Several psychiatric diseases, such as depression, anxiety, panic attacks, psychotic symptoms and even suicide, can be observed in individuals during the pandemic. One study of COVID-19 reports that individuals have depression, anxiety and stress due to moderate or severe psychological changes due to the pandemic.<sup>5</sup> Pregnancy is a sensitive period in which psychological distress can negatively affect both mother and baby.<sup>6</sup> A pregnancy experiencing uncertainty during the COVID-19 pandemic can cause stress, anxiety and even depression in pregnant women, adversely affecting their psychosocial health.<sup>7,8</sup> Constant and high levels of prenatal stress, anxiety, and depression symptoms increase the risk of postpartum depression as well as the rates of prenatal infection and illness.<sup>7,8</sup> Prenatal stress, anxiety, and depression can cause miscarriage, premature birth, low birth weight, fetal motor inactivity, and cognitive development problems.<sup>9,10</sup> Therefore, mental health problems are as important as physical health problems in pregnant women, and they should not be ignored during the COVID-19 pandemic.<sup>11</sup>

Due to the potential negative psychological sequelae of psychological, health and financial uncertainty and social isolation, it is important to determine the prevalence of psychological problems in pregnant women during this pandemic to activate early intervention methods and implement evidence-based practices. For this reason, it is argued that evaluating and addressing the current mental health symptoms of pregnant women during the pandemic will support the improvement of fetus and newborn health. In addition, identifying risk factors for the diagnosis and prevention of prenatal distress in pregnant women is extremely important in terms of mother-baby health, pregnancy and postpartum period. This study aimed to determine the level of stress, anxiety and depression symptoms in pregnant women diagnosed with COVID-19 or contacted with someone who had a confirmed case of COVID-19 and to compare them with healthy pregnant women.

## MATERIALS AND METHODS

**Ethical Status:** Before starting the study, ethical approval was obtained from the Non-Invasive Clinical Research and Publication Ethics Committee (Date: 01.05.2021, decision no: 2020/1358) and written permission from the provincial health direc-

torate (Number: E-13389845-799). In addition, COVID-19 scientific research permission was received from the Republic of Türkiye Ministry of Health (Form Code: 2020-12-03T23\_59\_27).

**Research Population and Sampling:** This study is an internet-based longitudinal study. Study data were collected between December 2021 and May 2022. The first part of the study data was done by retrospectively examining the records of the health directorate in the province. Women in their trimesters were included in the study. According to the polymerase chain reaction (PCR) test, (1) pregnant women with COVID-19 (+), (2) pregnant women who were in contact with COVID-19 (+), and (3) healthy pregnant women in the records of the directorate were included in the sample.

The study examined nine months of COVID-19 records from March to December 2021. According to the records of the health directorate, it was determined that 105 pregnant women were in contact with COVID-19 (+), 96 pregnant women were in contact with COVID-19 (+), and 270 healthy pregnant women (n=471). This work was completed in two stages. The first stage was applied in the prenatal period, and the second stage was applied in the first 6 months postpartum. In this study, all pregnant women who were COVID (+) at the data collection date and in contact with COVID (+) were taken. Randomisation was not performed because all pregnant women were included in the study. The women were invited to fill out a web-based questionnaire. Research questionnaires were developed using the Google Forms app (<https://docs.google.com/forms>), and links to the questionnaires were sent to women via WhatsApp. The study was completed with the prenatal and postpartum results of 385 women. (Figure 1).

**Measures:** The questionnaire administered during the prenatal period consisted of three parts, where first part included questions about sociodemographic and obstetric characteristics, the second part included questions about knowledge and attitudes about COVID-19, and the third part included the Revised Prenatal Distress Questionnaire (NuPDQ) and Beck Anxiety Inventory (BAI). The Edinburgh Postpartum Depression Scale (EPDS) was included in the questionnaire administered to the women in the postpartum period. Information about the study was given on the first page of both online questionnaires.

**The first part of the questionnaire:** This part included questions about the pregnant women's sociodemographic and obstetric characteristics such as age, education level, employment status, income level, number of pregnancies, and gestational week.

**The second part of the questionnaire:** This part was created by the researchers based on previous stud-



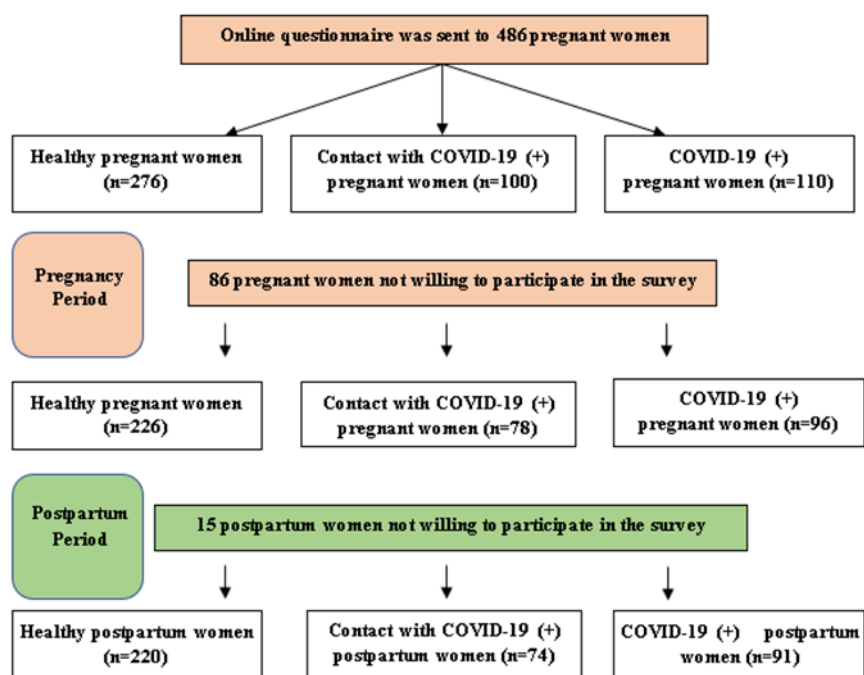


Figure 1. Definition of participation process by flow-chart.

ies.<sup>5,12</sup> Pregnant women were asked the following statements/questions about COVID-19: “Do you think that the COVID-19 pandemic can affect your pregnancy process?” and “Do you think that COVID-19 pandemic can affect your baby's health?”. They answered these questions as "yes or no".

Pregnant women answered other questions by scoring from 0 to 10. These questions are:

- Please describe the level of knowledge about the COVID-19 pandemic: 0= “I have no idea,” 10 = “My knowledge is perfect.”
- Do you think the COVID-19 pandemic has affected your psychological health?: 0 = “no,” 10 = “absolutely”
- Do you think that the social isolation due to the pandemic has affected your psychological health: 0 = “no,” 10 = “absolutely”

**The third part of the questionnaire:** NuPDQ, BAI and EPDS

**NuPDQ:** The 17-item NuPDQ, revised by Lobel et al. (2008), determines the pregnant women’s social relationships, physical and emotional symptoms, and anxiety levels about themselves and their babies during pregnancy. The Turkish validity and reliability study of the scale was conducted by Yüksel and Durna (2011), where the Cronbach's alpha internal consistency coefficient was determined as 0.85. The lowest and highest scale scores are 0 and 34, respectively. A higher score indicates a higher level of prenatal distress perceived by pregnant women. The

scale does not have a cut-off score.<sup>13,14</sup> In this study, the Cronbach's alpha internal consistency coefficient of the scale was found as 0.88.

**BAI:** The scale was adapted to Turkish by Ulusoy et al. (1998) and is used to determine the level of anxiety experienced by individuals. The scale consists of 21 items in total. The lowest and highest scale scores are 0 and 63, respectively. BAI scores are classified as minimal (0-7), mild anxiety (8-15), moderate anxiety (16-25), and severe anxiety (26-63). The Cronbach's alpha internal consistency coefficient of the scale was found as 0.93.<sup>15</sup> In this study, the Cronbach's alpha internal consistency coefficient was determined as 0.93.

**EPDS:** The Turkish validity and reliability study of the scale, which is used to screen depressive symptoms in individuals, was performed by Engindeniz et al. (1996). The Cronbach's alpha internal consistency coefficient of the scale was found as 0.79. The EPDS consists of 10 items in total. This is a 4-point Likert-type scale, scoring from 0 (none) to 3 (severe). The lowest and highest scale scores are 0 and 30, respectively. A higher total score indicates a higher risk for depression. The cut-off score on the scale is 12. A score of 12 and above is considered a risk for depression.<sup>16</sup> In this study, the Cronbach's alpha internal consistency coefficient of the scale was found as 0.85.

**Data Analysis:** The data were analysed using the Statistical Package for the Social Sciences 25.0 for Windows (SPSS, Chicago, IL, USA). The chi-square

test was used to compare categorical independent variables, and a one-way analysis of variance was used to compare continuous independent variables. Tukey test was used to determine the difference between groups. Independent samples-t test was used to analyse the data that met the parametric conditions, and the Mann-Whitney-U test to analyse the data that did not meet the parametric conditions. Pearson correlation analysis was used to analyse the relationship between the psychological effects of the

COVID-19 pandemic and social isolation on pregnant women and their NuPDQ, BAI, and EPDS mean scores.

**RESULTS**

There was no statistically significant difference between groups according to age, education level, employment status, number of pregnancies, number of children, gestational week, and presence of chronic disease ( $p>0.05$ ) (Table 1).

**Table 1.** Compares the sociodemographic and obstetric characteristics of pregnant women.

Variables	Healthy (n=220)	Contact with COVID-19 (+) (n=74)	COVID-19 (+) (n=91)	X <sup>2</sup> and p-value	
	n (%)	n (%)	n (%)		
Age (Mean ± SD)	30.33±5.36	28.96±4.68	30.02±5.14	-	
Age	18-27	69 (52.7)	31(23.7)	31 (23.7)	$\chi^2=7.332$ p=0.119
	28-34	100 (55.9)	36 (20.1)	43 (24.0)	
	≥ 35	51 (68.0)	7 (9.3)	17 (22.7)	
Education level	Primary school	17 (42.2)	7 (19.4)	12 (33.3)	$\chi^2=7.034$ p=0.134
	High school	89 (58.9)	35 (23.2)	27 (17.9)	
	University	114 (57.6)	32 (16.2)	52 (26.3)	
Employment status	Employed	66 (50.4)	28 (21.4)	37 (28.2)	$\chi^2=3.851$ p=0.146
	Unemployed	154 (60.6)	46 (18.1)	54 (21.3)	
Number of pregnancies	Primigravid	68 (52.3)	29 (22.3)	33 (25.4)	$\chi^2=2.030$ p=0.362
	Multigravid	152 (59.6)	45 (17.6)	58 (22.7)	
Number of children	1	84 (58.7)	29 (20.3)	30 (21.0)	$\chi^2=1.488$ p=0.829
	2	42 (53.8)	14 (17.9)	22 (28.2)	
	≥ 3	94 (57.3)	31 (18.9)	39 (23.8)	
Trimester	1. trimester	62 (68.1)	17 (18.7)	12 (13.2)	$\chi^2=9.266$ p=0.055
	2. trimester	105 (56.1)	34 (18.2)	48 (25.7)	
	3. trimester	53 (49.5)	23 (21.5)	31 (29.0)	
Presence of chronic disease	Yes	16 (47.1)	9 (26.5)	9 (26.5)	$\chi^2=1.810$ p=0.405
	No	204 (58.1)	65 (18.5)	82 (23.4)	

Table 2 compares the knowledge and attitudes of pregnant women regarding stress, anxiety, depression and COVID-19. Accordingly, 32.1% of the pregnant women diagnosed with COVID-19 reported that COVID-19 affected their pregnancy, while 34.2% reported that it affected their baby. On the other hand, 61.4% of the healthy pregnant women considered that COVID-19 did not affect their pregnancy, while 64.5% considered that it did not affect their baby ( $p<0.05$ ). In addition, 60.6% of the healthy pregnant women had mild anxiety, 29.0% of the pregnant women who contacted a person with confirmed COVID-19 also had moderate anxiety, and 51.4% of the pregnant women diagnosed with COVID-19 had severe anxiety ( $p<0.001$ ). While there was no depression in 67.8% of the healthy pregnant women, 27.5% of the pregnant women who contacted a person with confirmed COVID-19,

and 28.7% of the pregnant women diagnosed with COVID-19 had depression ( $p<0.001$ ). The pregnant women diagnosed with COVID-19 had higher BAI and NuPDQ mean scores than both those who contacted a person with confirmed COVID-19 and healthy pregnant women ( $p<0.001$ ). Moreover, the pregnant women diagnosed with COVID-19 and those who contacted a person with confirmed COVID-19 had higher EPDS mean scores than the healthy pregnant women ( $p<0.001$ ). The effect of COVID-19 and social isolation on psychological health was higher in the pregnant women diagnosed with COVID-19 and those who contacted a person with confirmed COVID-19 than in the healthy pregnant women ( $p<0.001$ ) (Table 2).

**Table 2.** Comparison of participants' stress, anxiety, postpartum depression levels, knowledge, and attitudes about COVID-19.

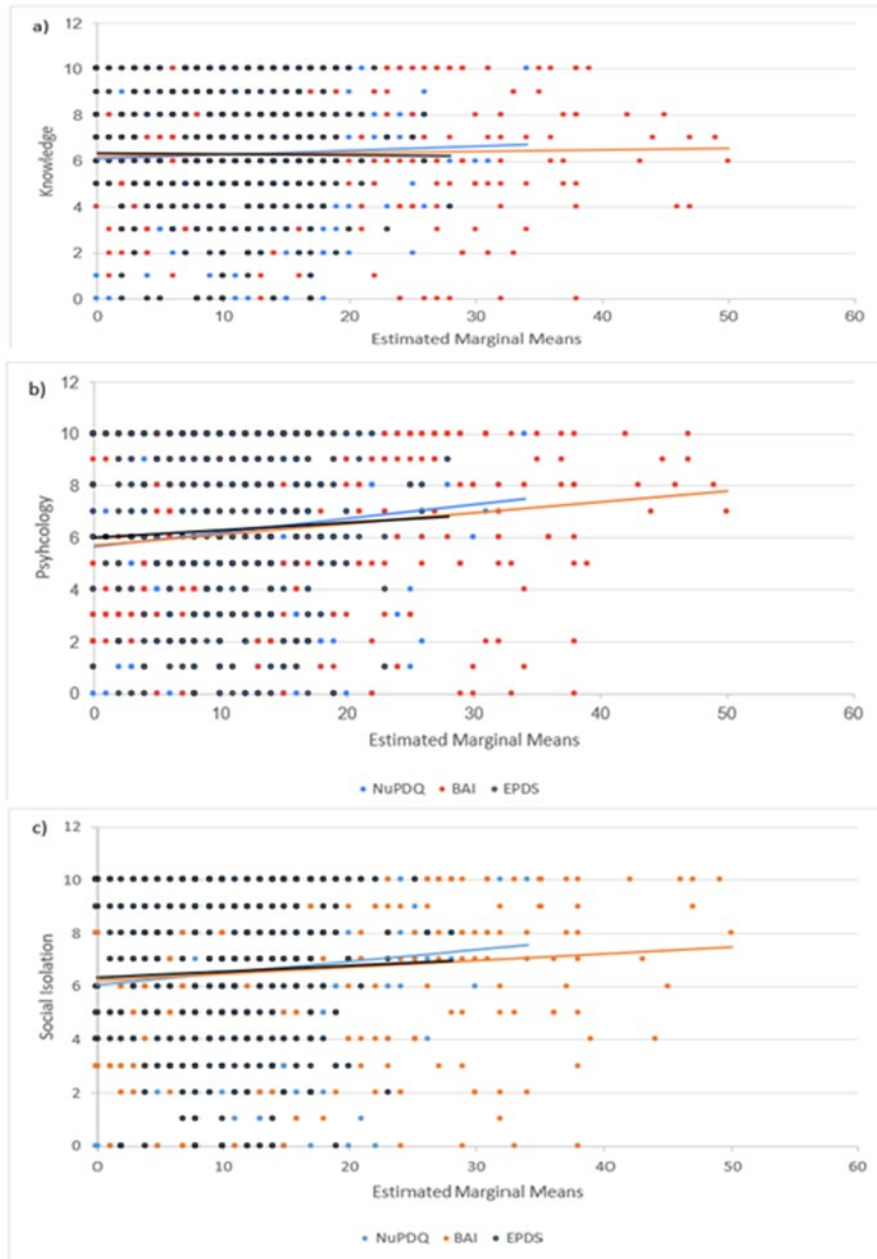
Variables		Healthy (n=220) n (%)	Contact with COVID-19 (+) (n=74) n (%)	COVID-19 (+) (n=91) n (%)	$\chi^2$ and p-value
<b>COVID-19 affects pregnancy</b>	Yes	66 (49.3)	25 (18.7)	43 (32.1)	$\chi^2=8.486$ <b>p=0.014</b>
	No	154 (61.4)	49 (19.5)	48 (18.1)	
<b>COVID-19 affects the fetus</b>	Yes	49 (40.8)	30 (25.0)	41 (34.2)	$\chi^2=19.324$ <b>p&lt;0.001</b>
	No	171 (64.5)	44 (16.6)	50 (18.9)	
<b>BAI group</b>	Minimal (0-7 scores)	106 (77.4)	17 (12.4)	14 (10.2)	$\chi^2=67.236$ <b>p&lt;0.001</b>
	Mild (8-15scores)	66 (60.6)	24 (22.0)	19 (17.4)	
	Moderate (16-25 scores)	27 (39.1)	20 (29.0)	22 (31.9)	
	Severe (26-63 scores)	21 (30.0)	13 (18.6)	36 (51.4)	
<b>EPDS group</b>	Yes ( $\geq 12$ scores)	75 (43.9)	47 (27.5)	49 (28.7)	$\chi^2=23.710$ <b>p&lt;0.001</b>
	No ( $< 12$ scores)	145 (67.8)	27 (12.6)	42 (19.6)	
		<b>Mean <math>\pm</math> SD</b>	<b>Mean <math>\pm</math> SD</b>	<b>Mean <math>\pm</math> SD</b>	
<b>Knowledge of COVID-19 (0-10 scale)</b>		6.17 $\pm$ 2.67	6.54 $\pm$ 2.57	6.54 $\pm$ 2.43	F=0.938 p= 0.392
<b>The effect of COVID-19 on psychology (0-10 scale)</b>		5.55 $\pm$ 3.10 <sup>a</sup>	7.35 $\pm$ 2.85 <sup>b</sup>	7.37 $\pm$ 2.72 <sup>c</sup>	F=17.457 <b>p&lt;0.001</b> c,b>a
<b>The effect of social isolation on psychology (0-10 scale)</b>		5.96 $\pm$ 2.94 <sup>a</sup>	7.24 $\pm$ 3.00 <sup>b</sup>	7.68 $\pm$ 2.45 <sup>c</sup>	F=13.997 <b>p&lt;0.001</b> c,b>a
<b>BAI Total</b>		10.73 $\pm$ 9.19 <sup>a</sup>	15.56 $\pm$ 10.49 <sup>b</sup>	21.21 $\pm$ 12.74 <sup>c</sup>	F=33.705 <b>p&lt;0.001</b> c>b>a
<b>NuPDQ Total</b>		10.04 $\pm$ 5.92 <sup>a</sup>	12.47 $\pm$ 7.03 <sup>b</sup>	14.93 $\pm$ 7.10 <sup>c</sup>	F=19.313 <b>p&lt;0.001</b> c>b>a
<b>EPDS Total</b>		9.70 $\pm$ 4.77 <sup>a</sup>	12.32 $\pm$ 5.14 <sup>b</sup>	11.61 $\pm$ 6.57 <sup>c</sup>	F=8.594 <b>p&lt;0.001</b> b,c>a

Figure 2a-c presents the relationship between pregnant women's COVID-19 knowledge levels, psychological effects of the COVID-19 pandemic and social isolation on them, and their NuPDQ, BAI and EPDS mean scores. There was no statistically significant relationship between the pregnant women's COVID-19 knowledge levels and their NuPDQ (r=0.007), BAI (r=0.061), and EPDS (r=0.007) mean scores (p>0.05). A weak positive relationship was found between the psychological effects of COVID-19 and social isolation on pregnant women and their NuPDQ (r=0.316, r=0.279, respectively), BAI (r=0.337, r=0.293) and EPDS (r=0.333, r=0.311, respectively) mean scores (p<0.01).

**DISCUSSION AND CONCLUSION**

Although there is a lot of research evidence regarding the clinical consequences of infectious diseases in pregnant women, the psychological effects of pandemics on pregnant women (including non-infected) have been mentioned by very few studies

in the literature. This study revealed that the COVID-19 pandemic has a significant psychological impact on pregnancy stress and postpartum anxiety, and depression. According to the study results, it was determined that the pregnant women who were positive for COVID-19 experienced more stress and anxiety, and the postpartum depression level of the women who were contacted and positive was higher than the healthy pregnant women (Table 2). One study examining the effects of the COVID-19 pandemic on maternal anxiety during pregnancy reported that pregnant women already had high levels of stress and anxiety and that the pandemic doubled their anxiety and stress levels.<sup>7</sup> One study comparing the depression symptoms experienced by mothers before and after the COVID-19 pandemic concluded that the COVID-19 pandemic adversely affected the mothers' mental health, and the symptoms of depression increased significantly.<sup>17</sup> Another study conducted to determine the emotional levels of pregnant women during the COVID-19 pandemic has



**Figure 2.** The relationship between a) participants’ COVID-19 knowledge levels, b) psychological effects of COVID-19 pandemic on participants, c) psychological effects of social isolation on participants and their NuPDQ, BAI and EPDS mean scores.

reported that pregnant women have high levels of depression, anxiety and stress during the pandemic.<sup>18</sup> These results support the results of this study. The present study examined the knowledge levels of pregnant women about COVID-19, the psychological effects of the COVID-19 pandemic and social isolation on them, and the relationship between these disease-related variables and their NuPDQ, BAI, and EPDS mean scores. There was a positive correlation between the psychological effects of the COVID-19 pandemic and social isolation on pregnant women

and their NuPDQ, BAI and EPDS mean scores (Figure 2b-c), but the relationship between their knowledge levels and NuPDQ, BAI and EPDS mean scores was not statistically significant (Figure 2a). Accordingly, the study revealed that pregnant women were psychologically affected by the COVID-19 pandemic and social isolation, but found no significant relationship between the stress, anxiety, and depression levels of those with high levels of knowledge. There are studies with results similar to those of the present study.

A meta-analysis study of the psychological effects of the COVID-19 pandemic on pregnant women reported that the prevalence of depression and anxiety increased significantly among pregnant women and suggested providing them with social support to reduce this situation.<sup>19</sup> Another study conducted for similar purposes stated that the COVID-19 pandemic had moderate to severe negative psychological effects on pregnant women.<sup>24</sup> A case-control study on the anxiety and depressive symptoms of pregnant women during the COVID-19 pandemic revealed that pregnant women had high levels of anxiety and depression during the pandemic and found that psychological and social isolation brought about by the disease had a significant effect on their anxiety and depression levels.<sup>12</sup> Another study on the effect of social isolation during the COVID-19 pandemic has stated that social isolation leads to loneliness, which is considered a risk factor for many mental disorders such as stress, anxiety, depression and even dementia later in life.<sup>20</sup>

In the study, a significantly high number of pregnant women who were diagnosed with COVID-19 reported that COVID-19 affected their pregnancy and baby (Table 2). Accordingly, pregnant women diagnosed with COVID-19 are more concerned about both themselves and their babies during the pandemic. This result may be due to the lack of clear evidence about the consequences of the disease in pregnant women and babies. As a matter of fact, the American College of Obstetricians and Gynecologists (ACOG) states that the effects of COVID-19 on pregnancy are still being investigated, whereby current studies have reported that pregnant women have a more severe risk of COVID-19 than non-pregnant women.<sup>21</sup>

In conclusion, this study revealed that pregnant women experience stress and anxiety during the COVID-19 pandemic, significantly related to COVID-19-specific concerns about risks to their own lives, their babies' health, and social isolation. However, it has been determined that these intense psychological problems experienced during pregnancy also affect the postpartum period, and women exhibit higher levels of postpartum depression symptoms than before COVID-19. In addition, the study findings show that pregnant women are vulnerable to mental status changes during the COVID-19 pandemic and deserve special care to deal with the high levels of anxiety and associated high postpartum depression caused by a period of uncertainty and stress. However, how long the effect of postpartum depression symptoms caused by COVID-19 last is an important point that requires extra attention, which is not yet known. Early detection of mental health problems is important in the perinatal period. Healthcare professionals should be aware of the ten-

dency of pregnant women to have anxiety during pandemics and consider the potential impact of pandemic-related symptoms on their physical and mental health. By prioritising effective screening strategies for depression and anxiety symptoms during the pandemic, early detection of health problems may allow obstetricians to make appropriate treatment plans with mental health professionals and provide public health education and mental health services, especially for pregnant women.

**Ethics Committee Approval:** Ethical approval was obtained from the Non-Invasive Clinical Research and Publication Ethics Committee (Date: 01.05.2021, decision no: 2020/1358) and written permission from the provincial health directorate (Date: 08.12.2020, No: E-13389845-799). In addition, COVID-19 scientific research permission was received from the Republic of Turkey Ministry of Health (Form Code: 2020-12-03T23\_59\_27). All pregnant women who participated were informed about the study on the first page of the questionnaire, and they were explained that their personal information would be kept confidential.

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

**Author Contributions:** Concept – SÖC, EKO; Supervision – SÖC, EG, ESB; Materials- EKO, EG; Data Collection and/or Processing - EG, ESB, TU; Analysis and/or Interpretation - EG, ESB, TU; Writing - EG, ESB, TU.

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## Comparison of I-Gel and Auragain in Airway Management

### Havayolu Yönetiminde I-Gel ile Auragain Kullanımının Karşılaştırılması

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#### ABSTRACT

**Objective:** We aimed to compare the superiority of I-Gel and Auragain, the second-generation supraglottic airway devices (SGAD) with different cuff structures, in terms of speed and ease of placement, oropharyngeal leak pressure (OLP), resistance of gastric contents, and post-operative oropharyngeal pain.

**Materials and Methods:** A total of 70 patients aged 18-65 years, with ASA scores I-II, who used I-Gel or Auragain to provide airways under general anesthesia were included in the study. Patients were divided into two groups as I-Gel and Auragain according to the type of SGAD used.

**Results:** OLP, placement duration and Visual Analogue Score (VAS) were found to be statistically significantly higher in the Auragain group ( $p<0.05$ ). In addition, a moderate positive correlation was found between VAS score and placement duration and number of attempts ( $p<0.05$ ). Gastric decompression success was similar in both groups ( $p>0.05$ ).

**Conclusion:** The use of I-Gel provides faster airway and less postoperative throat ache. The use of Auragain provides more efficient ventilation and higher OLP values. In addition, throat ache increases with the number of attempts and the duration of placement in both groups.

**Keywords:** Airway management, Auragain, I-Gel, oropharyngeal leak pressure

#### ÖZ

**Amaç:** Kaf yapıları birbirinden farklı olan ikinci nesil supraglottik havayolu araçları (SGAD)'ndan I-Gel ve Auragain'in yerleştirme hızı ve kolaylığı, oluşturdukları orofaringeal kaçak basıncı (OKB), mide içeriğinin dirençli, post-operatif orofarinkste neden oldukları ağrı bakımından birbirlerine olan üstünlüklerini karşılaştırılmayı amaçladık.

**Materyal ve Metot:** Çalışmaya 18-65 yaş arası, ASA skoru I-II olan, genel anestezi altında havayolu sağlanması için I-Gel veya Auragain kullanılan toplam 75 hasta dahil edildi. Hastalar kullanılan SGAD türüne göre I-Gel ve Auragain olarak iki gruba ayrıldı.

**Bulgular:** OKB, yerleştirme süresi ve Vizüel Analog Skala (VAS) skorlarının Auragain grubunda istatistiksel olarak anlamlı düzeyde yüksek olduğu bulundu ( $p<0.05$ ). Ayrıca VAS skoru ile yerleştirme süresi ve deneme sayısı arasında pozitif yönde orta düzey korelasyon saptandı ( $p<0.05$ ). Her iki grubun mide dekompresyonu başarısı ise benzer bulundu ( $p>0.05$ ).

**Sonuç:** I-Gel kullanımı ile daha hızlı havayolu sağlanmakta ve daha az postoperatif boğaz ağrısı oluşmaktadır. Auragain kullanımı ise daha etkin ventilasyon ve daha yüksek OKB değeri sağlamaktadır. Ayrıca her iki grupta da deneme sayısı ve yerleştirme süresinin fazla olması ile boğaz ağrısı artmaktadır.

**Anahtar Kelimeler:** Auragain, havayolu yönetimi, I-Gel, orofaringeal kaçak basıncı

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## INTRODUCTION

Difficulty in airway management is a major cause of morbidity and mortality in anesthesia practice. Every anesthesiologist aims to start anesthesia with confidence.<sup>1</sup> The introduction of the Laryngeal Mask Airway (LMA) has eased the approach to airway management. There have also been changes in airway management application algorithms. New supraglottic airway devices (SGAD) have been a powerful alternative to tracheal intubation.<sup>2</sup> Despite these advantages SGAD also have disadvantages such as difficulty in placement, inability to provide effective ventilation and risk of aspiration of gastric contents. The second-generation SGAD are superior to the previous generation with easier placement, more effective ventilation and lower aspiration risk with their structures suitable for airway anatomy and the gastric canal they contain.<sup>3</sup> I-Gel and Auragain are second generation SGAD that provide perilyngeal closure with these properties.<sup>4</sup>

I-Gel is an innovative supraglottic airway device with a soft, gel-like, and transparent structure made of thermoplastic elastomer suitable for medical use. Its non-inflated cuff structure separates the pharyngeal, laryngeal and perilyngeal structures and, unlike inflatable cuffs, prevents trauma due to compression.<sup>4</sup> Ambu Auragain is an airway device used as an alternative to a face mask to establish and maintain the airway in emergency and routine anesthesia applications. It allows gastric access and intubation.<sup>4</sup>

In this study, we aimed to compare the superiority of I-Gel and Auragain, the second-generation SGAD with different cuff structures, in terms of speed and ease of placement, oropharyngeal leak pressure (OLP), resistance of gastric contents, and post-operative oropharyngeal pain.

## MATERIALS AND METHODS

**Ethics Committee Approval:** Our study was approved by the University of Health Sciences, Haydarpaşa Numune Training and Research Hospital, Ethics Committee (Date: 18.04.2022, decision no: 79). The study was carried out in accordance with international guidelines. Written informed consent was obtained from all patients before the procedure.

**Research Design:** Between 04.05.2022 and 14.07.2022, 75 patients aged 18-65 years, with American Society of Anesthesiologists (ASA) score I-II, who used I-Gel or Auragain to provide airway under general anesthesia were included in the study. Patients younger than 18 years and older than 65 years, ASA score 3 or more, obese (BMI >35), with predicted general anesthesia duration of 3 hours or longer, with risk of difficult airway (mallampathy 3-4) or history of difficult intubation, with oral and

pharyngeal pathology, having nausea-vomiting and with aspiration risk were excluded. Patients were divided into two groups as I gel (Group I) or Auragain (Group II) according to the supraglottic airway device used.

**Data Collection:** All patients were premedicated with midazolam 0.05 mg/kg/iv 30 min before elective surgery. Patients brought to the operating room were monitored with DII-lead electrocardiography, blood pressure (non-invasive), peripheral oxygen saturation (SpO<sub>2</sub>).

All patients underwent induction of general anesthesia with 1-2 mcg/kg fentanyl, 2 mg/kg propofol and 0.6-1.2 mg/kg rocuronium bromide protocol, which is the standard protocol in our hospital. The patient was ventilated with 100% FiO<sub>2</sub> on manual/bag ventilation with a face mask. After loss of eyelash reflex, airway was established using either I-Gel or Auragain airway instruments and the patient was connected to the anesthesia device. The study included anesthesiology and reanimation clinic physicians with at least 4 years of experience. The type and size of SGAD used by the anesthesia team for the patient were recorded. Duration of successful placement, number of attempts, and transition to tracheal intubation in case of unsuccessful placement were recorded. Successful placement duration was measured as the time between the end of bag-valve ventilation and the connection of the placed SGAD to the breathing circuit and the appearance of square waves on the capnograph.

After the cuff was inflated, the cuff pressure was measured with a cuff manometer and lowered so that it did not rise above 40 cmH<sub>2</sub>O. In both groups, the measurement of OLP after SGAD placement was determined and recorded using manometer stability test. During the manometer stability test, the Adjustable Pressure-Limiting valve was closed to 40 cmH<sub>2</sub>O to prevent barotrauma and if no leakage sound was still heard, this value was recorded in the case report form.

After successful placement, the largest lumen aspiration catheter that could pass through the gastric canal of the two SGAD was advanced. The epigastric region was auscultated while 20 ml of air was sent into the stomach with an aspiration probe using a syringe to avoid gastric regurgitation. The probe that reached the stomach was aspirated with a syringe and successful cases were recorded.

After the surgical procedure was completed, intravenous and inhaled anesthetic agents used for maintenance of anesthesia were discontinued and the patient was awaited to wake up. After the patient's airway protective reflexes returned and the patient was able to respond to verbal commands, the SGAD was removed. The duration of SGAD use (from ini-



tial placement to removal) was recorded as the duration of the operation.

After awakening from general anesthesia, patients were taken to the recovery room for complete recovery and observation. The patients were monitored by two nurses on duty until transferred to ward. At 60 minutes in the postoperative recovery room, the responsible researcher asked the patient to evaluate the presence or absence of sore throat according to the Visual Analog Scale (VAS) score (0= no pain, 10= intolerable pain) and the score declared by the patient was recorded on the case report form.<sup>5</sup>

**Power Analysis:** The minimum number of patients to be included in the study was found to be 50 in the sample size analysis calculated by taking type 1 error 0.05, type 2 error 0.05, effect size 0.94 (reference values group 1=20.83±2.90 (n=30) group 2=20.93±3.11 (n=30)).<sup>6</sup> Considering the possible losses, 70 patients were included in the study to increase the statistical power.

**Statistical Analysis:** IBM SPSS Statistics 22 (IBM SPSS Türkiye) program was used for data analysis. While evaluating the study data, conformity of the parameters to normal distribution was evaluated

using the Shapiro Wilks test. While evaluating the study data, in the context of comparing descriptive statistical methods (Mean, Standard deviation, frequency) and comparing quantitative data, Student t test was used for comparison of normally distributed parameters between two groups and Mann Whitney U test was used for comparison of non-normally distributed parameters between two groups. Chi-Square test was used to compare qualitative data. Significance was evaluated at p<0.05.

**RESULTS**

The mean age of the 70 patients included in our study was 45.61±12.59 years (min=18, max=65). Demographic characteristics, ASA and Mallampati Scores of the patients according to the groups are presented in Table 1.

The success of gastric decompression according to the type of SGAD was similar in both groups (Table 2).

According to the type of SGAD, OLP, placement duration and VAS scores were found to be statistically significantly higher in the Auragain group (Table 3).

**Table 1.** Sociodemographic characteristics and ASA and Mallampati Scores by groups.

		SGAD Type n (%) or 'Mean±SD'		p
		I-Gel (n:35)	AG (n:35)	
Gender	Female	18(56.3)	14(43.8)	0.472
	Male	17(44.7)	21(55.3)	
ASA	1	5(62.5)	3(37.5)	0.710
	2	30(48.4)	32(51.6)	
Age		45.49±12.07	45.74±13.26	0.874
BMI		26.25±3.71	24.88±3.32	0.055
Mallampati I/II		15/20	15/20	1

SGAD: Supraglottic Airway Devices; SD: Standard deviation AG: Auragain; ASA: American Society of Anesthesiologists; BMI: Body Mass Index.

**Table 2.** Comparison of gastric decompression by type of SGAD.

			SGAD Type		p
			I-GEL	AG	
Gastric Decompression	Yes	n	21	24	0.618
		%	46.7	53.3	
	No	n	14	11	
		%	56.0	44.0	

SGAD: Supraglottic Airway Devices; AG: Auragain; SD: Standard deviation.

**Table 3.** Comparison of duration and pressures by SGAD type.

	SGAD						
	Mean	I-GEL SD	Median	Mean	AG SD	Median	p
OLP (cmH <sub>2</sub> O)	22.45	10.87	20.0	33.71	8.68	40.0	<b>0.001</b>
Placement Duration (seconds)	26.25	14.58	22.0	29.34	7.82	28.0	<b>0.001</b>
SGAD Size	4.37	.64	4.0	4.45	0.70	5.0	0.461
Number of Attempts	1.40	.91	1.0	1.25	0.56	1.0	0.866
Operation Duration (minutes)	69.42	28.27	60.0	61.14	20.7	60.0	0.375
VAS Score	2.14	1.11	2.0	2.77	1.08	2.0	<b>0.011</b>

SGAD: Supraglottic Airway Devices; AG: Auragain, SD: Standard deviation; OLP: Oropharyngeal Leak Pressure; VAS: Visual Analogue Score.

There was no significant difference in the distribution of the number of I-Gel and Auragain attempts (Table 4).

There was a moderate positive correlation between VAS score and placement duration and number of attempts (Table 5).

**Table 4.** Distribution of the number of attempts by SGAD type.

		SGAD		
		I-GEL	AG	
<b>Number of Attempts</b>	1.0	n	28	28
		%	80.0	80.0
	2.0	n	3	5
		%	8.6	14.3
	3.0	n	1	2
		%	2.9	5.7
	Tracheal	n	3	0
		%	8.6	0.0

SGAD: Supraglottic Airway Devices; AG: Auragain.

**Table 5.** Correlation between VAS score and measurements.

		VAS score
Operation duration	r	0.092
	p	0.450
SGAD Body	r	0.023
	p	0.850
Placement Duration	r	0.405
	p	<b>0.001</b>
Oropharyngeal Leak Pressure	r	0.183
	p	0.130
Number of Attempts	r	0.419
	p	<b>0.001</b>

VAS: Visual Analogue Score; SGAD: Supraglottic Airway Devices.

**DISCUSSION AND CONCLUSION**

The most characteristic feature of the second generation SGAD is that they allow easier placement of gastric resistance tubes. They also reduce the risk of aspiration by closing the esophagus and increasing pharyngolaryngeal separation. This improves ventilation quality and safety.<sup>7</sup> There are studies measuring the amount of aspiration of gastric contents.<sup>8,9</sup> In these studies, the content aspirated from the stomach was expressed as the mean volume between the groups and successful gastric aspiration was not evaluated for each patient. In our study, gastric access of the aspiration catheter was confirmed by epigastric auscultation in all patients. In patients whose gastric contents could be aspirated, there was no statistically significant difference between the two groups.

OLP is the most important marker of placement success and effective ventilation in SGAD use.<sup>10</sup> In many studies conducted with SGAD and monitoring OLP, average OLP values in the range of 22-34 cmH<sub>2</sub>O for I-Gel and 18.6-32.8 cmH<sub>2</sub>O for Auragain were given.<sup>8,11-13</sup> Pradeep et al.<sup>14</sup> also found a significantly (p<0.0001) higher mean OLP value in the Auragain group. Based on these results, it can be concluded that the inflatable cuff structure in the

Auragain structure provides better perilaryngeal localization compared to I-Gel.<sup>10</sup>

In the literature, there are also studies with I-Gel and Auragain in which no significant difference was observed between OLP values.<sup>8,11-13</sup> Kim et al.<sup>15</sup> found that the mean OLP value in I-Gel (23.3cm H<sub>2</sub>O) was significantly (p<0.001) higher than Auragain (18.6 cm H<sub>2</sub>O) in a study conducted in pediatric patients without the use of neuromuscular blockers.

Looking at the placement durations in studies comparing I-Gel and Auragain, there are results where I-Gel placement duration is shorter, as in our study.<sup>13,14,16</sup> The most important factor for the shorter I-Gel placement duration is the lack of an inflatable cuff structure.<sup>16</sup>

In different studies, placement durations were reported in the range of 8-50.53 seconds for I-Gel and 13-72.03 seconds for Auragain.<sup>8,11,14,15</sup> Among the reasons for these significant differences between placement durations are the difference in the interval chosen for the placement time, practitioner experience and the number of attempts.

Some studies did not find significant results between I-Gel and Auragain placement durations.<sup>8,11,15</sup> Sarma et al.<sup>17</sup> found the mean placement duration of I-Gel

(28.73 sec) longer than Auragain (25.07 sec) in their study.

In our study, first-attempt placement, and overall placement success for I-Gel and Auragain were similar. In studies, the first placement success rate for I-Gel was 66.7-100% and 60-100% for Auragain.<sup>8,11,14,15</sup> Some studies reported success for I-Gel and Auragain at first attempt in all patients.<sup>8,11,15</sup> These differences in the success rate may be attributed to the use of muscle relaxant agents during induction of anesthesia and the experience of the practitioner. Kriege et al.<sup>18</sup> reported 75% initial placement success with experienced practitioners and 68% with inexperienced practitioners. The study emphasized that practitioner experience is an important determinant of the success of SGAD deployment.

SGAD's cuff structure, which contributes to the perilaryngeal seal, presses against the surrounding tissue to provide a seal for ventilation. However, excessive and prolonged pressure transmitted by the cuff to the pharyngeal mucosa may exceed the mucosal capillary perfusion pressure and cause complications.<sup>19</sup> One of the most common complications in this situation is postoperative throat ache. In our study, VAS score was verbally inquired with the patients in the recovery room at the 1st hour postoperatively. Studies reported that throat ache was more common in the Auragain group, although not statistically significant.<sup>12,17</sup> Deepak et al.<sup>12</sup> found that mean OLP values were very similar between Auragain and I-Gel groups at different cuff pressures, and postoperative throat ache was higher in Auragain groups compared to I-Gel, although not significantly. Lakshmi et al.<sup>16</sup> found more postoperative throat ache in the I-Gel (13%) group than in the Auragain (10%) group, although not statistically significant.

In our study, a moderate positive correlation was observed between the number of multiple placements attempts and the duration of attempts, and VAS score in both groups. Taniguchi et al.<sup>20</sup> also found that the length of operation duration ( $p=0.026$ ) and the length of placement duration ( $p=0.018$ ) were significant in the occurrence of post-op throat ache after I-Gel use in 426 patients. In addition, although it was not statistically significant in the I-Gel group ( $p=0.658$ ), throat ache was more common in those with a higher number of attempts.

The limitations of our study are that hemodynamic parameters of the patients were not recorded; perioperative analgesic agents could not be standardized, and postoperative throat ache was inquired only in the operating room follow-up and not during the ward follow-up. According to the results of our study, the use of I-Gel, a supraglottic airway device, provides faster airway and less postoperative throat ache. The use of Auragain provides more efficient ventilation and higher OLP values. In addition,

throat ache increased with the number of attempts and the duration of placement in both groups. We believe that further studies are needed to support these findings.

**Ethics Committee Approval:** Our study was approved by the University of Health Sciences, Haydarpaşa Numune Training and Research Hospital, Ethics Committee (Date: 18.04.2022, decision no: 79).

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

**Author Contributions:** Concept – GE, ÖD, SG, OE; Supervision – ÖD, OE; Materials – GE, ÖD; Data Collection and/or Processing – GE, ÖD, SG; Analysis and/or Interpretation – GE, ÖD; Writing – GE, ÖD.

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## In-Hospital Clinical Outcomes of Covid-19 Patients Treated with Oral Anticoagulants

### Oral Antikoagülan Kullanan Covid-19 Hastalarının Hastane İçi Klinik Sonuçları

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#### ABSTRACT

**Objective:** We aimed to investigate the effects of warfarin and new-generation oral anticoagulants on the prognosis of patients diagnosed with coronavirus disease 2019 (COVID-19).

**Materials and Methods:** Patients diagnosed with COVID-19 were divided into two groups depending on whether they were using warfarin or a new-generation oral anticoagulant. The types of chronic diseases, drugs used, hematological and biochemical parameters, and prognoses in each group were statistically analysed.

**Results:** Twenty-three patients (37.1%) using warfarin and 39 (62.9%) patients using new-generation oral anticoagulants were included in the study. There was no significant difference between the two groups regarding demographic characteristics and laboratory data. The mortality rates for the warfarin and new-generation anticoagulant groups were similar (39.1% vs. 43.6%, respectively;  $p = 0.731$ ). Also, there was no significant difference in the results of major bleeding and intubation rates between the two groups.

**Conclusion:** There was no difference in the effects of warfarin and new-generation oral anticoagulants on mortality, intubation and major bleeding among the patients with COVID-19.

**Keywords:** Anticoagulation, coronavirus, Covid-19, thrombosis

#### ÖZ

**Amaç:** Çalışmamızda varfarin ve yeni nesil oral antikoagülanların COVID-19 hastalığının prognozu üzerine etkilerini araştırmayı amaçladık.

**Materyal ve Metot:** COVID-19 tanısı alan hastalar, varfarin veya yeni nesil oral antikoagülan kullanıp kullanılmalarına göre iki gruba ayrıldı. Her gruptaki kronik hastalık tipleri, kullanılan ilaçlar, hematolojik ve biyokimyasal parametreler ve prognozlar istatistiksel olarak analiz edildi.

**Bulgular:** Varfarin kullanan 23 (%37,1) hasta ve yeni nesil oral antikoagülan kullanan 39 (%62,9) hasta çalışmaya dahil edildi. Her iki grup arasında demografik özellikler ve laboratuvar verileri açısından anlamlı fark yoktu. Varfarin ve yeni nesil antikoagülan gruplarında mortalite oranları benzerdi (sırasıyla %39,1 ve %43,6;  $p = 0,731$ ). Ayrıca majör kanama ve entübasyon oranları sonuçlarında da iki grup arasında anlamlı fark yoktu.

**Sonuç:** COVID-19 hastalarında varfarin ve yeni nesil oral antikoagülanların entübasyon, majör kanama ve mortalite üzerine etkileri arasında fark yoktu.

**Anahtar Kelimeler:** Antikoagülasyon, Covid-19, koronavirus, tromboz

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## INTRODUCTION

The coronavirus disease 2019 (COVID-19) virus, or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is an RNA virus. Infection with this virus can lead to a wide range of symptoms, from mild to lung infection with severe respiratory failure.<sup>1</sup> COVID-19 has been classified as a pandemic by the World Health Organization.<sup>2</sup> Patients with COVID-19 may be asymptomatic; however, the disease may also present with symptoms such as fever, chills, cough, shortness of breath, myalgia, and headache. The case fatality rate is 2%–3%. The laboratory tests for COVID-19 are nonspecific and include creatine kinase, lactate dehydrogenase, D-dimer (a specific fibrin degradation product), hemogram, white blood cell count, serum C-reactive protein (CRP), sedimentation rate and procalcitonin. Low lymphocytes and platelets can be seen in COVID-19 patients. Pathological changes in these parameters are also used as prognostic factors.<sup>3</sup>

Since the COVID-19 pandemic is new, copious studies about the characteristics and treatment of the virus and the disease are being added to the literature. However, despite many new scientific studies in the literature daily, there needs to be more sufficient and definitive information about COVID-19 and its treatment. Although it is emphasised that impaired coagulation parameters are associated with a poor prognosis in COVID-19,<sup>4</sup> there are limited data in the literature on warfarin, new-generation oral anticoagulants (NOAC) and low-molecular-weight heparin treatments for the disease.<sup>5</sup>

In this study, we aimed to investigate the effects of warfarin and NOAC use on the prognosis of patients diagnosed with COVID-19.

## MATERIALS AND METHODS

**Ethical Statement:** Approval for this study was obtained from the ethics committee of Sakarya University, Faculty of Medicine (Date: 27/04/2020, decision no: 71522473/050.01.04/463). The study was carried out following the international declaration, guidelines, etc.

**Patients:** Sixty-two patients diagnosed with COVID-19, treated in intensive care, and followed up in our hospital were included in the study. Following ethics committee approval, the patient's data were collected retrospectively through the electronic medical records. Clinical findings, laboratory parameters, computed tomography and SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) were used to diagnose the patients with COVID-19. The patients were divided into two groups depending on the use of either warfarin or NOACs. The NOACs used were apixaban, rivaroxaban,

dabigatran and edoxaban. The types of chronic diseases, drugs used, hematological and biochemical parameters and prognoses in each group were statistically analysed.

**Sample Collection, Nucleic Acid Isolation and RT-PCR Reactions:** Combined nasopharynx and oropharynx swab samples were taken with a Dacron swab, placed in a viral transport medium, and immediately transported to the laboratory at 2°C–8°C. The samples were sent to the laboratory following the cold chain rules using the triple transport system and following infection prevention and control procedures. After the samples had been accepted in the microbiology laboratory, they were taken to a third-level biosecurity negative pressure room. The Bio-Speedy® Viral Nucleic Acid Isolation Kit was used to isolate total nucleic acid from samples (Bioeks, İstanbul, Turkey). The isolation procedure was carried out in line with the manufacturer's recommendations. The Bio-Speedy® Covidien work for RT-PCR Detection Kit-19 RT-qPCR (Bioeks, İstanbul, Turkey) was used. The manufacturer's recommendations carried out PCR amplification and the evaluated the results.

**Statistical Analysis:** Descriptive analyses were performed to provide information on the general characteristics of the study population. Visual (i.e., probability plots, histograms) and analytical (Kolmogorov–Smirnov test, Shapiro–Wilk test) methods were used to determine whether the data were normally distributed. The descriptive analyses were presented using medians and interquartile ranges for the non-normally distributed variables. The Mann–Whitney *U* test was used for the nonparametric tests to compare these parameters. Pearson's chi-square test was used to compare the categorical variables between the two groups. The categorical variables were presented as the frequency (% percentage). A *p*-value <0.05 was considered statistically significant. The analyses were performed using SPSS Statistics version 22.0 (IBM Corporation, Armonk, NY).

## RESULTS

When the demographic characteristics of the patients were compared, no significant differences were found between the two groups other than the use of insulin and alpha-blocker therapy. While all the patients using NOAC were taking the drug due to atrial fibrillation (AF), 19 of the patients using warfarin were using it because of AF, and four had a prosthetic heart valve (Table 1).

**Table 1.** Comparison of baseline characteristics and the drug they use of the warfarin and NOAC groups.

	Warfarin, n = 23 (37.1%)	NOAC, n = 39 (62.9%)	p	
Sex, n (%)	Female, n = 11 (47.8) Male, n = 12 (52.2)	Female, n = 16 (41.0) Male, n = 23 (59.0)	0.602	
Hypertension, n (%)	18 (78.3)	27 (69.2)	0.441	
Diabetes Mellitus, n (%)	11 (47.8)	12 (30.8)	0.179	
CAD history, n (%)	3 (13.0)	9 (23.1)	0.323	
CVD history, n (%)	8 (34.8)	6 (15.4)	0.078	
PAD history, n (%)	0 (0.0)	2 (5.1)	0.526	
COPD history, n (%)	3 (13.0)	10 (25.6)	0.338	
CKD, n (%)	3 (13.0)	6 (15.4)	0.928	
Hyperlipidemia, n (%)	3 (13.0)	8 (30.5)	0.516	
CHF, n (%)	4 (17.4)	7 (17.9)	0.978	
DRUGS (Already taken)	ACE/ARB, n (%)	14 (60.6)	24 (61.5)	0.998
	CCBs, n (%)	10 (43.5)	14 (35.9)	0.597
	Diuretics, n (%)	18 (78.3)	26 (66.7)	0.331
	Beta blockers, n (%)	13 (56.5)	27 (69.2)	0.312
	Digoxin, n (%)	4 (17.4)	9 (23.1)	0.751
	Alfa blockers, n (%)	0 (0.0)	8 (20.5)	<b>0.021</b>
	Antiplatelet agent, n (%)	9 (39.1)	14 (35.9)	0.799
	OAD, n (%)	6 (26.1)	7 (17.9)	0.447
	Insülin, n (%)	5 (21.7)	0 (0.0)	<b>0.005</b>
	Bronchodilators, n (%)	2 (8.7)	5 (12.8)	0.620
	Statins, n (%)	3 (13.0)	6 (15.4)	0.770
	MRA, n (%)	5 (21.7)	7 (17.9)	0.715

CAD: Coronary Artery Disease; CVD: Cerebrovascular Disease; PAD: Peripheral Artery Disease; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease; CHF: Congestive Heart Failure; ACE: Angiotensin-converting Enzyme; ARB: Angiotensin Receptor Blocker; CCB: Calcium Channel Blocker; OAD: Oral Antidiabetic; MRA: Mineralocorticoid Receptor Antagonist.

When the laboratory values of the patients in the two groups were compared, no differences were found except that the prothrombin time and international

normalised ratio (PT-INR) values were higher in the warfarin group (Table 2).

**Table 2.** Comparison of laboratory test results of the two groups.

	Warfarin, n = 23	NOAC, n = 39	p
WBC count, kU/l	9.6 ± 5.8	11.3 ± 6.7	0.453
Hemoglobin, g/dL	10.5 ± 3.2	11.6 ± 2.2	0.170
Hematocrit, %	35.1 ± 8.5	37.5 ± 7.2	0.407
Lymphocyte 10 <sup>3</sup> /uL	1.2 ± 0.5	1.3 ± 1.4	0.839
Neutrophile, 10 <sup>3</sup> /uL	8.0 ± 5.7	9.2 ± 6.0	0.429
Platelet, 10 <sup>3</sup> /uL	199 ± 93	206 ± 88	0.829
Prothrombin time, seconds	40.4 ± 31.3	15.2 ± 40.7	<b>0.001</b>
APTT, seconds	51.5 ± 42.4	32.8 ± 7.2	0.085
INR	3.9 ± 3.2	1.4 ± 0.4	<b>0.001</b>
D-DİMER, ng/mL	2661 ± 5595	1920 ± 1689	0.757
Hs-cTnI, ng/L	941 ± 3299	217 ± 787	0.759
Ferritin, ng/mL	675.5 ± 402.3	423.3 ± 387.3	0.400
Glucose, mg/dL	101.1 ± 93.1	104.2 ± 82.1	0.204
Urea, mg/dL	84.8 ± 23.6	94.9 ± 30.3	0.651
Creatinine, mg/dL	2.2 ± 2.4	1.4 ± 0.9	0.460
Albumin, g/dL	3.1 ± 0.4	3.2 ± 0.5	0.555
Lactate dehydrogenase, U/L	399.2 ± 85.3	349.5 ± 128.4	0.565
C reactive protein, mg/dL	68.8 ± 62.9	75.0 ± 95.1	0.257
Prokalsitonin, ng/mL	3.9 ± 3.5	10.8 ± 31	0.348
Sedimentation, mm/hour	65.4 ± 40.5	45.6 ± 28.7	0.129
Fibrinogen, g/L	400 ± 80	372 ± 95	0.431
CK-MB, IU/L	15.0 ± 4.1	25.2 ± 24.3	0.099
Lactate, mmol/L	2.9 ± 1.8	2.5 ± 1.7	0.427

WBC; White Blood Cell; APTT; Activated Partial Thromboplastin Time; INR; International Normalized Ratio; Hs-cTnI; High sensitive Cardiac Troponin I; CK-MB; Creatine Kinase Myocardial Band.

When the subgroup mortality analysis was performed, 14 of the 23 (37.0%) patients with diabetes ( $p = 0.020$ ), 7 of the 9 (14.5%) patients with chronic renal failure ( $p = 0.018$ ), and 3 of the 11 (17.7%) patients with heart failure ( $p = 0.003$ ) died. These chronic diseases were statistically significant in terms of death among the COVID-19 patients. In the patients with exitus, the hemoglobin ( $10.2 \pm 2.7$  &  $12 \pm 2.3$ , respectively;  $p = 0.012$ ) and hematocrit ( $34.3 \pm 7.5$  &  $38 \pm 7.7$ , respectively;  $p = 0.045$ ) levels were lower compared to the patients who survived. Furthermore, these patients' CRP levels ( $103$

$\pm 110$  &  $44 \pm 54$ , respectively;  $p = 0.047$ ), procalcitonin levels ( $16 \pm 35$  &  $1 \pm 2.5$ , respectively;  $p = 0.005$ ), and sedimentation rates ( $62 \pm 34$  &  $42 \pm 23$ , respectively;  $p = 0.005$ ) were significantly different from those who were discharged in good health (Table 2). In the warfarin group, only eight patients with INR were in the therapeutic range target value. The treatment of the patients with either warfarin or NOAC continued during their time in the ICU, and there was no difference between the two groups in terms of in-hospital mortality (Table 3).

**Table 3.** In-hospital clinical outcomes of the study groups.

	Warfarin, n = 23	NOAC n = 39	p
<b>Intubation</b>	3 (13.0)	10 (25.6)	0.338
<b>Major Bleeding</b>	0 (0.0)	2 (5.1)	0.526
<b>Mortality n, (%)</b>	9 (39.1)	17 (43.6)	0.731

## DISCUSSION AND CONCLUSION

While COVID-19 can be asymptomatic, it can lead to flu-like symptoms, severe respiratory failure, multi-organ dysfunction and death.<sup>3,6</sup> Some laboratory parameters may also increase and decrease in the presence of COVID-19 infection depending on the pathogenesis of the disease. Low lymphocytes, albumin and platelets, and high CRP, procalcitonin, lactate dehydrogenase, creatinine, and D-dimer have been highlighted as poor prognostic factors.<sup>1,3,7,8</sup>

Thrombotic complications cause serious problems in patients who are positive for COVID-19.<sup>9</sup> As with viral infections, COVID-19 infection also activates coagulation and can cause the excessive activation of platelets. In addition, causing an inflammatory response systemically can affect the procoagulant and anticoagulant mechanisms in hemostasis and disrupt the balance between the two.<sup>10,12</sup> In autopsies of patients who died due to COVID-19, thrombus in the capillaries and small vessels and many microthrombi in the liver venous portal system were present.<sup>13</sup>

In severe COVID-19 cases, high D-dimer levels are encountered, revealing that they are associated with mortality. Again, these patients often have a coagulation disorder.<sup>14</sup>

In our study, the effects of warfarin and new-generation oral anticoagulants used to treat patients with COVID-19 were examined, and it was determined that there was no difference in the impact of these two groups of drugs on mortality. As expected, the PT-INR levels were significantly higher in the group using warfarin, but no significant difference was found in the other laboratory parameters.

In conclusion, based on the results of our study, neither warfarin nor NOACs were superior in treating patients with COVID-19 in terms of in-hospital clinical outcomes. The relatively low number of cases in this study was considered a limitation. Multicentre studies with more case numbers should be conducted to verify these results.

**Ethics Committee Approval:** Our study was approved by the Sakarya University Ethics Committee (Date: 27/04/2020, decision no: 71522473/050.01.04/463). The study was carried out following the international declaration, guidelines, etc.

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## The Factors Affecting the Level of Job Satisfaction of Family Physicians and their Relationship with Professional Self-Esteem

### Aile Hekimlerinin İş Doyumu Düzeyini Etkileyen Faktörler ve Mesleki Benlik Saygısı İle İlişkisi

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#### ABSTRACT

**Objective:** The study aimed to investigate the relationship between job satisfaction and professional self-esteem levels of family medicine practitioners working in Family Health Center.

**Materials and Methods:** Between April 2021 and April 2022, 128 family physicians who volunteered from 155 family physicians working in family health centres in Giresun province were included in the study. The socio-demographic descriptive form, the Minnesota Job Satisfaction and Occupational Self-Esteem Scales were administered face-to-face and online (via WhatsApp groups and e-mail communities).

**Results:** There was no significant relationship between job satisfaction and its sub-dimensions with age, gender, marital status, specialisation status, physical conditions of the Family Health Center, total years of practice and years of training in family medicine ( $p>0.05$ ). The mean level of occupational self-esteem was 112.48. It was found to be significantly positively correlated with age, total years of practice, years of family medicine practice and average number of patients seen ( $p=0.05$ ,  $p=0.004$ ,  $p=0.004$ ,  $p=0.004$ ,  $p=0.009$ , respectively).

**Conclusion:** Professional self-esteem levels increase as professional age, total years of profession, and total years of working in family medicine increase.

**Keywords:** Family physicians, job satisfaction, professional self-esteem

#### ÖZ

**Amaç:** Bu çalışmada Aile Sağlığı Merkezi'nde görev yapan aile hekimliği uygulayıcılarının iş doyumları ile mesleki benlik saygısı düzeyleri arasındaki ilişkisini araştırmak amaçlanmıştır.

**Materyal ve Metot:** Nisan 2021- Nisan 2022 tarihleri arasında Giresun ilinde aile sağlığı merkezlerinde görev yapan 155 aile hekiminden gönüllü olan 128 aile hekimi çalışmaya dahil edilmiştir. Sosyo-demografik tanımlayıcı form, Minnesota İş Doyum ve Mesleki Benlik Saygısı Ölçekleri yüz yüze ve online (whatsapp grupları, e-posta toplulukları aracılığıyla) olarak uygulandı.

**Bulgular:** İş doyum ve alt boyutları ile yaş, cinsiyet, medeni durum, uzmanlık durumu, Aile Sağlığı Merkezinin fiziki koşulları, toplam çalışma yılı ve aile hekimliği çalışma yılı arasında anlamlı bir ilişki bulunmamıştır ( $p>0,05$ ). Mesleki benlik saygısı düzeyi ortalaması 112,48 bulunmuş olup yaş, toplam meslek yılı, aile hekimliğinde çalışma süresi ve ortalama bakılan hasta sayısı ile anlamlı pozitif ilişkili bulunmuştur (sırasıyla  $p=0,05$ ,  $p=0,004$ ,  $p=0,004$ ,  $p=0,009$ ).

**Sonuç:** Mesleki yaş, toplam meslek yılı, aile hekimliğinde toplam çalışma yılı arttıkça mesleki benlik saygısı düzeyleri artmaktadır.

**Anahtar Kelimeler:** Aile hekimliği, iş doyum, mesleki benlik saygısı

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## INTRODUCTION

Primary health care is an important part of a country's health care system and plays a central role.<sup>1</sup> It is the first contact area of individuals with the health care system.<sup>2</sup> Burnout is more common among frontline physicians, as in family medicine.<sup>3</sup>

Job satisfaction can be defined as the general attitude of employees towards certain elements of their work, such as their job, work environment and communication with coworkers.<sup>3</sup> It is considered an indicator of the sustainability of the health system and quality of work-life.<sup>4</sup> It directly affects patient satisfaction due to the interaction of employees with patients.<sup>4</sup>

Professional self-esteem is a concept that has a significant impact on behavioural achievements, and can predict individual professional achievements which has a significant impact on clinical trials.<sup>5</sup> The process of forming a professional self is a unique journey. It is affected by many internal and external factors.<sup>6</sup> On this basis, professional self-esteem can be defined as the subjective acceptance of the characteristics of a physician with professionalism and clinical skill.<sup>7</sup> In addition, the identity of a physician is defined as an individual in whom the medical profession's characteristics, values and norms are internalised and, as a result, thinks, acts and feels like a doctor.<sup>8</sup> High self-esteem has been shown to increase productivity.<sup>9</sup> Family medicine practitioners struggle alone with limited resources in more isolated conditions.<sup>10</sup> Among the factors affecting job satisfaction, which is one of the important determinants for physicians to be successful, happy and productive autonomy can be affected by a variety of features, such as colleagues/staff/patient relationships, income, health resources, social reputation, personal leisure time, management, restrictions and regulations, and working hours.<sup>11</sup> The steps to be taken to determine and improve the level of job satisfaction will increase the efficiency of family physicians and the level of satisfaction with primary health care services.<sup>12</sup> Finally, no study has been found in Türkiye on professional self-esteem for Family Medicine.

In this context, our study was planned considering that family physicians can comparatively examine the factors affecting job satisfaction, determine the factors that decrease satisfaction, make suggestions that can increase satisfaction, and contribute to the connection with professional self-esteem.

## MATERIALS AND METHODS

**Ethical Aspect of the Study** Our study was approved by the Giresun University Non-Interventional Ethics Committee (Date: 18.03.2021, decision No: 25). Approval numbered E-41544352-799 was obtained from the Provincial Health Directorate. The study

was conducted by the International Declaration of Helsinki.

**Information and Parameters:** The descriptive cross-sectional study was conducted between April 2021 and April 2022. Our population consists of 155 individuals practising Family Medicine in Giresun province. Epi Info (Centers for Disease Control and Prevention) was used for sample selection. The population size was calculated as 126 with a 5% margin of error at 99% confidence interval. One hundred twenty-eight individuals were reached.

**Subjects and Methods:** A three-part data collection form was applied to family medicine practitioners who agreed to participate in the research. Socio-demographic descriptive and job-related questions (age, gender, marital status, speciality status, professional years, total professional years in family medicine, number of patients cared for daily, and physical status of the family health centre, as well as the Minnesota Job Satisfaction Scale and the Arıcak Professional Self-Esteem scales were applied. The survey was applied face-to-face and online (via WhatsApp groups, and mail communities).

**The Minnesota Job Satisfaction Scale (MISS):** It was developed by Dawis, Weiss, England, and Lofquist in 1967 in the form of one hundred questions.<sup>13</sup> It was adapted into Turkish, and its validity and reliability study was carried out by Baycan<sup>14</sup> in 1985, with the internal consistency coefficient being found to be 0.77. According to the reliability analysis of the Minnesota Job Satisfaction Scale, which we used to measure the level of job satisfaction in our study, the Cronbach-alpha values of general, intrinsic and extrinsic job satisfaction were found to be 0.932, 0.917 and 0.83, respectively. The scale was designed as a long and short form and, in our study, a short form consisting of twenty items with features that detect intrinsic and extrinsic satisfaction factors was used. The scale is a five-point Likert type scored between 1 and 5 with the scoring conducted as '1=Not at all satisfied, 2=Not satisfied, 3=I am undecided, 4=I am satisfied, and 5=Very satisfied'. Using the scale, general satisfaction, internal and external satisfaction scores can be determined.

**The Arıcak Professional Self-Esteem Scale** aims to measure the attitudes of individuals aged seventeen and over who have received training or were practising a profession based on their respect for the job.<sup>15</sup> In 1999, the "Arıcak Professional Self-Esteem" scale developed by Arıcak, consisting of 30 items was used. In Arıcak's study, the Cronbach's alpha reliability coefficient of the scale was 0.93, and the test-retest reliability coefficient was 0.90. For content validity, 34 experts from 9 different universities were consulted. The items accepted by 75% of the expert group were included in the scale, while

the others were removed. Factor analysis technique was used to test construct validity. There is no cut-off value, and high scores indicate increased professional self-esteem. According to the reliability analysis of the professional self-esteem scale of the family physicians participating in our study, the Cronbach Alpha value was found to be 0.706. In our study, the professional self-esteem score also increases as the age variable increases. The scale was prepared in a five-point Likert type. The evaluation was as follows: In the positive sentences in the Professional Self-Esteem Scale, Totally Agree 5, Agree 4, Undecided 3, Disagree 2, and Never Disagree 1 were scored. Any negative sentences were scored oppositely.

**Statistical Analysis:** IBM SPSS v20.0 program was used for the data analysis. According to the results of normality tests, a student t-test and the Pearson Correlation Coefficient test were used when the data met the normal distribution condition, and the Mann-Whitney U test, Kruskal-Wallis test and Spearman Correlation test were used when the data did not meet the normal distribution conditions. The statistical significance level was accepted as  $p < 0.05$ .

**RESULTS**

The demographic data of 128 physicians who participated in the survey were categorised according to frequency distributions. Of the physicians who participated in the study, 70.3% were male and 29.7% were female. Considering the age distribution of the physicians participating in the study, the highest participation was found in the 41-50 age group, while the lowest participation was found in the 26-30 age group with 5.5%. When the speciality status of the physicians was examined, 86.7% were general practitioners, 7.8% were family medicine specialists, and 5.5% received speciality training with Family medicine speciality training to be provided to Contractual Family Physicians (CFPs) (Table 1).

The mean and standard deviation values of Minnesota general job satisfaction were calculated based on the age variable. This table explains that the mean of general job satisfaction of 7 individuals between the ages of 26-30 was  $61.86 \pm 16.25$ , and the mean of general job satisfaction of 18 individuals between the ages of 31-35 was  $59.33 \pm 15.22$ . It is seen that the age group with the highest mean of general job satisfaction is individuals aged 51-55 with a value of 62.81, and the age group with the

**Table 1:** Demographic data.

Variables		All individuals n (%)
<b>Gender</b>	Male	90 (70.3)
	Female	38 (29.7)
<b>Ages</b>	Between 26-30	7 (5.5)
	Between 31-35	18 (14.1)
	Between 36-40	26 (20.3)
	Between 41-50	49 (38.3)
	Between 51-55	16 (12.5)
	56 and over	12 (9.4)
<b>Marital Status</b>	Single	14 (10.9)
	Married	114 (89.1)
<b>Your Specialization</b>	I am a family medicine specialist	10 (7.8)
	I am a general practitioner	111 (86.7)
	I am Contractual Family Physicians (CFPs)	7 (5.5)
<b>Your Total Professional Years</b>	Between 2-12 years	45 (35.2)
	Between 13-22 years	45 (35.2)
	Between 23-32 years	29 (22.7)
	32 years and more	9 (7.0)
<b>How Many Years Working in a Family Medicine Practice?</b>	Between 1-5	32 (25.0)
	Between 6-10	33 (25.8)
	11 and more	63 (49.2)
<b>How Many Patients Do You Examine in a Day?</b>	Between 20-40	30 (23.4)
	Between 41-60	48 (37.5)
	Between 61-80	41 (32.0)
	81 and more	9 (7.0)
<b>Are You Satisfied with the FHC's Physical Conditions?</b>	I'm undecided	15 (11.7)
	I agree	59 (46.1)
	I do not agree	31 (24.2)
	I totally agree	10 (7.8)
	I totally disagree	13 (10.2)

lowest mean of general job satisfaction is individuals over 56 with a value of 57.92 (Table 2).

Whether there is a relationship between the numerical variable "How many years have you been working in family medicine practice?" and the variables of the professional self-esteem scale, Minnesota general job satisfaction, intrinsic job satisfaction and extrinsic job satisfaction were examined one by one. The Spearman Correlation test was used to analyse the data. When the results are examined, it is seen that the p-value of the age variable and the number of occupational self's scale variables is 0.004. p-value less than 0.05 indicates that there is a relationship between these two variables. If it is concluded that there is a relationship between them, then the correlation coefficient is examined to look at the degree and direction of the relationship. The correlation coefficient was found to be 0.25. This value indicates a positive relationship. A value between 0 and 0.25 indicates a very weak relationship, between 0.26 and 0.49 indicates a weak relationship, between 0.50 and 0.69 indicates a moderate relationship, be-

tween 0.70 and 0.89 indicates a high relationship, and a value greater than 0.90 indicates a strong relationship. In this case, it shows that there is a weak positive relationship between the numerical variable "How many years have you been working in family medicine practice?" and the scale of professional self-esteem. In other words, as the value of how many years you have been working in family medicine practice increases, the professional self-esteem score also increases (Table 3).

No significant relationship was found between the specialisation status of family physicians and the physical conditions of the FHCs they work with and their professional self-esteem. It has been concluded that there is a moderate positive relationship between professional self-esteem and general job satisfaction and internal job satisfaction, and a weak positive relationship with external job satisfaction. The professional self-esteem score was found to be 112.48 in family physicians, and a similar result was obtained with the mean scores of other occupational groups (Table 4).

**Table 2.** Numerical values of Minnesota General Job Satisfaction by age variable.

Age range	Minnesota Overall Job Satisfaction	
	Mean±SD	n
26-30	1.86±16.25	7
31-35	59.33±15.22	18
36-40	60.46±13.48	26
41-50	58.08±15.04	49
51-55	62.81±15.35	16
56 and over	57.92±11.45	12
<b>Total</b>	<b>59.52±14.38</b>	<b>128</b>

**Table 3.** How many years have you been working in Family Medicine Practice?.

Spearman Correlation Test		Years of work in Family Medicine	Professional Self-Esteem Scale	Minnesota Overall Job Satisfaction	Intrinsic Job Satisfaction	Extrinsic Job Satisfaction
Years of work in Family Medicine	Correlation Coefficient	1.000	0.250*	0.052	0.053	0.107
	p-value	0.05	0.004	0.557	0.554	0.230
	n	128	128	128	128	128

\*: The correlation coefficient was found to be 0.250; This value indicates a positive relationship.

**Table 4.** Family medicine speciality status, Professional Self and General Job Satisfaction and its sub-dimensions.

		Profesyonel Self-Esteem Scale	Minnesota Overall Job Satisfaction	Intrinsic Job Satisfaction	Extrinsic Job Satisfaction
<b>Total Mean±SD</b>		112.48±18.37	2.97±0.71	3.08±0.76	2.81±0.76
<b>Your Specialization Mean±SD</b>	<b>I am a family medicine specialist</b>	122±13.92	2.78±0.81	3.0±1.12	2.43±0.06
	<b>I am a general practitioner</b>	111.8±17.95	2.99±0.71	3.08±0.73	2.86±0.76
	<b>I am Contractual Family Physicians (CFPs)</b>	108.43±27.62	3.0±0.77	3.22±0.86	2.66±0.77
	<b>p-value</b>	0.186	0.448	0.479	0.144

## DISCUSSION AND CONCLUSION

We accessed 128 of 155 family physicians working in the Giresun province family health centres, and we reached two important results in our study examining the factors affecting the level of job satisfaction of family physicians and its relationship with professional self-esteem. The first of these is the conclusion that the professional self-esteem levels of family physicians are positively related to age, total professional years, total working years in family medicine and the average number of patients cared for daily. The other is a moderately positive and significant relationship between professional self-esteem levels and general and internal job satisfaction, as well as a weak positive significant relationship between professional self-esteem and external job satisfaction.

In a study on job satisfaction among family physicians in Saudi Arabia, it was reported that physicians were highly satisfied with their career choices, regardless of gender, age, public or private, and marital status.<sup>16</sup> In another study on effort-reward imbalance and job satisfaction of 1,105 family medicine practitioners in China, it was revealed that age, education, job rank, type of institution, working year and monthly income, were factors affecting job satisfaction and that the general job satisfaction level was relatively low.<sup>17</sup> In this study, no significant relationship was found between age, gender and marital status as demographic factors of job satisfaction of family physicians and general job satisfaction and its sub-dimensions.

In a study on the job satisfaction of primary care physicians in China, physicians with longer years of service were reported to be less satisfied than other physicians.<sup>18</sup> Another study reported that those who worked in their occupations for 16-20 years were more satisfied with their jobs.<sup>17</sup> In this study, a significant positive result was obtained between the total professional years in medicine and the level of professional self-esteem in family medicine practice. According to this, it was observed that the level of professional self-esteem increased as the total number of professional years in medicine and working years in family medicine increased. As the value of professional self-esteem increases, the values of general job satisfaction, internal job satisfaction and external job satisfaction also increase.

In a study comparing the factors associated with occupational satisfaction/dissatisfaction among family physicians in two regions affiliated with the Ministry of Health, it was shown that 84% and 78% of family medicine participants were satisfied and that most of them were willing to choose the same speciality another time if given a chance.<sup>19</sup> In this study, general job satisfaction, internal job satisfaction and external job satisfaction were found to be moderate

by the literature, and internal job satisfaction was higher than external job satisfaction.

Professional self-esteem reflects an individual's professional self-understanding, self-esteem, and behavioural orientations, including knowledge, skills, flexibility, leadership, communication ability, and satisfaction with their profession.<sup>5</sup> Again, in a study conducted with 1,083 nursing faculty students in China, it was shown that a positive professional self-concept reduces the level of academic burnout.<sup>20</sup> An awareness of burnout has increased significantly in recent years.<sup>21</sup> In this study, it was found that 50.8% of family medicine practitioners respected their profession greatly, and were not affected by the speciality and the physical conditions of the FHC. In addition, it was concluded that professional self-esteem increased significantly as the total working time in medicine, the total time worked in family medicine practice and the average number of patients cared for daily increased.

In conclusion, a positive relationship was found between job satisfaction and professional self-esteem among family medicine physicians, as with other occupational groups. This is a praise for Family Medicine as a medical speciality. We are moving towards our goals of high service satisfaction and adopting a healthy lifestyle in line with our country's strong primary healthcare vision. There are many deficiencies and weak points in our study. These are the following: not being able to access all our family physicians; conducting the study only in a city centre; not making a distinguishing between urban and rural; and not evaluating the results according to the family medicine class. The originality of our study is that it is the first study to examine the relationship between job satisfaction and professional self-esteem in family physicians. With our study results, more studies are needed to reach definitive conclusions.

**Ethics Committee Approval:** Our study was approved by the Giresun University Non-Interventional Ethics Committee (Date: 18.03.2021, decision No: 25). Approval numbered E-41544352-799 was obtained from the Provincial Health Directorate. The study was conducted by the International Declaration of Helsinki.

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## The Factors Affecting the Level of Job Satisfaction of Family Physicians and their Relationship with Professional Self-Esteem

### Aile Hekimlerinin İş Doyumu Düzeyini Etkileyen Faktörler ve Mesleki Benlik Saygısı İle İlişkisi

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#### ABSTRACT

**Objective:** The study aimed to investigate the relationship between job satisfaction and professional self-esteem levels of family medicine practitioners working in Family Health Center.

**Materials and Methods:** Between April 2021 and April 2022, 128 family physicians who volunteered from 155 family physicians working in family health centres in Giresun province were included in the study. The socio-demographic descriptive form, the Minnesota Job Satisfaction and Occupational Self-Esteem Scales were administered face-to-face and online (via WhatsApp groups and e-mail communities).

**Results:** There was no significant relationship between job satisfaction and its sub-dimensions with age, gender, marital status, specialisation status, physical conditions of the Family Health Center, total years of practice and years of training in family medicine ( $p>0.05$ ). The mean level of occupational self-esteem was 112.48. It was found to be significantly positively correlated with age, total years of practice, years of family medicine practice and average number of patients seen ( $p=0.05$ ,  $p=0.004$ ,  $p=0.004$ ,  $p=0.004$ ,  $p=0.009$ , respectively).

**Conclusion:** Professional self-esteem levels increase as professional age, total years of profession, and total years of working in family medicine increase.

**Keywords:** Family physicians, job satisfaction, professional self-esteem

#### ÖZ

**Amaç:** Bu çalışmada Aile Sağlığı Merkezi'nde görev yapan aile hekimliği uygulayıcılarının iş doyumları ile mesleki benlik saygısı düzeyleri arasındaki ilişkisini araştırmak amaçlanmıştır.

**Materyal ve Metot:** Nisan 2021- Nisan 2022 tarihleri arasında Giresun ilinde aile sağlığı merkezlerinde görev yapan 155 aile hekiminden gönüllü olan 128 aile hekimi çalışmaya dahil edilmiştir. Sosyo-demografik tanımlayıcı form, Minnesota İş Doyum ve Mesleki Benlik Saygısı Ölçekleri yüz yüze ve online (whatsapp grupları, e-posta toplulukları aracılığıyla) olarak uygulandı.

**Bulgular:** İş doyum ve alt boyutları ile yaş, cinsiyet, medeni durum, uzmanlık durumu, Aile Sağlığı Merkezinin fiziki koşulları, toplam çalışma yılı ve aile hekimliği çalışma yılı arasında anlamlı bir ilişki bulunmamıştır ( $p>0,05$ ). Mesleki benlik saygısı düzeyi ortalaması 112,48 bulunmuş olup yaş, toplam meslek yılı, aile hekimliğinde çalışma süresi ve ortalama bakılan hasta sayısı ile anlamlı pozitif ilişkili bulunmuştur (sırasıyla  $p=0,05$ ,  $p=0,004$ ,  $p=0,004$ ,  $p=0,009$ ).

**Sonuç:** Mesleki yaş, toplam meslek yılı, aile hekimliğinde toplam çalışma yılı arttıkça mesleki benlik saygısı düzeyleri artmaktadır.

**Anahtar Kelimeler:** Aile hekimliği, iş doyum, mesleki benlik saygısı

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## INTRODUCTION

Primary health care is an important part of a country's health care system and plays a central role.<sup>1</sup> It is the first contact area of individuals with the health care system.<sup>2</sup> Burnout is more common among frontline physicians, as in family medicine.<sup>3</sup>

Job satisfaction can be defined as the general attitude of employees towards certain elements of their work, such as their job, work environment and communication with coworkers.<sup>3</sup> It is considered an indicator of the sustainability of the health system and quality of work-life.<sup>4</sup> It directly affects patient satisfaction due to the interaction of employees with patients.<sup>4</sup>

Professional self-esteem is a concept that has a significant impact on behavioural achievements, and can predict individual professional achievements which has a significant impact on clinical trials.<sup>5</sup> The process of forming a professional self is a unique journey. It is affected by many internal and external factors.<sup>6</sup> On this basis, professional self-esteem can be defined as the subjective acceptance of the characteristics of a physician with professionalism and clinical skill.<sup>7</sup> In addition, the identity of a physician is defined as an individual in whom the medical profession's characteristics, values and norms are internalised and, as a result, thinks, acts and feels like a doctor.<sup>8</sup> High self-esteem has been shown to increase productivity.<sup>9</sup> Family medicine practitioners struggle alone with limited resources in more isolated conditions.<sup>10</sup> Among the factors affecting job satisfaction, which is one of the important determinants for physicians to be successful, happy and productive autonomy can be affected by a variety of features, such as colleagues/staff/patient relationships, income, health resources, social reputation, personal leisure time, management, restrictions and regulations, and working hours.<sup>11</sup> The steps to be taken to determine and improve the level of job satisfaction will increase the efficiency of family physicians and the level of satisfaction with primary health care services.<sup>12</sup> Finally, no study has been found in Türkiye on professional self-esteem for Family Medicine.

In this context, our study was planned considering that family physicians can comparatively examine the factors affecting job satisfaction, determine the factors that decrease satisfaction, make suggestions that can increase satisfaction, and contribute to the connection with professional self-esteem.

## MATERIALS AND METHODS

**Ethical Aspect of the Study** Our study was approved by the Giresun University Non-Interventional Ethics Committee (Date: 18.03.2021, decision No: 25). Approval numbered E-41544352-799 was obtained from the Provincial Health Directorate. The study

was conducted by the International Declaration of Helsinki.

**Information and Parameters:** The descriptive cross-sectional study was conducted between April 2021 and April 2022. Our population consists of 155 individuals practising Family Medicine in Giresun province. Epi Info (Centers for Disease Control and Prevention) was used for sample selection. The population size was calculated as 126 with a 5% margin of error at 99% confidence interval. One hundred twenty-eight individuals were reached.

**Subjects and Methods:** A three-part data collection form was applied to family medicine practitioners who agreed to participate in the research. Socio-demographic descriptive and job-related questions (age, gender, marital status, speciality status, professional years, total professional years in family medicine, number of patients cared for daily, and physical status of the family health centre, as well as the Minnesota Job Satisfaction Scale and the Arıcak Professional Self-Esteem scales were applied. The survey was applied face-to-face and online (via WhatsApp groups, and mail communities).

**The Minnesota Job Satisfaction Scale (MISS):** It was developed by Dawis, Weiss, England, and Lofquist in 1967 in the form of one hundred questions.<sup>13</sup> It was adapted into Turkish, and its validity and reliability study was carried out by Baycan<sup>14</sup> in 1985, with the internal consistency coefficient being found to be 0.77. According to the reliability analysis of the Minnesota Job Satisfaction Scale, which we used to measure the level of job satisfaction in our study, the Cronbach-alpha values of general, intrinsic and extrinsic job satisfaction were found to be 0.932, 0.917 and 0.83, respectively. The scale was designed as a long and short form and, in our study, a short form consisting of twenty items with features that detect intrinsic and extrinsic satisfaction factors was used. The scale is a five-point Likert type scored between 1 and 5 with the scoring conducted as '1=Not at all satisfied, 2=Not satisfied, 3=I am undecided, 4=I am satisfied, and 5=Very satisfied'. Using the scale, general satisfaction, internal and external satisfaction scores can be determined.

**The Arıcak Professional Self-Esteem Scale** aims to measure the attitudes of individuals aged seventeen and over who have received training or were practising a profession based on their respect for the job.<sup>15</sup> In 1999, the "Arıcak Professional Self-Esteem" scale developed by Arıcak, consisting of 30 items was used. In Arıcak's study, the Cronbach's alpha reliability coefficient of the scale was 0.93, and the test-retest reliability coefficient was 0.90. For content validity, 34 experts from 9 different universities were consulted. The items accepted by 75% of the expert group were included in the scale, while

the others were removed. Factor analysis technique was used to test construct validity. There is no cut-off value, and high scores indicate increased professional self-esteem. According to the reliability analysis of the professional self-esteem scale of the family physicians participating in our study, the Cronbach Alpha value was found to be 0.706. In our study, the professional self-esteem score also increases as the age variable increases. The scale was prepared in a five-point Likert type. The evaluation was as follows: In the positive sentences in the Professional Self-Esteem Scale, Totally Agree 5, Agree 4, Undecided 3, Disagree 2, and Never Disagree 1 were scored. Any negative sentences were scored oppositely.

**Statistical Analysis:** IBM SPSS v20.0 program was used for the data analysis. According to the results of normality tests, a student t-test and the Pearson Correlation Coefficient test were used when the data met the normal distribution condition, and the Mann-Whitney U test, Kruskal-Wallis test and Spearman Correlation test were used when the data did not meet the normal distribution conditions. The statistical significance level was accepted as  $p < 0.05$ .

**RESULTS**

The demographic data of 128 physicians who participated in the survey were categorised according to frequency distributions. Of the physicians who participated in the study, 70.3% were male and 29.7% were female. Considering the age distribution of the physicians participating in the study, the highest participation was found in the 41-50 age group, while the lowest participation was found in the 26-30 age group with 5.5%. When the speciality status of the physicians was examined, 86.7% were general practitioners, 7.8% were family medicine specialists, and 5.5% received speciality training with Family medicine speciality training to be provided to Contractual Family Physicians (CFPs) (Table 1).

The mean and standard deviation values of Minnesota general job satisfaction were calculated based on the age variable. This table explains that the mean of general job satisfaction of 7 individuals between the ages of 26-30 was  $61.86 \pm 16.25$ , and the mean of general job satisfaction of 18 individuals between the ages of 31-35 was  $59.33 \pm 15.22$ . It is seen that the age group with the highest mean of general job satisfaction is individuals aged 51-55 with a value of 62.81, and the age group with the

**Table 1:** Demographic data.

Variables		All individuals n (%)
<b>Gender</b>	Male	90 (70.3)
	Female	38 (29.7)
<b>Ages</b>	Between 26-30	7 (5.5)
	Between 31-35	18 (14.1)
	Between 36-40	26 (20.3)
	Between 41-50	49 (38.3)
	Between 51-55	16 (12.5)
	56 and over	12 (9.4)
<b>Marital Status</b>	Single	14 (10.9)
	Married	114 (89.1)
<b>Your Specialization</b>	I am a family medicine specialist	10 (7.8)
	I am a general practitioner	111 (86.7)
	I am Contractual Family Physicians (CFPs)	7 (5.5)
<b>Your Total Professional Years</b>	Between 2-12 years	45 (35.2)
	Between 13-22 years	45 (35.2)
	Between 23-32 years	29 (22.7)
	32 years and more	9 (7.0)
<b>How Many Years Working in a Family Medicine Practice?</b>	Between 1-5	32 (25.0)
	Between 6-10	33 (25.8)
	11 and more	63 (49.2)
<b>How Many Patients Do You Examine in a Day?</b>	Between 20-40	30 (23.4)
	Between 41-60	48 (37.5)
	Between 61-80	41 (32.0)
	81 and more	9 (7.0)
<b>Are You Satisfied with the FHC's Physical Conditions?</b>	I'm undecided	15 (11.7)
	I agree	59 (46.1)
	I do not agree	31 (24.2)
	I totally agree	10 (7.8)
	I totally disagree	13 (10.2)

lowest mean of general job satisfaction is individuals over 56 with a value of 57.92 (Table 2).

Whether there is a relationship between the numerical variable "How many years have you been working in family medicine practice?" and the variables of the professional self-esteem scale, Minnesota general job satisfaction, intrinsic job satisfaction and extrinsic job satisfaction were examined one by one. The Spearman Correlation test was used to analyse the data. When the results are examined, it is seen that the p-value of the age variable and the number of occupational self's scale variables is 0.004. p-value less than 0.05 indicates that there is a relationship between these two variables. If it is concluded that there is a relationship between them, then the correlation coefficient is examined to look at the degree and direction of the relationship. The correlation coefficient was found to be 0.25. This value indicates a positive relationship. A value between 0 and 0.25 indicates a very weak relationship, between 0.26 and 0.49 indicates a weak relationship, between 0.50 and 0.69 indicates a moderate relationship, be-

tween 0.70 and 0.89 indicates a high relationship, and a value greater than 0.90 indicates a strong relationship. In this case, it shows that there is a weak positive relationship between the numerical variable "How many years have you been working in family medicine practice?" and the scale of professional self-esteem. In other words, as the value of how many years you have been working in family medicine practice increases, the professional self-esteem score also increases (Table 3).

No significant relationship was found between the specialisation status of family physicians and the physical conditions of the FHCs they work with and their professional self-esteem. It has been concluded that there is a moderate positive relationship between professional self-esteem and general job satisfaction and internal job satisfaction, and a weak positive relationship with external job satisfaction. The professional self-esteem score was found to be 112.48 in family physicians, and a similar result was obtained with the mean scores of other occupational groups (Table 4).

**Table 2.** Numerical values of Minnesota General Job Satisfaction by age variable.

Age range	Minnesota Overall Job Satisfaction	
	Mean±SD	n
26-30	1.86±16.25	7
31-35	59.33±15.22	18
36-40	60.46±13.48	26
41-50	58.08±15.04	49
51-55	62.81±15.35	16
56 and over	57.92±11.45	12
<b>Total</b>	<b>59.52±14.38</b>	<b>128</b>

**Table 3.** How many years have you been working in Family Medicine Practice?.

Spearman Correlation Test		Years of work in Family Medicine	Professional Self-Esteem Scale	Minnesota Overall Job Satisfaction	Intrinsic Job Satisfaction	Extrinsic Job Satisfaction
Years of work in Family Medicine	Correlation Coefficient	1.000	0.250*	0.052	0.053	0.107
	p-value	0.05	0.004	0.557	0.554	0.230
	n	128	128	128	128	128

\*: The correlation coefficient was found to be 0.250; This value indicates a positive relationship.

**Table 4.** Family medicine speciality status, Professional Self and General Job Satisfaction and its sub-dimensions.

		Profesyonel Self-Esteem Scale	Minnesota Overall Job Satisfaction	Intrinsic Job Satisfaction	Extrinsic Job Satisfaction
<b>Total Mean±SD</b>		112.48±18.37	2.97±0.71	3.08±0.76	2.81±0.76
<b>Your Specialization Mean±SD</b>	<b>I am a family medicine specialist</b>	122±13.92	2.78±0.81	3.0±1.12	2.43±0.06
	<b>I am a general practitioner</b>	111.8±17.95	2.99±0.71	3.08±0.73	2.86±0.76
	<b>I am Contractual Family Physicians (CFPs)</b>	108.43±27.62	3.0±0.77	3.22±0.86	2.66±0.77
	<b>p-value</b>	0.186	0.448	0.479	0.144

## DISCUSSION AND CONCLUSION

We accessed 128 of 155 family physicians working in the Giresun province family health centres, and we reached two important results in our study examining the factors affecting the level of job satisfaction of family physicians and its relationship with professional self-esteem. The first of these is the conclusion that the professional self-esteem levels of family physicians are positively related to age, total professional years, total working years in family medicine and the average number of patients cared for daily. The other is a moderately positive and significant relationship between professional self-esteem levels and general and internal job satisfaction, as well as a weak positive significant relationship between professional self-esteem and external job satisfaction.

In a study on job satisfaction among family physicians in Saudi Arabia, it was reported that physicians were highly satisfied with their career choices, regardless of gender, age, public or private, and marital status.<sup>16</sup> In another study on effort-reward imbalance and job satisfaction of 1,105 family medicine practitioners in China, it was revealed that age, education, job rank, type of institution, working year and monthly income, were factors affecting job satisfaction and that the general job satisfaction level was relatively low.<sup>17</sup> In this study, no significant relationship was found between age, gender and marital status as demographic factors of job satisfaction of family physicians and general job satisfaction and its sub-dimensions.

In a study on the job satisfaction of primary care physicians in China, physicians with longer years of service were reported to be less satisfied than other physicians.<sup>18</sup> Another study reported that those who worked in their occupations for 16-20 years were more satisfied with their jobs.<sup>17</sup> In this study, a significant positive result was obtained between the total professional years in medicine and the level of professional self-esteem in family medicine practice. According to this, it was observed that the level of professional self-esteem increased as the total number of professional years in medicine and working years in family medicine increased. As the value of professional self-esteem increases, the values of general job satisfaction, internal job satisfaction and external job satisfaction also increase.

In a study comparing the factors associated with occupational satisfaction/dissatisfaction among family physicians in two regions affiliated with the Ministry of Health, it was shown that 84% and 78% of family medicine participants were satisfied and that most of them were willing to choose the same speciality another time if given a chance.<sup>19</sup> In this study, general job satisfaction, internal job satisfaction and external job satisfaction were found to be moderate

by the literature, and internal job satisfaction was higher than external job satisfaction.

Professional self-esteem reflects an individual's professional self-understanding, self-esteem, and behavioural orientations, including knowledge, skills, flexibility, leadership, communication ability, and satisfaction with their profession.<sup>5</sup> Again, in a study conducted with 1,083 nursing faculty students in China, it was shown that a positive professional self-concept reduces the level of academic burnout.<sup>20</sup> An awareness of burnout has increased significantly in recent years.<sup>21</sup> In this study, it was found that 50.8% of family medicine practitioners respected their profession greatly, and were not affected by the speciality and the physical conditions of the FHC. In addition, it was concluded that professional self-esteem increased significantly as the total working time in medicine, the total time worked in family medicine practice and the average number of patients cared for daily increased.

In conclusion, a positive relationship was found between job satisfaction and professional self-esteem among family medicine physicians, as with other occupational groups. This is a praise for Family Medicine as a medical speciality. We are moving towards our goals of high service satisfaction and adopting a healthy lifestyle in line with our country's strong primary healthcare vision. There are many deficiencies and weak points in our study. These are the following: not being able to access all our family physicians; conducting the study only in a city centre; not making a distinguishing between urban and rural; and not evaluating the results according to the family medicine class. The originality of our study is that it is the first study to examine the relationship between job satisfaction and professional self-esteem in family physicians. With our study results, more studies are needed to reach definitive conclusions.

**Ethics Committee Approval:** Our study was approved by the Giresun University Non-Interventional Ethics Committee (Date: 18.03.2021, decision No: 25). Approval numbered E-41544352-799 was obtained from the Provincial Health Directorate. The study was conducted by the International Declaration of Helsinki.

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## The Effect of Prognostic Factors on Survival in Endometrioid Type Adenocancer

### Endometrioid Tip Adenokanserde Prognostik Faktörlerin Sağkalıma Etkisi

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#### ABSTRACT

**Objective:** The study aims to investigate the prognostic factors in uterine endometrioid adenocarcinoma that affect survival outcomes.

**Materials and Methods:** This retrospective study includes 144 cases which underwent surgical treatment for uterine endometrioid adenocarcinoma. Demographic data and tumour characteristics were evaluated for lymph node metastasis. Stage I and grade 1-2 tumours were divided into lymphadenectomy and non-lymphadenectomy groups, and 5-year survival was assessed.

**Results:** The presence of myometrial invasion of more than 1/2, adnexal metastasis and lymphovascular space invasion were found to be associated with lymph node metastasis ( $p=0.010$  ve  $0.019$  ve  $0.015$ ). In our study, the 5-year survival rate was 87.4%. Survival rate was correlated with age, myometrial invasion, and tumour grade. The 5-year survival rates were 89.8% in lymphadenectomy group and 85.2% in non-lymphadenectomy group, and no statistically significant difference was observed ( $p=0.575$ ).

**Conclusion:** Myometrial invasion, grade and the age of diagnosis were detected as important prognostic factors of uterine endometrioid adenocarcinomas. We concluded that lymphadenectomy did not increase the survival rate of stage I grade 1-2 endometrioid tumours. Lymphadenectomy may not be performed in stage I grade 1-2 tumours; thus, the morbidities of lymphadenectomy can be avoided.

**Keywords:** Endometrial cancer, lymphadenectomy, prognostic factors

#### ÖZ

**Amaç:** Uterusun endometrioid tip adenokanserlerinde prognostik faktörlerin sağ kalıma etkisini saptamayı amaçladık.

**Materyal ve Metot:** Kliniğimizde 2006 Mayıs- 2012 Mayıs arasında endometrium kanseri nedeniyle cerrahi tedavi uygulanan histolojik tipi Endometrioid Adenokarsinom olan 144 olgu çalışmaya dahil edildi. Demografik veriler ve tümör özelliklerinin lenf nodu metastazı ve sağ kalıma ilişkisi değerlendirildi. Evre I grade 1-2 tümörler lenfadenektomi yapılanlar ve yapılmayanlar olarak gruplandırılarak 5 yıllık sağ kalım değerlendirildi.

**Bulgular:** Miyometriyal invazyonun  $>1/2$  den fazla olmasının, adneksiyal tutulumun ve lenfovasküler alan invazyon varlığının lenf nodu metastazı ile ilişkili olduğu izlenmiştir ( $p=0,010$ ,  $0,019$  ve  $0,015$ ). 5 yıllık sağ kalım %87,4 olarak bulunmuştur. Yaş, miyometriyal invazyon ve tümörün grade'nin sağ kalım ile ilişkili olduğu gözlenmiştir. 5 yıllık sağ kalım lenfadenektomi yapılan grupta %89,8, lenfadenektomi yapılmayan grupta ise %85,2 olarak hesaplanmıştır ve aralarında istatistiksel olarak anlamlı bir fark izlenmemiştir ( $p=0,575$ ).

**Sonuç:** Miyometriyal invazyon, adneksiyal tutulum ve lenfovasküler alan invazyon varlığının önemli birer prognostik faktör olduğunu belirledik. Evre I grade 1-2 tümörlerde lenfadenektominin sağ kalımı arttırmadığını saptadık. Evre I grade 1-2 tümör varlığında lenfadenektomi yapılmayabilir. Böylece lenfadenektominin hastaya yükleyeceği morbiditeden kaçınılabılır.

**Anahtar Kelimeler:** Endometrium kanseri, lenfadenektomi, prognostik faktör

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## INTRODUCTION

Endometrial cancer is the most common malignancy of the female urogenital system in developed countries and the second most common cancer after cervical cancer in developing countries.<sup>1</sup> According to the International Agency for Research on Cancer, 382069 new cases are reported each year.<sup>2</sup> In the United States, uterine corpus cancer is the fourth most common cancer, and in 2023 approximately 66200 new cases are expected to be reported and 13030 cases to result in death.<sup>3</sup>

The main risk factor of endometrial cancer is unopposed estrogen. In postmenopausal women, adipose tissue is an important source of endogenous estrogen, and obesity is an important risk factor for endometrial cancer.<sup>6</sup>

It is essential to determine endometrial cancer's clinical and histopathological features for optimal treatment. The rates of pelvic and paraaortic lymph node metastasis in all patients diagnosed with endometrial cancer are 9% and 5%, respectively.<sup>7</sup> Nowadays, systemic pelvic lymph node dissection has no proven benefit or harm at stage 1 endometrial carcinoma.<sup>8</sup> But, many retrospective studies have shown that the role of systemic pelvic and para-aortic lymphadenectomy was to increase the survival of patients with moderate and high risk for lymph node metastasis.<sup>9</sup>

We aimed to analyse the prognostic factors in endometrioid adenocarcinoma and to evaluate the correlation between the characteristics of the tumour and survival.

## MATERIALS AND METHODS

**Ethics Committee Approval:** This study was supported by Kocaeli University Scientific Research Projects Coordination Unit as KÜ GOKAEK 2018/9 scientific research project and approved by the ethics committee. (Date: 19.01.2018, decision no: 2018/9).

**Material and Methods:** The study included 206 patients with tumour histologic type Endometrioid Adenocarcinoma treated for endometrial cancer between May 2006 and May 2012 in Kocaeli University Faculty of Medicine, Department of Obstetrics and Gynecology. The data from 144 patients were accessed and incorporated into this study. The data was derived from the patient's pathology report. The demographic data, including age, diabetes mellitus (DM), hypertension (HT), parity, concomitant malignant disease, family history and smoking, were retrospectively evaluated from the records. At the same time, the pathology reports were examined to determine the surgical stages, tumour size, myometrial invasion, cervical involvement, adnexal involvement, peritoneal cytology, lymphovascular space invasion, and lymph node metastasis. The

patients were divided into two groups according to lymph node metastasis. The demographic data and tumour characteristics correlation between lymph node metastasis were evaluated. The factors affecting survival were analysed as multiple and single. Stage I grade 1-2 tumours were divided into two groups as performing lymphadenectomy or not, and 5-year survival was evaluated. The effects of lymphadenectomy on survival were compared between these two groups.

**Statistical Analysis:** All statistical analyses were performed using the IBM SPSS Statistics 20 statistical data program. Continuous variables were expressed as means with standard deviations or medians with quartiles, and categorical variables were expressed as frequencies and percentages. The significance of the difference between the groups was evaluated by Student's t-test. Categorical variables were assessed with Pearson's Chi-square test and Fisher's Exact Test. A p-value of <0.05 was considered statistically significant. The survival rate was estimated with Kaplan-Meier. The factors affecting survival outcomes were evaluated with the Cox Regression test. A p-value of <0.05 was considered statistically significant.

## RESULTS

The study included 206 patients with tumour histologic type Endometrioid Adenocarcinoma who were treated for endometrial cancer between May 2006 and May 2012 in Kocaeli University Faculty of Medicine, Department of Obstetrics and Gynecology. The data from 144 patients were accessed and incorporated into this study.

The mean age of the patients was 58.51±10.15 years, and the mean BMI was 33.42±6.74. 29 (20.10%) of the patients were diagnosed in the premenopausal period, and 115 (79.9%) were diagnosed in the postmenopausal period. It was observed that 69 (47.9%) of the patients had HT, 39 (27.1%) had DM, and 15 (10.4%) were smokers. When the histopathological results of the patients were evaluated, 73 patients had grade 1 tumours, 58 had grade 2 tumours, and 13 had grade 3 tumours. When the patients were examined in terms of myometrial invasion, it was observed that the tumour was limited to the endometrium in 19 patients (12.5%), 98 patients (68.1%) had less than 1/2 and 28 patients (19.4%) had more than 1/2 myometrial invasion. Of the patients (n=99) in whom tumour size was reached in histopathology results, 27 (27.3%) had a tumour size below 2 cm, and 72 (72.7%) had a tumour size above 2 cm. Pelvic lymph node involvement was observed in 8 (7%) of 115 patients who underwent pelvic lymphadenectomy. Paraaortic lymph node involvement was observed in 2 of 48 patients (4.20%) who underwent

paraaortic lymphadenectomy. When the histopathology results were analysed, it was observed that lymphovascular invasion was present in 8 of 106 patients. The cervical stromal invasion was found in 1 patient (0.70%) and adnexal involvement in 10 patients (7.00%). Detailed characteristics of patients are shown in Table 1.

It was demonstrated that pelvic lymph node metastasis was observed in 5 (4.35%) patients with more than 1/2 of myometrial invasion. Therefore, the correlation between more than 1/2 of myometrial invasion and pelvic lymph node metastasis was consid-

ered as statistically significant (p=0.010). 3 (2.61%) patients had both adnexal metastasis and pelvic lymph node metastasis. Adnexal metastasis was associated with pelvic lymph node metastasis (p=0.015). There was a significant correlation between lymphovascular spread and pelvic lymph node metastasis (p=0.019). Lymph node metastasis was observed in 1 patient (5%) with a tumour size <2 cm and 6 (10%) patients with a tumour size ≥2 cm. There was no significant correlation between tumour size and pelvic lymph node metastasis (p=0.667) (Table 2).

**Table 1.** Characteristics of patients.

Characteristics		Statistical Data
Age, Mean ± SD		58.51 ± 10.15
Parity, Mean ± SD		2.98 ± 2.01
BMI, Mean ± SD		33.42 ± 6.74
Hypertension, n (%)		69 (47.90)
DM, n (%)		39 (27.10)
Smoking, n (%)		15 (10.40)
Menopause, n (%)	Premenopause	29 (20.10)
	Postmenopause	115 (79.90)
Tumour grade, n (%)	Grade 1	73 (50.70)
	Grade 2	58 (40.30)
	Grade 3	13 (9.00)
	-	19 (12.50)
Myometrial invasion, n (%)	Less than 1/2	98 (68.10)
	More than 1/2	28 (19.40)
	-	27 (27.30)
Tumour size, n (%)	Less than 2 cm	27 (27.30)
	More than 2 cm	72 (72.70)
Lymphovascular space invasion, n (%)	Negative	98 (92.50)
	Positive	8 (7.50)
Pelvic lymph node metastasis, n (%)	Negative	107 (93.00)
	Positive	8 (7.00)
Paraaortic lymph node metastasis, n (%)	Negative	46 (95.80)
	Positive	2 (4.20)
Cervical invasion, n (%)	Negative	122 (84.70)
	Stromal invasion	1 (0.70)
	Glandular invasion	21 (14.60)
Adnexal metastasis, n (%)	Negative	134 (93.10)
	Positive	10 (6.90)

BMI: Body mass index; DM: Diabetes Mellitus.

**Table 2.** Myometrial invasion, adnexal metastasis, lymphovascular space invasion, tumour size and pelvic lymph node metastasis.

Characteristics		Pelvic Lymph Node Metastasis		p*
		Negative, n (%)	Positive, n (%)	
Myometrial invasion	Less than 1/2	88 (76.5)	3 (2.61)	0.010
	More than 1/2	19 (16.52)	5 (4.35)	
Adnexal metastasis	Negative	101 (87.20)	5 (5.00)	0.015
	Positive	6 (5.21)	3 (2.61)	
Lymphovascular space invasion (n=80)	Negative	72 (90.00)	1 (1.25)	0.019
	Positive	5 (6.25)	2 (2.50)	
Tumour size (n=99)	Less than 2 cm	26 (26.26)	1 (1.01)	0.667
	More than 2 cm	66 (66.66)	6 (6.06)	

\*: Fisher Exact Test

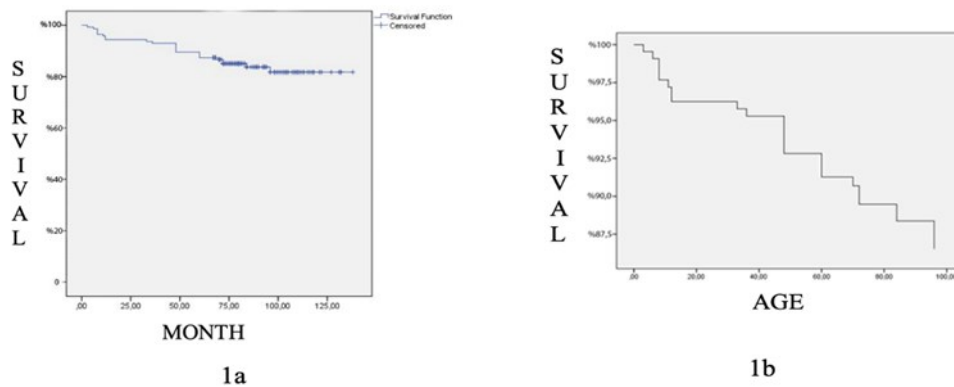


In this study, the 5-year survival rate was calculated as 87.4%. The graph of overall survival is shown in Figure 1a. Comparing age and survival was relatively significant when evaluated alone ( $p=0.000$ ). The relationship between age and survival is shown in Figure 1b.

When survival outcomes were compared with menopause, DM, HT, and smoking, no significant correlation was observed with each other. Comparing age and survival was relatively significant when evaluated alone but was not found to be statistically significant in the multivariate analysis ( $p=0.000$ ;  $\text{Exp}(B)=1.09$ ). A significant correlation was found between myometrial invasion and survival, and myometrial invasion of less than 1/2 was observed to improve

survival by 8.74 times ( $p=0.022$ ;  $\text{Exp}(B)=8.74$ ). There was a significant correlation between grade and survival. Patients' survival with grade 1 tumours was found to be associated with 11.05 times better prognosis than grade 3 tumours ( $p=0.023$ ;  $\text{Exp}(B)=11.05$ ) (Table 3).

Patients with stage 1 grade 1-2 tumours were compared in terms of survival in two groups: 28 patients did not undergo lymphadenectomy, and 88 patients underwent lymphadenectomy. 5-year survival rate was 85.2% in patients without lymphadenectomy, and survival in the group with lymphadenectomy was 89.8%; no statistically significant difference was observed between them ( $p=0.575$ ) (Table 4).



**Figure 1.** Survival rates. **1a:** Overall survival (Kaplan-Meier), **1b:** The relationship between age and survival rate (Kaplan-Meier).

**Table 3.** Factors related to survival rate.

Characteristics	p*	Relative Risk
Age	0.000	1.09
Menopause	0.074	-
DM	0.189	-
HT	0.349	-
Grade	0.023	11.05
Myometrial invasion	0.022	8.74
Pelvic lymph node involvement	0.606	-
Adnexal metastasis	0.712	-
Tumour size	0.305	-
Lymphovascular space invasion	0.573	-

DM: Diabetes Mellitus; HT: Hypertension; \*: Cox regression analysis.

**Table 4.** Stage I Grade 1-2 tumours pelvic lymph node dissection and survival.

Stage I Grade 1-2 tumours	n (%)	5-year survival	p*
Lymph node	Dissection +	88 (75.9)	89.8%
	Dissection -	28 (24.1)	85.2%

\*: Cox Regression Analysis.

## DISCUSSION AND CONCLUSION

Endometrial cancer is typically a disease of the peri / post-menopausal period. The mean age at diagnosis was 63 years, and 90% of cases were above 50.<sup>10</sup> In our study, the mean age of the patients was 58.51 ± 10.15 years. 9 (6.25%) patients were under the age of 40.

Ruterbusch et al.<sup>14</sup> reported the effect of comorbid conditions and racial differences on the survival rates in patients with endometrial cancer. They reported that DM and obesity are not significantly associated with the risk of death due to endometrial cancer in both black and white women. However, they have shown that HT reduces the risk of death in both groups. McVicer et al.<sup>15</sup> reported in a meta-analysis that death rates due to all causes were increased by 42%, and recurrent disease was increased by 23% in diabetic endometrial carcinoma patients. In our study, DM, HT, smoking, and BMI were not found to be significantly associated with survival in the uterine endometrioid adenocarcinoma.

Bak et al.<sup>16</sup> compared grade 1 and grade 2 cases in a group of 171 low-risk endometrial cancer patients in their study and reported that there was a statistically significant difference in disease-free survival (97.5% - 79.3%), although no significant difference in overall survival. In the study of Han et al.<sup>17</sup>, the tumour grade was higher in Stage IB patients compared to Stage IA. They concluded that myometrial invasion in stage IA disease and the histological grade of the tumour in stage IB disease were associated with disease-free survival. Wang et al.<sup>18</sup> have revealed in a meta-analysis that the presence of myometrial invasion of more than ½ is associated with worse survival outcomes. In our study, there was a significant correlation between grade and survival in endometrial cancer, which is consistent with the literature.

The ASTEC study<sup>26</sup> evaluated 1408 patients with endometrial cancer; 704 patients with lymphadenectomy and 704 patients without lymphadenectomy were compared. The 5-year overall survival rate was 81% in the group without lymphadenectomy and 80% in the lymphadenectomy group. Panici et al.<sup>27</sup> compared 264 patients with lymphadenectomy and 250 patients without lymphadenectomy. Early and late postoperative complications were more frequent in the lymphadenectomy group. The 5-year disease-free and overall survival rates were similar in two groups; in patients who underwent lymphadenectomy rates were 81-85.9%; without lymphadenectomy were 81.7-90%. In a study by Zhang et al.,<sup>28</sup> patients with endometrial cancer who underwent surgery were investigated. It was concluded that lymphadenectomy may be avoided in patients with low risk. In our study, patients with Stage 1 grade 1-2 tumours, 28 patients who underwent lymphadenectomy without lymphadenectomy and 88 patients who

underwent lymphadenectomy were compared in terms of survival. In patients without lymphadenectomy, 5-year survival was 85.2%, and the survival rate was 89.8% in patients with lymphadenectomy. No statistically significant difference was observed between them. Our study was found to be compatible with the literature. The missing aspects of our study; the number of patients with advanced stage and lymph node metastasis is low, and cervical involvement was present in only 1 patient. On the other hand, since most of the study patients had stage I tumours, this study provides information about the effect of lymphadenectomy on survival in stage I grade 1-2 tumours.

Endometrial cancer is an important cause of morbidity and mortality among women. Therefore, it is important to determine the risk factors of the disease, to determine the prognostic factors and to standardise the treatment modality.

In conclusion, we found in our study that myometrial invasion, adnexal metastasis and lymphovascular spread were prognostic factors for lymph node metastasis which is an important prognostic factor for endometrial cancer. Our findings were consistent with the current literature. When the factors affecting survival are investigated; we determined that myometrial invasion, grade and age of diagnosis are important prognostic factors for endometrial adenocarcinoma. We concluded that lymphadenectomy does not increase the survival rate in stage I grade 1-2 tumours. Thus, the morbidity of lymphadenectomy to the patient can be avoided. Treatment should be individualised according to the patient's condition when the decision is made for lymphadenectomy.

**Ethics Committee Approval:** This study was supported by Kocaeli University Scientific Research Projects Coordination Unit as KÜ GOKAEK 2018/9 scientific research project and approved by the ethics committee. (Date: 19.01.2018, decision no: 2018/9).

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**Author Contributions:** Concept – MB, AC; Supervision – AC; Materials – MB; Data Collection and Processing – MB, MÇK, LA, EK; Analysis and Interpretation – MB, EK, MÇK, LA; Writing – MB, LA, MÇK, EK.

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## Evaluation of Thyroid Dysfunction in Patients with Atrial Fibrillation

### Atrial Fibrilasyonu olan Hastalarda Tiroid Fonksiyon Bozukluğunun Değerlendirilmesi

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#### ABSTRACT

**Objective:** Atrial fibrillation is a common cardiac arrhythmia and is an important risk factor for ischemic stroke and heart failure. Thyroid hormones have important effects on the cardiovascular system. In this study, we aimed to evaluate the relationship between atrial fibrillation (AF) and thyroid disorders.

**Materials and Methods:** 587 newly diagnosed AF patients who applied to the Cardiology Clinic between January and December 2022 were included in this study. Thyroid function tests of the patients were examined.

**Results:** The mean age of the patients included in the study was  $62.2 \pm 9.8$  years. 62% of the patients were female, and 38% were male. Euthyroid in 539 patients (91.7%), hypothyroidism in 2 patients (0.3%), subclinical hypothyroidism in 11 patients (2%), hyperthyroidism in 23 patients (3.9%), and subclinical hyperthyroidism in 12 patients (2.1%).

**Conclusion:** Atrial Fibrillation is associated with both hyperthyroidism and hypothyroidism. Thyroid dysfunctions are more common in patients with AF than in the normal population. Patients with AF should be screened for thyroid disorders.

**Keywords:** Atrial Fibrillation, hyperthyroidism, hypothyroidism

#### ÖZ

**Amaç:** Atriyal fibrilasyon yaygın bir kardiyak aritmidir ve iskemik inme ve kalp yetmezliği için önemli bir risk faktördür. Tiroid hormonlarının kardiyovasküler sistem üzerinde önemli etkileri vardır. Bu çalışmada atrial fibrilasyon (AF) ile tiroid bozuklukları arasındaki ilişkiyi değerlendirmek amaçlandı.

**Materyal ve Metot:** Bu çalışmaya Ocak – Aralık 2022 arasında Kardiyoloji Kliniğine başvuran yeni tanı almış 587 AF'li hasta alındı. Hastaların tiroid fonksiyon testleri incelendi.

**Bulgular:** Çalışmaya alınan hastaların yaş ortalaması  $62.2 \pm 9.8$  idi. Hastaların %62'si kadın %38'i erkekti. 539 hasta ötiroid (%91,7), 2 hastada hipotiroidi (%0,3), 11 hastada subklinik hipotiroidi (%2), 23 hastada hipertiroidi (%3,9) ve 12 hastada subklinik hipertiroidi (%2,1) tespit edildi.

**Sonuç:** Atrial Fibrilasyon hem hipertiroidi ve hem hipotiroidi ile ilişkilidir. Tiroid fonksiyon bozuklukları AF'li hastalarda normal popülasyona göre daha sık görülür. AF'li hastalar tiroid bozuklukları açısından taranmalıdır.

**Anahtar Kelimeler:** Atrial Fibrilasyon, hipertiroidi, hipotiroidi

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## INTRODUCTION

Atrial fibrillation (AF) is a supraventricular arrhythmia characterized by disorganized, high-rate atrial electrical activity. Atrial fibrillation is the most common arrhythmia worldwide. The prevalence of AF is estimated at 4 per thousand in the general population and increases with age. In two separate studies, the prevalence was reported as 2-4% in the population over 60 years of age and 11.6% in those over 75 years of age. The incidence of AF is also age-related, increasing approximately twice for every ten years in adults. Incidence is given as 2-3 per thousand for the ages 55-64 per year, and 35 per thousand for the age range 85-94 years. AF is an independent risk factor for both cerebrovascular diseases and congestive heart failure.<sup>1-3</sup>

Thyroid hormones affect many systems, especially the cardiovascular system, and urogenital system in the body. The cardiovascular effects of thyroid hormones have been known for a long time. Hyperthyroidism is associated with AF. Subclinical hyperthyroidism is associated with a high resting heart rate, increased atrial and ventricular premature beat frequency, increased left ventricular mass index, and cardiac output. Previous studies on subclinical hyperthyroidism have suggested an increased risk of developing atrial fibrillation. However, overt hypothyroidism is associated with bradycardia, dyslipidemia, hypertension, atherosclerosis, decreased heart rate variability, and increased risk of myocardial infarction. It has been reported in the literature that neither subclinical nor overt hypothyroidism has been found to be a risk factor for AF.<sup>4-6</sup>

In this study, we aimed to reveal the frequency of thyroid dysfunction in newly diagnosed AF patients.

## MATERIALS AND METHODS

**Ethical Statement:** Our study was approved by the xxx University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Date: 14/10/2022, decision no: 310). The study was carried out by the Helsinki Declaration.

**Subject and Study Design:** Patients with atrial fibrillation over the age of 18, who were newly diagnosed with atrial fibrillation, and who applied to the cardiology outpatient clinic of our hospital between 01-01-2022 and 31-12-2022 were included in our study. The diagnosis of AF was made according to the ESC (European Society of Cardiology) 2020 Atrial Fibrillation guidelines.<sup>3</sup>

Irregular R-R intervals (in cases where atrioventricular conduction is not impaired), absence of prominent repetitive P waves and presence of irregular atrial activation in electrocardiography (ECG) were accepted as AF.

Demographic data, chronic disease history, TSH

(Thyroid Stimulating Hormone), and fT<sub>4</sub> (free thyroxine) values of the patients were found using the hospital database.

Patients previously diagnosed with atrial fibrillation, osteoporosis, thyroid dysfunction (hypothyroidism, hyperthyroidism, taking a thyroid hormone, using thyroid medication), thyroid cancer, with a history of radiotherapy to the head and neck region, using amiodarone, digoxin, bisphosphonate, and vitamin K antagonists were excluded from the study.

**Evaluation of Data:** Subclinical hypothyroidism, hypothyroidism, euthyroidism, subclinical hyperthyroidism, and hyperthyroidism diagnoses of the patients were made based on the Turkish Endocrinology and Metabolism Association Thyroid Diseases Diagnosis and Treatment Guide 2020. Patients with TSH > 4.5 µU/L and fT<sub>4</sub> values within normal limits have subclinical hypothyroidism, patients with TSH > 4.5 µU/L and fT<sub>4</sub> values below 22 pmol/L hypothyroidism, TSH (0.35 – 4.5 µU/L) and fT<sub>4</sub> (9-22 pmol) /L) patients with normal limits were considered euthyroid, patients with TSH < 0.35 µU/L and fT<sub>4</sub> values were considered subclinical hyperthyroidism, and patients with TSH < 0.35 µU/L and fT<sub>4</sub> values above 22 pmol/L were considered hyperthyroid.

**Statistical Analysis:** All statistical analyzes were performed using SPSS for Windows (SPSS 20, Inc.). When producing descriptive statistics, continuous variables were presented as mean ± standard or median, and nominal variables as several cases (n) and percentage (%).

## RESULTS

A total of 587 patients were included in the study, 364 (62%) were female, and 223 (38%) were male. The mean age of the patients was 62.2 years. The youngest mean age with a mean age of 60.1 was found in the euthyroid patient group, and the most advanced mean age with a mean age of 70.8 was found in the subclinical hyperthyroidism group. According to the results of thyroid function tests, the patients were divided into five groups subclinical hypothyroidism, hypothyroidism, euthyroidism, subclinical hyperthyroidism, and hyperthyroidism. Euthyroid in 539 patients (91.7%), hypothyroidism in 2 patients (0.3%), subclinical hypothyroidism in 11 patients (2%), hyperthyroidism in 23 patients (3.9%), and subclinical hyperthyroidism in 12 patients (2.1%) (Table 1).

The patients were evaluated in terms of thyroid function tests. The mean thyroid stimulating hormone values were  $1.86 \pm 2.42$  µU/L, and the mean free thyroxine values were  $15.92 \pm 6.28$  pmol/L (Table 2).

**Table 1.** Demographic data.

	Hypothyroid	Subclinical Hypothyroid	Euthyroid	Subclinical Hyperthyroid	Hyperthyroid	Total
F/M (n)	7/4	1/1	335/204	8/4	13/10	587
Age Mean (year)	63.3 ± 8.3	64.8 ± 9.2	60.1 ± 9.5	70.8 ± 10.4	62.1 ± 7.8	62.2 ± 9.8

F/M: Female/Male.

**Table 2.** Thyroid Hormone values.

	Hypothyroid	Subclinical Hypothyroid	Euthyroid	Subclinical Hyperthyroid	Hyperthyroid	Total
TSH (µU/L)	18,64 ± 15,86	7.22 ± 5,44	1.54±1.2	0.084	0.036 ± 0.022	1,86 ± 2.42
ft <sub>4</sub> (pmol/L)	1,94 ± 0.98	2.16 ± 1,42	15.2±3.67	16.86	22.26 ± 8.36	15.92 ± 6,28

The patients were also evaluated in terms of their chronic disease history. Backgrounds of Hypertension, Ischemic Heart Disease, Peripheral Vascular Disease, Cerebrovascular Disease, Chronic Obstructive Pulmonary Disease, Diabetes Mellitus, Conges-

tive Heart Failure, and Chronic Kidney Failure were questioned. The three most common chronic diseases were found to be Hypertension (n:35), Diabetes Mellitus (n:22), and Ischemic Heart Disease (n:18) (Table 3).

**Table 3.** Additional diseases.

	Hypothyroid	Subclinical Hypothyroid	Euthyroid	Subclinical Hyperthyroid	Hyperthyroid	Total
HT (n)	2	1	21	5	6	35
IHD (n)	1	0	16	1	0	18
PVD (n)	0	0	1	0	0	1
CVD (n)	0	0	5	0	1	6
COPD (n)	0	0	3	0	0	3
DM (n)	2	1	15	3	1	22
CHF (n)	1	0	12	1	0	14
CRH (n)	0	0	1	0	0	1
Malignancy (n)	0	0	2	1	0	3

HT: Hypertension; IHD: Ischemic Heart Disease; PVD: Peripheral Vascular Disease; CVD: Cerebrovascular Disease; COPD; Chronic Obstructive Pulmonary Disease; DM: Diabetes Mellitus; CHF: Congestive Heart Failure; CRF: Chronic Renal Failure.

## DISCUSSION AND CONCLUSION

When the literature is examined, we see that in most of the articles and reviews, cardiological pathologies in thyroid diseases are discussed. Our study investigated thyroid dysfunction in patients who applied to the cardiology outpatient clinic. This makes our study different and valuable from other studies.

The presence of autoimmune thyroid disease affects cardiac functions, even if thyroid hormones are in excess or low in venous blood and even thyroid hormone levels are within normal limits.

The prevalence of hypothyroidism over the age of 12 is 0.3% for overt hypothyroidism and 4.3% for subclinical hypothyroidism. The incidence of hypothyroidism is annual; It is given as 3.5 per 1000 for women and 0.6 for men. Hypothyroidism is seen 5-8 times more in women than in men.<sup>7-9</sup> When we examined the cardiovascular effects of subclinical hypothyroidism or overt thyroidism, it was associated with diastolic hypertension, sinus bradycardia, heart failure, tamponade, pericardial effusion, dyslipidem-

ia, and atherosclerosis. There is no data revealing its relationship with AF.

In our study, we found hypothyroidism in 2 patients (0.3%) and subclinical hypothyroidism in 11 patients (2%). Our subclinical + clinical hypothyroidism rate was 2.3% in total. This rate was lower than expected in the normal population. 8 of the 13 patients were female, and five were male. The number of women was more than men. Our findings are consistent with the knowledge that hypothyroidism is not associated with AF and that hypothyroidism is more common in women.

Subclinical and hyperthyroidism are seen in 1.9-2.7% of women and 0.16-0.23 of men. The incidence in women is about ten times higher than in men. The incidence increases with age. The most common pathology caused by hyperthyroidism in the heart is tachyarrhythmias. Among the tachyarrhythmias, AF is the most common, and sinus tachycardia, which continues even at rest.<sup>7-10</sup>

In our study, hyperthyroidism was detected in 23

patients (3.9%) and subclinical hyperthyroidism in 12 patients (2.1%). Our subclinical + clinical hyperthyroidism rate was found to be 6% in total. This rate was higher than expected in the normal population. Again, of the 35 patients, twenty-one were female, and fourteen were male. The number of women was more than men. The fact that the rate of hyperthyroidism is higher in patients with AF compared to the normal population reveals a relationship between AF and hyperthyroidism.

Studies have shown that hyperthyroidism increases coronary blood flow by over 50%. The increase in oxygen consumption of the myocardium and the fact that the consumption of the atria is higher than that of the ventricles suggests that it prepares the ground for AF.<sup>1</sup> When the thyroid function tests of patients with atrial arrhythmia were examined in a study, 5% of the patients were found to have hyperthyroidism.<sup>10</sup> In another study, subclinical hyperthyroidism was found in 10% of patients with AF.<sup>11</sup> In a study, the incidence of AF in hyperthyroidism was found to be 12%, and it was shown that the frequency of AF was low in young hyperthyroid patients and increased significantly in the geriatric group.<sup>12</sup>

The most important limitation of our study is the number of cases. As another limitation, the relationship between AF and autoimmune thyroid diseases could be examined by looking at thyroid autoantibodies, but since our study was retrospective, these tests could not be examined because they could not be requested from the cardiology outpatient clinic. The other limitation of our study, free or total  $t_3$  level was not included in the laboratory examinations. Therefore, it is impossible to evaluate especially  $T_3$  toxicosis in the subclinical hyperthyroidism group. The fact that the number of cases was not higher and examining the autoimmune disease relationship would have made our study more valuable.

In conclusion, thyroid dysfunction, especially hyperthyroidism, is more common in patients with AF compared to the normal population and plays a role in its pathophysiology. Therefore, patients with AF should be evaluated for thyroid dysfunction and thyroid function tests should be routinely requested.

**Ethics Committee Approval:** Our study was approved by the xx University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Date: 14/10/2022, decision no: 310). The study was carried out by the Helsinki Declaration.

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

**Author Contributions:** Concept – PV; Supervision; Materials – PV; Data Collection and/or Processing – TD; Analysis and Interpretation – PV; Writing – PV.

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## The Effects of Eccentric-Concentric Isokinetic Muscle Strength Training on Quadriceps Femoris Muscle Architecture, Muscle Strength and Proprioception in Healthy Young People

### Eksentrik-Konsentrik İzokinetik Kas Kuvveti Eğitiminin Sağlıklı Gençlerde Kuadriseps Femoris Kas Mimarisi, Kas Kuvveti ve Propriyosepsiyon Üzerine Etkileri

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#### ABSTRACT

**Objective:** This study aimed to compare and evaluate the efficacy of eccentric and concentric training on quadriceps femoris muscle architecture, muscle strength and proprioception in healthy young people.

**Materials and Methods:** Sixty healthy subjects were divided into two groups concentric training (n=30), and eccentric training (n=30). The outcome measurements were Quadriceps Femoris (QF) muscle architecture, muscle strength and knee proprioception. The training was carried out on the subjects' dominant side leg (right), and the participants were trained three times a week for 12 weeks. The measurements were applied before and after training. QF muscle architecture was assessed by using ultrasonography. Isokinetic muscle strength and knee proprioception were assessed with the isokinetic dynamometer.

**Results:** The results showed a significant increase in QF architecture, muscle strength and knee proprioception after the training in the two groups (p<0.05). When we compared the training groups, there were no differences regarding the outcome of all variables between groups (p>0.05).

**Conclusion:** Training techniques, including eccentric and concentric training, positively affected QF muscle architecture, muscle strength, and knee proprioception (p<0.05), but there is no superiority between each other (p>0.05).

**Keywords:** Eccentric training, muscle architecture, muscle strength, quadriceps femoris, proprioception

#### ÖZ

**Amaç:** Bu çalışmanın amacı sağlıklı kişilerde eksentrik ve konsentrik eğitimlerin kuadriseps femoris kasının kas mimarisi, kas kuvveti ve propriyosepsiyona etkilerini değerlendirmek ve karşılaştırmaktır.

**Materyal ve Metot:** 60 sağlıklı kişi konsentrik (n=30) ve eksentrik (n=30) kas eğitimi olarak iki gruba ayrıldı. M. Kuadriseps Femoris (QF) kas mimarisi, kas kuvveti ve diz propriyosepsiyonu değerlendirildi. Eğitim dominant taraf bacak (sağ) üzerinde uygulandı ve katılımcılar haftada 3 kez, 12 hafta boyunca eğitime devam etti. Değerlendirmeler eğitim öncesi ve eğitim sonrası olarak yapıldı. QF kas mimarisi ultrason ile değerlendirildi. Kas kuvveti ve diz propriyosepsiyonu izokinetik dinamometre ile değerlendirildi.

**Bulgular:** Bu çalışmanın sonuçlarına göre QF kas mimarisi, kas kuvveti ve diz propriyosepsiyonu her iki grupta benzer şekilde artış gösterdi (p<0,05). Eğitim gruplarını karşılaştırdığımızda tüm değerlendirme sonuçları açısından her iki grup arasında fark bulunmadı (p>0,05).

**Sonuç:** Sonuçlar eksentrik ve konsentrik eğitimlerin QF kas mimarisi, kas kuvveti ve diz propriyosepsiyonu üzerine pozitif etkilerinin olduğunu (p<0,05), fakat birbirleri üzerine üstünlüklerinin olmadığını işaret etmiştir (p>0,05).

**Anahtar Kelimeler:** Eksentrik eğitim, kas mimarisi, kas kuvveti, kuadriseps femoris, propriyosepsiyon

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## INTRODUCTION

Gaining better muscle strength depends on a more active life in healthy people because it leads to the formation of better muscular function.<sup>1</sup> Muscular strength is defined as the force generated with a maximal effort by a muscle or group of muscles against resistance. Sufficient muscle strength better protects the person against joint and muscle injuries.<sup>2,3</sup> Therefore, it is important to implement strength training programs within the scope of preventive physiotherapy in healthy people as well. Isometric, concentric, eccentric, and isokinetic exercises are the main exercises to improve muscle strength.<sup>4</sup> Isokinetic exercises increase muscle strength the most. With isokinetic devices, the maximum load can be imposed on the muscle at predetermined fixed angular velocities. These systems allow the implementation of concentric and eccentric training of muscles.<sup>5-7</sup>

Knowledge of the architectural features of the muscle, the basic element of muscle function, will enable effective evaluation and improvement of muscle function. Muscle architecture enables the muscle development process to be understood and interpreted macroscopically.<sup>8</sup> It is known that muscle strength training programs cause changes in muscle structure. It has been reported that both eccentric training and concentric plus eccentric training increase fascicle length.<sup>9</sup> Trainings, including resistance training exercises and eccentric strengthening programs, have been observed to result in increased muscle cross-sectional area and fibre length.<sup>8</sup>

Proprioception can be defined as the combined stimuli from mechanoreceptors in the joint capsules, tendons, ligaments, muscles, and skin being transmitted to the central nervous system.<sup>10</sup> The proprioceptive sense includes joint position sensation and kinesthesia and ensures dynamic joint stability by contributing to the muscle reflex and motor planning necessary to achieve nerve-muscle control.<sup>11</sup> The scientific literature suggests that proprioception and postural stability are also extremely important for preventing sports injuries. Studies have also reported that proprioception is considerably associated with the performance of elite athletes.<sup>12</sup>

Despite many studies, controversy remains regarding the effects of different types of resistance training on muscle strength and hypertrophy.<sup>13,14</sup> The purpose of this study was to determine the effect of eccentric-concentric isokinetic muscle strength training on muscle architecture, muscle strength, and proprioception of healthy quadriceps femoris muscle and to compare this training program on proprioception, muscle architecture, and strength.

## MATERIALS AND METHODS

**Ethics Committee Approval:** The study was approved by the Clinical Research Ethics Committee of Suleyman Demirel University, Faculty of Medicine (Date: 08.02.2017, decision no. 72867572.050.01-29921). The study was carried out following the international declaration, guidelines, etc.

**Study Design and Data Collection:** The exclusion criteria were severe pain, acute injuries of muscle-tendon structures, nonconformity of the participant during the test, cases with insufficient soft tissue healing, the presence of severe effusion and severe limitation of joint movement, the presence of an orthopedic illness in the knee or ankle, and the presence of a systemic disease that prevents performance on the isokinetic dynamometer. In addition, volunteer participants were encouraged to stay away from all sports activities and strengthening methods that could affect the increase in muscle strength during the program.

**Outcome Measurements:** 60 subjects completed the program. The study included participants who were right limb-dominant. In the study groups, the participants' dominant extremity's quadriceps femoris muscle was studied. Participants were divided into; an eccentric (ECC) exercise group (30 participants) and a concentric (CON) exercise group (30 participants). A strength training program comprising 3 sets with 10 repetitions a day, 3 days a week for a total of 12 weeks, was conducted.

A form was created to evaluate the age, educational status, sex, height, weight, dominant lower extremity, and type of strength training program of the participants. All participants were evaluated twice before and after strength training with the following assessment methods.

In this study, we evaluated the pennation angle of the vastus lateralis muscle and the anteroposterior diameter, namely, the thickness of the muscle using the Toshiba Aplio 500 ultrasound system. Participants were evaluated after being rested for 10 min before the ultrasonography. In addition, it was ensured that the participants did not engage in intense physical activity 48 h before the evaluation. Three images were obtained for each region.<sup>4</sup> The evaluation was performed on the patient lying with the knee in extension and the muscles relaxed.<sup>15-17</sup> Images were obtained at the midline from between the trochanter major and the lateral condyle of the femur.<sup>17,18</sup>

The isokinetic muscle strength test was performed at a velocity of 60°–240°/s at concentric/concentric mode during the concentric strength testing and at a velocity of 60°–120°/s at eccentric/eccentric mode during the eccentric strength testing.<sup>6,19</sup>

Proprioception measurements in the knee joint were performed using an isokinetic dynamometer. In evaluating knee joint proprioception, the joint position sense was measured using the active and passive methods. Values recorded when the targeted angle of 30°, 45°, and 75° was reached were recorded as deviation values.<sup>19</sup>

The isokinetic exercise program was applied to the dominant right knee of the participants. An isokinetic exercise program comprising 3 sets of 10 repetitions and 90 s of rest period after each set of 10 repetitions was implemented at an angular velocity of 180°/s in the concentric exercise group and at an angular velocity of 120°/s to the eccentric exercise group.<sup>6</sup>

**Statistical Analysis:** The *t*-test or Mann–Whitney U test was used for comparing the pre-training parameters of patients in the two exercise groups after the data was tested for normal distribution. In comparing pre-training and post-training differences in the exercise groups, the Wilcoxon test was separately used in the eccentric and concentric groups for data not following normal distribution, and the repeated measures analysis of variance was used for data following normal distribution.<sup>20</sup> The evaluations were made using the SPSS 20 software, and a *p*-value of <0.05 was considered statistically significant.

**RESULTS**

The present study investigated the effects of 12 weeks of eccentric and concentric isokinetic muscle strength training on muscle architecture, muscle strength, and proprioception of healthy quadriceps femoris muscle.

There was no statistically significant difference between the eccentric and concentric groups for age, (ECC; 22.77±1.45, CON; 22.07±1.14) gender (ECC; female:n;14, CON; male:n;16) and body mass index (ECC; 22.92±3.11, CON; 21.66±2.77) (*p*>0.05).

There was a statistically significant difference between the pre-training and post-training active proprioception at 30 degrees (AP30) (*p*=0.048) and active proprioception at 75 degrees (AP75) (*p*=0.0001) values of the participants in the eccentric exercise group. Post-training AP30 and AP75 values were significantly decreased compared to pre-training values (*p*<0.05). However, there was no statistically significant difference between active proprioception at 45 degrees (AP45) values (*p*=0.280). There was a statistically significant difference between the pre-training and post-training passive proprioception at 30 degrees (PP30) (*p*=0.0001), passive proprioception at 45 degrees (PP45) (*p*=0.003) and passive proprioception at 75 degrees (PP75) (*p*=0.001) values of the participants in the eccentric exercise group. There was a significant decrease in all post-training values compared with the pre-training values (Table 1).

There was a statistically significant difference between the pre-training and post-training AP45 (*p*=0.001) and AP75 (*p*=0.039) values of the participants in the concentric exercise group. Post-training AP45 and AP75 values decreased significantly compared to pre-training values (*p*<0.05). However, there was no statistically significant difference between AP30 values (*p*=0.163). There was a statistically significant difference between the pre-training and post-training PP30 (*p*=0.004), PP45 (*p*=0.003

**Table 1.** Comparison of proprioceptive sense measurements of participants in the eccentric exercise group before and after training.

Parameters	Before Training		After Training		p*
	Mean± SD	Median (Min-max)	Mean ± SD	Median (Min-max)	
AP30	3.43±3.98	2 (0-14)	1.73±2.36	1 (0-10)	0.048
AP45	3.00±2.75	2 (0-9)	2.33±2.81	1.5 (0-11)	0.280
AP75	4.33±4.61	3 (0-22)	1.60±2.61	0.5 (0-12)	0.0001
PP30	2.40±2.27	2 (0-10)	0.70±1.02	0 (0-4)	0.0001
PP45	1.27±1.28	1 (0-5)	0.43±0.97	0 (0-5)	0.003
PP75	2.57±2.42	2 (0-10)	0.70±1.12	0 (0-4)	0.001

SD: Standard Deviation; Min: Minimum; Max: Maximum; AP30: Active proprioception at 30 degrees; AP45: Active proprioception at 45 degrees; AP75: Active proprioception at 75 degrees; PP30: Passive proprioception at 30 degrees; PP45: Passive proprioception at 45 degrees; PP75: Passive proprioception at 75 degrees; \*: Wilcoxon Test.

and PP75 (p=0.0001) values of the participants in the concentric exercise group. There was a significant decrease in all post-training values compared with the pre-training values (Table 2).

There was no statistically significant difference between the eccentric and concentric groups regarding pre-training and post-training changes in the AP30 (p=0.561), AP45 (p=0.202), AP75 (p=0.243), PP30

**Table 2.** Comparison of proprioceptive sense measurements of participants in the concentric exercise group before and after training.

Parameters	Before Training		After Training		p*
	Mean±SD	Median (Min-max)	Mean ± SD	Median (Min-max)	
AP30	3.37±2.78	2.5 (0-9)	2.34±2.19	2 (0-8)	0.163
AP45	3.60±3.31	3 (0-14)	1.55±2.18	1 (0-8)	0.001
AP75	3.63±3.25	2.5 (0-14)	1.93±1.71	2 (0-5)	0.039
PP30	2.60±2.50	2 (0-10)	0.93±1.36	0 (0-5)	0.004
PP45	2.07±1.74	1.5 (0-7)	0.59±1.24	0 (0-5)	0.003
PP75	3.63±3.75	3 (0-15)	0.83±1.04	0 (0-4)	0.0001

SD: Standard Deviation; Min: Minimum; Max: Maximum; AP30: Active proprioception at 30 degrees; AP45: Active proprioception at 45 degrees; AP75: Active proprioception at 75 degrees; PP30: Passive proprioception at 30 degrees; PP45: Passive proprioception at 45 degrees; PP75: Passive proprioception at 75 degrees; \*: Wilcoxon Test.

(p=0.649), PP45 (p=0.262) and PP75 (p=0.539) parameters. Negative values in the descriptive statistics show that a decrease has occurred after training (Table 3).

The 60-degree quadriceps femoris concentric peak torque (QCON60) (GxT; F (1,58)=0.371, p=0.545), 60-degree quadriceps femoris eccentric peak torque (QECC60) (GxT; F (1,58)=0.840, p=0.363), 240-degree quadriceps femoris concentric peak torque (QCON240) (GxT; F (1,58)=1.303, p=0.258) and 120-degree quadriceps femoris eccentric peak torque (QECC120) (GxT; F (1,58)=1.982, p=0.165) values showed a similar level of increase in the eccentric and concentric exercise groups. Therefore, the interaction term was not statistically significant (p>0.05). There was a statistically significant difference in

terms of an increase between the pre-training and post-training QCON60 (T; F (1,58)=39.677, p=0.0001), QECC60 (T; F (1,58)=48.466, p=0.0001), QCON240 (T; F (1,58)=69.268, p=0.0001) and QECC120 (T; F (1,58)=34.106, p=0.0001) values in both groups. No statistically significant difference was found in terms of QCON60 (G; F (1,58)=0.007, p=0.934), QECC60 (G; F (1,58)=0.051, p=0.822), QCON240 (G; F (1,58)=0.199, p=0.657) and QECC120 (G; F (1,58)=0.116, p=0.735) measurements between the eccentric and concentric exercise groups (Table 4).

A similar increase was observed in the muscle thickness (MT) values of the eccentric and concentric exercise groups. Therefore, the interaction term was not statistically significant (Group × Time; F (1,58)

**Table 3.** Descriptive statistics and comparison of pre-training and post-training changes (differences) in the two groups (eccentric and concentric).

Before and After Education Difference	ECCENTRIC		CONCENTRIC		p*
	Mean ± SD	Median (Min-max)	Mean±SD	Median (Min-max)	
Difference _AP30	-1.70±4.23	-1 (-10 - 9)	-0.93±3.27	-1 (-9 - 7)	0.561
Difference _AP45	-0.66±3.88	-0.5 (-7 - 9)	-2.07±3.15	-1 (-13 - 3)	0.202
Difference _AP75	-2.73±3.44	-2 (-10 - 5)	-1.69±3.94	-1 (-12 - 4)	0.243
Difference _PP30	-1.70±2.25	-1.5 (-9 - 2)	-1.59±2.78	-1 (-10 - 4)	0.649
Difference _PP45	-0.83±1.44	-1 (-5 - 3)	-1.41±2.26	-1 (-7 - 4)	0.262
Difference _PP75	-1.87±2.76	-1 (-9 - 3)	-2.69±4.01	-2 (-14 - 4)	0.539

SD: Standard Deviation; Min: Minimum; Max: Maximum; AP30: Active proprioception at 30 degrees; AP45: Active proprioception at 45 degrees; AP75: Active proprioception at 75 degrees; PP30: Passive proprioception at 30 degrees; PP45: Passive proprioception at 45 degrees; PP75: Passive proprioception at 75 degrees; \*: Wilcoxon Test.

**Table 4.** Comparison of pre-training and post-training values of isokinetic muscle strength measurements in the eccentric and concentric exercise groups.

Parameters	Groups	TIME (T)		Statistics
		Before Training	After Training	
QCON60, Mean ± SD	Eccentric	129.23±51.28	157.60±49.08	G; F (1,58)=0.007, p=0.934 T; F (1,58)= 39.677, p=0.0001 GxT; F (1,58)= 0.371, p=0.545
	Concentric	130.63±55.33	154.00±59.62	
QECC60, Mean ± SD	Eccentric	140.07±44.15	164.80±41.82	G; F (1,58)=0.051, p=0.822 T; F (1,58)= 48.466, p=0.0001 GxT; F (1,58)= 0.840, p=0.363
	Concentric	134.00±39.14	166.23±45.29	
QCON240, Mean ± SD	Eccentric	74.53±31.93	93.60±32.89	G; F (1,58)=0.199, p=0.657 T; F (1,58)= 69.268, p=0.0001 GxT; F (1,58)= 1.303, p=0.258
	Concentric	73.40±28.32	87.87±29.75	
QECC120, Mean ± SD	Eccentric	152.90±48.24	174.47±53.71	G; F (1,58)=0.116, p=0.735 T; F (1,58)= 34.106, p=0.0001 GxT; F (1,58)= 1.982, p=0.165
	Concentric	150.33±42.36	185.60±62.58	

SD: Standard Deviation; T: Time; GxT: GroupxTime; QCON60: 60-degree quadriceps femoris concentric peak torque; QECC60: 60-degree quadriceps femoris eccentric peak torque; QCON240: 240-degree quadriceps femoris concentric peak torque; QECC120: 120-degree quadriceps femoris eccentric peak torque.

=0.008, p=0.931). In both groups, there was a statistically significant difference in terms of an increase between pre-training and post-training MT values (Time; F (1,58)=5.415, p=0.023). No statistically significant difference was found between the eccentric and concentric exercise groups regarding MT measurements (G; F (1,58)=0.116, p=0.734). The pennation angle (PA) values displayed a similar level of decrease in the eccentric and concentric exer-

cise groups. Therefore, the interaction term was not found to be statistically significant (Group × Time; F (1,58)=0.019, p=0.891). There was a statistically significant difference in decreasing the pre-training and post-training PA values in both groups (Time; F (1,58)=5.149, p=0.027). No statistically significant difference was found between the eccentric and concentric exercise groups in terms of PA measurements (Group; F (1,58)=0.009, p=0.926) (Table 5).

**Table 5.** Comparison of pre-training and post-training muscle thickness and pennation angle measurement values in the eccentric and concentric exercise groups.

Parameters	Group	TIME		Statistics
		Before Training	After Training	
MT, Mean ± SD	Eccentric	17.15±4.03	18.12±3.22	G; F (1,58)=0.116, p=0.734 T; F (1,58)= 5.415, p=0.023 GxT; F (1,58)= 0.008, p=0.931
	Concentric	16.89±3.38	17.79±4.07	
PA, Mean ± SD	Eccentric	10.53±3.70	9.43±2.76	G; F (1,58)=0.009, p=0.926 T; F (1,58)= 5.149, p=0.027 GxT; F (1,58)= 0.019, p=0.891
	Concentric	10.67±3.55	9.42±2.96	

SD: Standard Deviation; MT: Muscle thickness; PA: Pennation angle.

### DISCUSSION AND CONCLUSION

The differential impact of ECC or CON on strength gains is still a debatable issue, while the mechanisms regulating these adaptations have not yet been fully elucidated. Analysis of studies in the literature on concentric-eccentric strength increase after concentric-eccentric isokinetic exercise training revealed different results. Within the ponder by Bagheri et al. offbeat workout comes about in a more noteworthy increment in maximal isometric deliberate compression of the quadriceps muscle after 12 weeks of concentric and unconventional isokinetic workout preparing.<sup>21</sup> Douglas et al. reported that eccentric training could elicit greater improvements in muscle strength and mechanical muscle function than concentric or concentric-eccentric resistance training.<sup>21</sup> Conversely, a group of researchers have demonstrated that a similar increase occurred in the muscle strength of both the concentric and eccentric

groups after concentric and eccentric isokinetic exercise training.<sup>13,14,23,24</sup> Similarly, in our study, as in most studies reported in the literature, the eccentric and concentric peak torque strength values of the concentric and eccentric isokinetic exercise training groups showed a similar level of increase in both groups after 12 weeks of isokinetic muscle strength training.

There is ongoing controversy as to whether differences exist in the hypertrophic response to concentric vs. eccentric actions.<sup>24</sup> Only one study among muscle architecture studies conducted on the quadriceps muscle by evaluating the anatomical cross-sectional area of the muscle has revealed a difference between eccentric and concentric exercise training groups. In that study by Higbie et al., the anatomical cross-sectional area of the muscle was found to be greater in the eccentric group than in the concentric.<sup>25</sup> Other studies showed a similar increase

in MT in the concentric and eccentric exercise training groups.<sup>14,24,26</sup> Our study has also found similar results to the literature and revealed that a similar level of increase occurred in the MT of the concentric and eccentric isokinetic exercise training. This suggests that this result is associated with the eccentric and concentric peak torque strength values having a similar level of increase in both groups. The findings indicate the importance of including eccentric and concentric actions in muscle strength programs, as both effectively increase muscle hypertrophy.

We observed different results when we analysed muscle architecture studies in the literature in which PA was evaluated. In their study published in 2007, Blazeovich et al. reported that PA increased similarly in the concentric and eccentric exercise groups.<sup>27</sup> Conversely, Quinlan et al. have detailed in their study conducted in 2021 that the PA of the vastus lateralis muscle increased and that this increment was greater in the concentric exercise group than in the eccentric exercise group.<sup>26</sup> The studies of Raj et al. and the studies of Baroni et al. showed that there was no change in the pennation angle after the eccentric exercise training program.<sup>28,18</sup> Unlike the literature, a similar level of decrease occurred in PA values of the eccentric and concentric exercise groups in our study. We attribute this situation to different results in the literature.

Until now, many studies have investigated the effect of different training modules on position sense, but the majority focused on rehabilitation from musculoskeletal injuries. Unfortunately, the reports in healthy individuals on the impact of exercise on position sense are limited. Methenitis et al. reported that no significant changes were found in knee joint position sense for both concentric or eccentric groups.<sup>29</sup> In Shiravand et al. research, a factually noteworthy decrease was similarly found in the margin of error for proprioception after training compared with pre-training in the eccentric and concentric groups.<sup>30</sup> The results of our study are also similar; a factually noteworthy diminish similarly found in the margin of error for proprioception after training compared with pre-training in the eccentric and concentric groups. Because motor control loss in the knee joint is the most important cause that triggers proprioception loss, improved proprioception is an expected outcome of increased muscle strength. We believe that increasing the concentric and eccentric muscle strength increases the motor control and improves proprioception. We attribute the lack of proprioception difference between the two groups to the fact that there is no noteworthy contrast between the concentric and eccentric training groups in evaluating our other muscle strength and architecture parameters.

In conclusion, the present study has limitations. This limitation is the absence of a control group. In our study, it was observed that compared with the initial values, the post-exercise training values of all measurement parameters increased in both groups regardless of the training. This demonstrates that eccentric and concentric isokinetic strength training is effective in strengthening the quadriceps femoris muscle in healthy young individuals and that it is effective on muscle architecture and joint position sensation as well, which supports several previous studies performed in this regard. In addition, our study shows that eccentric and concentric isokinetic strength training in healthy young individuals has a similar effect on the quadriceps femoris muscle strength, muscle architecture, and joint position sensation. We accept that the results acquired from the research will act as a guideline for increasing the physical fitness of healthy individuals and athletes and determining the rehabilitation program for those with pathological conditions.

**Ethics Committee Approval:** The study was approved by the Clinical Research Ethics Committee of Suleyman Demirel University, Faculty of Medicine (Date: 08.02.2017, decision no. 72867572.050.01-29921). The study was carried out in accordance with the international declaration, guidelines, etc.

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

**Author Contributions:** Concept – TIP, ZCA; Supervision – TIP, ZCA UT, ST; Materials – TIP, ZCA UT, ST; Data Collection and/or Processing – TIP, ZCA UT, ST; Analysis and/or Interpretation – TIP; Writing – TIP.

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**Earthquake Victim Profile in a Hospital Far from the Earthquake Zone: The Case of Sakarya****Deprem Bölgesinden Uzaktaki Bir Hastaneye Başvuran Depremzede Hasta Profili: Sakarya İli Örneği**

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**ABSTRACT**

**Objective:** In our study, the effect of earthquake victims who applied to the emergency department (ED) of our hospital, despite being far from the earthquake area, on the workload and the need for additional precautions will be examined. As a result, it is aimed to create a guiding resource for future disasters.

**Materials and Methods:** This study was conducted with patients who applied to Sakarya Training and Research Hospital (STRH) Emergency Department within 15 days after the Kahramanmaraş earthquake and were diagnosed as X34-Earthquake Victims according to ICD-10.

**Results:** The mean age of the 405 patients were 20.98 years, and 52.6% were female. The ratio of the admitted patients to the total number of patients was 1.62%. Regarding resource use, the laboratory was requested for 32.3%, imaging examination for 55.1%, consultation for 19%, and 353 patients were discharged from the emergency department.

**Conclusion:** Although earthquake victims may apply to the emergency departments regardless of the distance after the earthquake, this number is insufficient to require additional measures regarding the workload it creates. However, since this study is the first analysis based on distance, it should be supported by similar studies.

**Keywords:** Earthquake, emergency department, precaution

**ÖZ**

**Amaç:** Bu çalışmada deprem bölgesinden uzakta olmasına karşın hastanemiz acil servislerine başvuran depremzedelerin acil servis iş yüküne etkisi ve ek bir önlem alınmasının gerekip gerekmediği yönünden analiz edilerek gelecekteki olası afetler için güncel bir kaynağın oluşturulması amaçlanmıştır.

**Materyal ve Metot:** Bu çalışma; Kahramanmaraş depremi sonrası ilk 15 günlük süreçte Sakarya Eğitim ve Araştırma Hastanesi (SEAH) acil servislerine başvuran ve Uluslararası Hastalık Sınıflandırması-10'a göre X34-Depremzede tanısı almış tüm hastaları içermektedir.

**Bulgular:** Çalışmaya dahil edilen toplam 405 hastanın yaş ortalamaları 20,98 yıl ve %52,6'sının ise kadın olduğu saptandı. Depremzede hastaların, toplam acil servis başvuru sayısına oranı % 1,62 olduğu gözlemlendi. Kaynak kullanım bakımından %32,3'üne en az bir laboratuvar istemi yapıldığı, %55,1'ine en az bir görüntüleme tetkiki istendiği, %19'una konsültasyon istendiği ve 353 hastanın ise direkt acil servisten taburcu edildiği tespit edildi.

**Sonuç:** Deprem sonrası mesafeden bağımsız acil servislere depremzede başvurusu olabilmesine karşın bu sayı oluşturduğu iş yükü bakımından ek bir önlem almayı gerektirecek kadar fazla değildir. Ancak bu çalışmanın, mesafe dikkate alınarak yapılan ilk analiz olmasından dolayı benzer çalışmalar ile desteklenmesi gerekmektedir.

**Anahtar Kelimeler:** Acil servis, deprem, önlem

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## INTRODUCTION

Earthquakes are natural disasters that cause death and significant loss of property due to seismic fluctuations caused by the energies in the earth's crust shaking the earth.<sup>1</sup> Turkey has active fault lines, and large-scale earthquakes occur regularly. Among the last century's earthquakes, one that caused the most death and property loss occurred in Kahramanmaraş on February 6, 2023 (Epicenter: Pazarcık district; Intensity: 7.7 Mw; Focal depth: 8.6 km). The fact that a second earthquake occurred approximately nine hours after the first earthquake (Epic Base: Elbistan district; Intensity: 7.6 Mw; Focal depth: 7 km), makes these earthquakes unique due to the size of the area and the large number of people affected.<sup>2</sup> More than 13.5 million people in 11 provinces (Kahramanmaraş, Gaziantep, Şanlıurfa, Diyarbakır, Adana, Adıyaman, Osmaniye, Hatay, Kilis, Malatya and Elazığ) and an area of 108,812 km<sup>2</sup> were affected by these earthquakes.<sup>2,3</sup>

The first days after an earthquake are critical for rescue activities and health services.<sup>4</sup> According to the information published by the official authorities, 42 310 people lost their lives, 108 281 people were injured, 21 859 injured people were treated, and 51 152 people were transferred to hospitals in other cities due to the earthquake in the first 15 days.<sup>5,6</sup> According to this information, it is understood that health services outside the earthquake zone should also be regulated. As a matter of fact, despite being far from the earthquake area, earthquake victims applied to our hospital. However, no study in the literature investigates the relationship between earthquake victims and the distance to the earthquake zone.

In our study, the effect of earthquake victims who applied to the emergency departments (ED) of our hospital, despite being far from the earthquake area, on the workload and the need for additional precautions will be examined. As a result, it is aimed to create a guiding resource for future disasters.

## MATERIALS AND METHODS

**Ethical Approvals and Permissions:** Approval for this study was obtained from the Sakarya University Faculty of Medicine Ethics Committee (Date: 27.02.2023, decision no: 61). The procedures were carried out by the 2004 Declaration of Helsinki.

**Research Type:** This study is a descriptive, cross-sectional, and retrospective study conducted between February 6 and February 20, 2023. Patients who applied to STRH Emergency Departments (Adults, Gynecology and Obstetrics, Child) and were diagnosed as X34-Earthquake Victims according to the International Classification of Diseases-10 were included in the study.

**Definitions:** Our tertiary hospital provides emergency departments in three different areas (Adults, Gynecology and Obstetrics, and Pediatrics). The annual number of applications is 739,776, and the total number of applications during the education period is 25.061. The approximate distance from the epicentre of the earthquake is 900 km.

**Inclusion Criteria:** All patients who applied within the first 15 days after the earthquake were diagnosed as X34-Earthquake Victims. Patients whose data can be fully accessed through the hospital automation system were included in the study.

**Exclusion Criteria:** Patients whose data cannot be accessed through the hospital automation system

**Data Collecting:** In the study, the patients; demographic characteristics (age, gender), the emergency department applied (Adult, Gynecology and Obstetrics, Child), whether there is an earthquake-related injury, affected area if there is an injury (head/neck, thorax, abdomen, pelvis, extremity, multiple injuries in case of injuries involving two or more regions), resource use (laboratory examination, ultrasonography, tomography, consultation request) and emergency room outcomes (discharge, service or intensive care admission) were recorded using the hospital automation system.

**Statistical Analysis:** IBM SPSS Statistics (Version 21.0. Armonk, NY: IBM Corp.) was used for statistical analysis. Kolmogorov-Smirnov ( $n \geq 50$ ) test was performed in the normality analysis of numerical data. Numerical variables were expressed as the average, along with the standard deviation. The chi-square test presented as numbers and percentages were used for categorical variables.

## RESULTS

After the Kahramanmaraş earthquake, the information regarding the applications made to the STRH Adult, Gynecology and Obstetrics and Pediatric EDs between 6-20 February 2023 is shown in Table 1. Accordingly, most applications were to the Pediatric ED. When applications on a unit basis are compared according to the total number of patients, the rates were found to be 0.89% in the Adult ED, 2.17% in Gynecology and Obstetrics ED, 3.2% in the Pediatric ED, and 1.62% in total.

The demographic characteristics of the patients, whether laboratory, imaging, and consultation, were requested, and the emergency department outcomes are shown in Table 2. It was determined that the mean age of the patients was 20.98 years, 52.6% were female, 32.3% were requested to be in the laboratory, 55.1% were imaging tests, 19% were consulted, and 353 people whose treatment was completed during the emergency department were discharged. It was observed that laboratory, imaging,

**Table 1.** Applications to adult, gynecology and obstetrics, and pediatric emergency departments.

ED	Earthquake Victim n (%)	Earthquake-Related Injury (%)	Total n (%)
Adult ED	148 (0.89)	118 (0.71)	16608 (100)
Pediatric ED	221 (3.2)	4 (0.05)	6799 (100)
GOED	36 (2.17)	0 (0)	1654 (100)
<b>Total</b>	<b>405 (1.62)</b>	<b>122 (0.48)</b>	<b>25061 (100)</b>

ED: Emergency Department; GOED: Gynecology and Obstetrics Emergency Department.

**Table 2.** Demographic characteristics of patients, resource use, emergency room outcome, and earthquake-related injuries.

		Adult (n: 148)	Gynecology and Obstetrics (n: 36)	Pediatric (n: 221)	Total (n: 405)
<b>Age (years)</b>		42.45	27.61	5.52	20.98
<b>Gender</b>	Female, n (%)	78 (52.7)	36 (100)	99 (44.8)	213 (52.6)
	Male, n (%)	70 (47.3)	0 (0)	122 (55.2)	192 (47.4)
<b>Laboratory</b>	Request, n (%)	68 (45.9)	6 (16.7)	57 (25.8)	131 (32.3)
	Not request, n (%)	80 (54.1)	30 (83.3)	164 (74.2)	274 (67.7)
<b>Scanning</b>	Request, n (%)	125 (84.5)	33 (91.7)	65 (29.4)	223 (55.1)
	Not request n (%)	23 (15.5)	3 (8.3)	156 (70.6)	182 (44.9)
<b>Consultation</b>	Request, n (%)	67 (45.3)	0 (0)	10 (4.5)	77 (19.0)
	Not request, n (%)	81 (54.7)	36 (100)	211 (95.5)	328 (81.0)
<b>Outcome</b>	Discharge, n (%)	121 (81.8)	28 (77.8)	204 (92.3)	353 (87.2)
	Standart room, n (%)	22 (14.9)	8 (22.2)	17 (7.7)	47 (11.6)
	Intensive care unit, n (%)	5 (3.4)	0 (0)	0 (0)	5 (1.2)
<b>Earthquake-related injury</b>	Having, n (%)	118 (79.7)	0 (0)	4 (1.8)	122 (30.1)
	Not having, n (%)	30 (20.3)	36 (100)	217 (98.2)	283 (69.9)

**Table 3.** Distribution of injuries to the lesion areas.

	Head/Neck n(%)	Thorax n(%)	Abdomen n(%)	Pelvis n(%)	Extremity n(%)	Multiple n(%)	Total n(%)
<b>Lesion Area</b>	24 (20)	16 (13)	2 (2)	9 (7)	60 (49)	11 (9)	122 (100)

and consultation requests were mostly requested from the adult emergency department. It was found that the patients who applied to the Gynecology and Obstetrics Emergency Department did not request a consultation.

A total of 122 patients with earthquake-related injuries came to the emergency department, and the majority (n: 118; 96.7%) applied to the Adult Emergency Department. (Table 2). Data on the affected areas after injury are shown in Table 3. It was observed that the extremities (60.49%) were affected the most, and the abdomen (2.20%) was the least affected.

## DISCUSSION AND CONCLUSION

Natural disasters have caused deaths and property losses all over the world throughout history.<sup>7</sup> Earthquakes stand out among these disasters regarding death, disability, and economic loss.<sup>8</sup> It has been reported that 125 million people were affected by earthquakes in the past 20 years, and approximately 750.000 people died.<sup>9</sup>

Health services were most affected by the earthquake; the most affected unit among health services is the emergency service. Especially in the first days after the earthquake, a density is expected due to the applications of earthquake victims. When we look at the publications on this subject, there is information that the rate of earthquake victims who applied to the emergency service after the earthquake was 75% and above in the first days.<sup>8,10,11</sup> Studies on this subject report that most hospital admissions are made within the first 1-2 days after the earthquake.<sup>10,12</sup> In our study, it is observed that there were no earthquake victims in the first 48 hours. This may have resulted from the response to the earthquake and its distance from the earthquake zone. In addition, when we look at the applications of the earthquake victims in the first 15 days, only 405 patients were identified, and this number corresponds to only 1.62% compared to the number of applications made in the same period, which is at a level that can be neglected when similar studies are examined.

In studies conducted on patients who came to the emergency department after an earthquake, it is seen that the number of discharges and hospitalisations is high.<sup>8,10</sup> Publications on the use of resources are limited in number. One study reported that 72.3% of the earthquake victims who came to the emergency department did not need any laboratory examination, and 12.2% did not need any imaging examination.<sup>10</sup> Our results support this study. An important reason for this situation may be that most earthquake victims were slightly injured. It has been reported in different studies that most of those who applied to the emergency department after a disaster had minor injuries.<sup>12-14</sup>

Our study revealed that only 52 (12.8%) of earthquake victims were hospitalised. It is seen that this figure corresponds to a rate of only 3.42% when compared to the hospitalizations from the emergency departments in the same period. In a study examining the post2020 Izmir earthquake, the subject reported that 85% of the patients were discharged after ED follow-up, 7% were hospitalized in the standard room, and 2% were hospitalized in intensive care.<sup>10</sup> Similarly, in another study examining the 2011 Van earthquake, it was reported that 72% of the earthquake victims were discharged after ED follow-up, 9% were referred to another hospital, and 19% were admitted to the standard room or intensive care unit.<sup>8</sup> Our study results were compatible with the literature, and 87.2% of the patients were discharged. All these results support the idea that after the earthquake, injuries that can be discharged (superficial injuries that are not of vital importance) are more prominent, especially in earthquake victims, rather than hospitalization.

General body injuries constitute an essential part of post-earthquake emergency services. The literature shows that most injuries occur in the extremities with a rate of 35-40%, and the lower extremities are the most common among extremities.<sup>10,11,15</sup> However, there are also many studies in which other systems, significantly the head/neck, and thorax, can be affected.<sup>10,15,16</sup> Our study results are consistent with the literature, and the number of patients admitted due to injury was approximately 30%, and isolated extremity trauma was 60.49%.

In conclusion, although earthquake victims may apply to the emergency departments regardless of the distance after the earthquake, this number is insufficient to require additional measures regarding the workload it creates. However, since this study is the first analysis based on distance, it should be supported by similar studies. The limitations of our study are; the distance of our city to the earthquake zone, being the only center of the study, and patients coming with their own will and means.

**Ethics Committee Approval:** Approval was obtained from the Non-Invasive Ethics Committee of Sakarya University Faculty of Medicine (Date:27.02.2023 and decision no: 61).

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

**Author Contributions:** Concept – NA; Supervision – NA, YY, BE, OK, FG; Materials –NA, SA, YY; Data Collection and Processing –NA, BE, FG, OK; Analysis and Interpretation – SA, NA, YY; Writing – NA, YY, SA.

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## Interferon-Gamma Inducible Protein-10: Not a Mortality Marker for COVID-19 Disease

### İnterferon-gamma ile İndüklenebilir Protein-10: COVID-19 Hastalığı için Bir Ölüm Göstergesi Değildir

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#### ABSTRACT

**Objective:** Interferon-gamma inducible protein-10 (IP-10) released from macrophages is associated with thrombosis. We aimed to investigate patients' biochemical markers following severe COVID-19, concentrating on the role of IP-10 in mortality.

**Materials and Methods:** In our study, we retrospectively evaluated data from 88 (females, 44.3%) severe patients followed in our university hospital's intensive care unit (ICU). We obtained demographic and laboratory data from our study population's files and electronic records, including D-dimer, ferritin, uric acid, IP-10 values, and other biochemical markers.

**Results:** The mean age of all 88 patients with COVID-19 infection followed in the ICU was 70.5 ±10 years. The median for lymphocyte count was 1.3 (1-2.1) vs 0.8 (0.5-1.1) K/uL, ferritin 151 (90.7-255) vs 624 (296-1254) mcg/L, D-dimer 386 (293.5-650) vs 1280 (871-2245) ug/L, LDH 220 (185-286) vs 429.5 (368-560) U/L with a p-value of <0.05 in survivors vs non-survivors respectively. On the other hand, the level of IP-10 was 21.3 (13.2-31.6) vs 26.6 (11.4-43.6) pg/mL with a p-value of 0.04.

**Conclusion:** In this study, in which non-survivors and survivors were compared in severe COVID-19 patients, it was found that ferritin and D-dimer were good predictors of mortality, while IP-10 could not be a predictor of mortality.

**Keywords:** Biomarker, COVID-19, IP-10, mortality

#### ÖZ

**Amaç:** Makrofajlardan salınan interferon-gama indüklenebilir protein-10 (IP-10) tromboz ile ilişkilidir. Bu çalışma, şiddetli COVID-19 nedeniyle takip edilen hastaların biyokimyasal belirteçlerini ve IP-10'un mortaliteyi göstermedeki rolünü araştırmayı amaçladı.

**Materyal ve Metot:** Bu çalışmada üniversite hastanesinin yoğun bakım ünitesinde (YBU) takip edilen 88 (Kadın % 44,3) ağır hastanın retrospektif verileri değerlendirildi. Demografik ve laboratuvar verileri ile D-dimer, Ferritin, Ürik asit, IP-10 değerleri ve diğer biyokimyasal belirteçlere ilişkin veriler ölen ve yaşayan hastaların dosyalarından elde edildi.

**Bulgular:** Yoğun bakımda takip edilen COVID-19 enfeksiyonlu 88 hastanın yaş ortalaması 70,5 ±10 idi. Hayatta kalan grupta, lenfosit sayısı 1,3 (1-2,1) K/uL, ferritin 151 (90,7-255), D-dimer 386 (293,5-650), LDH 220 (185-286) iken, ölen hastalarda ise, lenfosit sayısı 0,8 (0,5-1,1), ferritin 624 (296-1254) mcg/L, D-dimer 1280 (871-2245) ug/L, LDH 429,5 (368-560) U/L saptandı. Bu parametrelerde p değeri <0,05 idi. Buna karşılık, hayatta kalmayanlarda serum IP-10 seviyeleri hayatta kalanlar da 21,3 (1,2-31,6) pg/mL iken ölen hastalarda 26,6 (11,4-43,6) pg/mL, p=0,04.

**Sonuç:** Şiddetli COVID-19 hastalarında hayatta kalmayanlar ve hayatta kalanların karşılaştırıldığı bu çalışmada, ferritin, ve D-dimerin mortalite için iyi bir tahmin edici potansiyeli olduğu, IP-10'un ise bir belirleyici olamayacağı bulundu.

**Anahtar Kelimeler:** Biyobelirteç, COVID-19, IP-10, mortalite

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## INTRODUCTION

Early symptoms of patients with the new Coronavirus disease 2019 (COVID-19) are fever, non-productive cough, and fatigue. Still, it is closely related to multi-organ failure and high cytokine levels in severe patients.<sup>1</sup> Cytokine levels determine the course of symptoms. Cytokine production is related to individual immune function; therefore, some parameters may have a predictive role in estimating the severity of the COVID-19 course. The clinical spectrum of COVID-19 ranges from simple to severe and critical.<sup>2</sup> Criteria and indications for ICU admission, intubation, and therapy changed dynamically with time during the pandemic.

The host immune response against COVID-19 plays a principal role in the pathogenesis and progression.<sup>3</sup> Serum concentrations of proinflammatory cytokines are strongly associated with disease outcomes and are increased in patients with severe disease.<sup>4</sup> In severe cases, stimulated expression of inflammatory cytokines, especially TNF- $\alpha$  and Interleukin 6, is associated with lymphopenia, T-cell depletion, and increased macrophage and neutrophil counts, indicating immune pathways and cell distribution.<sup>5</sup>

In critical COVID-19 patients, inflammatory factors such as interleukins, colony-stimulating factor, interferon, tumour necrosis factor, growth factor, and chemokines usually increase.<sup>6</sup> Most cytokines are produced by T lymphocytes, fibroblasts, and mononuclear macrophages, which are, in turn, affected by them. Cytokines usually mediate inflammation; however, IL-10 has an anti-inflammatory effect. After natural killer cells (NK) and T cells are activated, proinflammatory cytokines and chemokines such as interferon-gamma inducible protein-10 (IP-10) increase. IP-10 is secreted via endothelial cells, monocytes, and adipose tissue. In a recent study, serum levels of interleukins (4, 19, and 1 $\beta$ ), MCP-1, and TNF- $\alpha$  were significantly higher in patients with COVID-19 compared to disease free.<sup>7</sup> However, the level of IP-10 levels was significantly lower in COVID patients.<sup>7</sup> IP-10 is associated with thrombosis.<sup>1,8</sup> Covid-19 was also described as a multiorgan disease with microthrombosis resulting from damage to the microvascular system.<sup>1,8</sup> In our study, we aimed to evaluate the role of several laboratory parameters, including IP-10, to determine whether they have any predictive role regarding the mortality of COVID-19 in patients followed up in our institution.

## MATERIALS AND METHODS

**Ethical Approval:** We obtained ethical committee approval from the Sakarya University Faculty of Medicine Ethical Committee (Date: 28.12.2020, decision no: E-71522473-050.01.04-619); we con-

ducted our study per the Declaration of Helsinki.

**Study:** Our study is a retrospective, single-center study involving 88 severe (39 female and 49 male) COVID-19 patients recruited from the ICU of our university hospital in Sakarya, western Türkiye. We included adult patients over 18 years who fulfilled COVID-19 disease severity criteria (Those with oxygen saturation less than 90 and or breathing more than 30 breaths per minute despite >5 litre O<sub>2</sub> support). We excluded those under 18 years, those with a history of malignancy or evidence of bacterial infection on ICU admission, and those immunocompromised.

**Study Group:** Our population included surviving and deceased COVID-19 patients admitted to the ICU. Clinical information and laboratory results were collected at the earliest time after hospitalisation. We split our patients into survivors (n=44) and non-survivors (n=44). To study IP-10, serum samples of the patients were drawn on the first day of ICU admission and then stored at -80 degrees. All serum IP-10 levels were measured using an ELISA kit. Clinical symptoms, COVID-19, and laboratory test results were analysed retrospectively.

**Follow-up of Patients and Treatment Protocol:** The diagnosis was made based on the constantly updated TR Ministry of Health's and COVID-19 diagnosis and treatment guidelines parallel to updated international guidelines.

**COVID-19 RNA Detection and Measurement of IP-10:** Nasopharyngeal swabs were tested using commercial reagent kits designed detection of SARS-CoV-2 RNA by PCR. Ready-made commercial kits (Bioxcen, Türkiye) were used for the test. Tests of samples were carried out in compliance with the manufacturer's instructions.

**Measurement of Human IP-10 (CXCL 10) Levels:** Collected samples were sent to our microbiology laboratory in yellow serum separate tubes (SST) biochemistry tube and centrifuged at 4000 rpm for 10 minutes. Collected serum samples were frozen and stored at -80°C until investigated for IP-10 using the micro-ELISA test. Using the ELISA kit, the level of Human IP-10 CXCL10 (Abcam Ltd, Cambridge, UK) was determined in an automatic micro-ELISA device (Grifols, Triturus, Spain). The micro-ELISA test procedure was carried out according to the manufacturer's (Abcam, Cambridge, USA) instructions. The serum levels of IP-10 were measured quantitatively by subtracting the cut-off and calibration curves. The detection range of the kit used is 12.5-800 pg/ml, with an analytical sensitivity of 2.6 pg/mL.

**Outcomes and Other Tests:** All information regarding patient outcomes and routinely monitored laboratory data were taken from hospital records and the



hospital management system.

**Statistical Analyses:** A descriptive analysis was performed to provide information on the general characteristics of the study population. We used Visual (probability plots, histograms) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk's test) to evaluate the normality of distribution. To compare normally distributed variables, we used mean and standard deviation. For non-normally distributed variables, the descriptive analyses were presented using median and interquartile range (IQR). We used the student's t-test for parametric variables and the Mann-Whitney U test for nonparametric ones. The categorical variables were presented as the frequency (% percentage). Categorical variables between the two groups were evaluated using Chi-square test. Automated analyses were performed by SPSS statistics software (IBM SPSS Statistics, Version 21.0). P-value <0.05 was considered significant.

**RESULTS**

This study included 88 patients (44 females & 44 males) confirmed by PCR. The mean age was 70,5

±10 years. We divided the patients into the Survivor (Group 1) and the non-survivor groups (Group 2). The mean age of group 1 was 69.1 ± 9.5 years, while 72 ± 10.3 years in group 2. The male sex ratio was 50.0% (n=22) and 61.40% (n=17) in group 1 and group 2, respectively. In the non-survivor group, the history of both COPD (n=9; 25%) as well as CKD (n=8; 18,2%) was higher than in the survival group. The non-survivor patients had lower lymphocyte accounts, higher neutrophil accounts, higher uric acid, higher alanine aminotransferase (AST), and lower serum albumin than survived patients. On the other hand, Troponin-I, CRP, and procalcitonin levels were higher than the survivor group. The median of IP-10 serum levels of all patients was 23.1 pg/mL (11.8-35.7). The median IP-10 level of the non-survived group was 26.6 pg/mL (11.4-43.6), whereas 21.3 pg/mL (13.2-31.6) in the survived group. However, this difference was statistically insignificant (Table 1).

As illustrated in Figure 1, the Level of ferritin and D-dimer was prominently higher in the nonsurvivor group (p=0,0). This was minimal concerning IP-10

**Table 1.** Characteristics and results of Survivor and non-survivor groups.

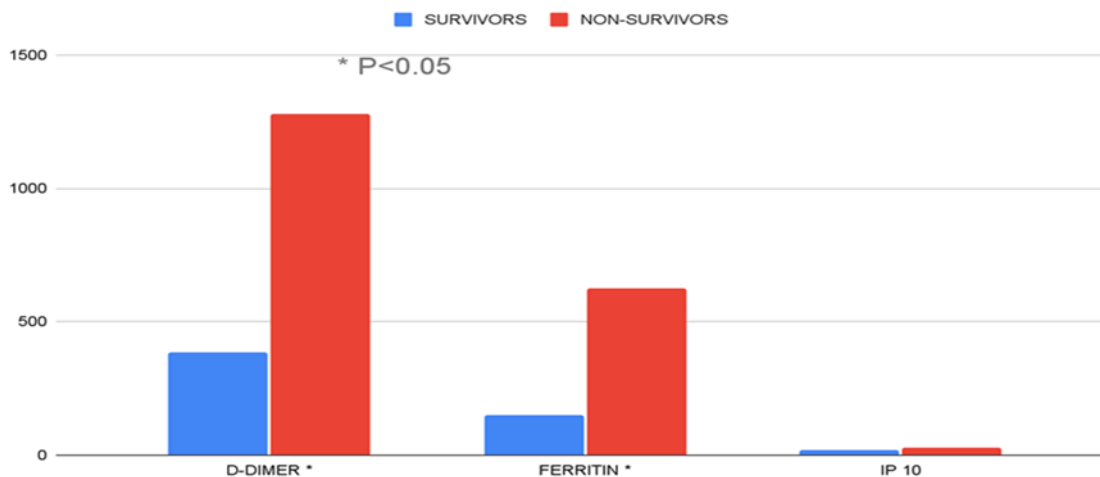
Characteristics	Survivor Group (n- 44)	Non-survivor Group (n- 44)	All patients (n- 88)	P
Age, Mean ± SD	69.1±9.5	72±10.3	70.5±10	0.177
Sex				
Female, n (%)	22 (50.0)	17 (38.60%)	39 (44.3%)	0.283
Male, n (%)	22 (50.0)	27 (61.40%)	49 (55.7%)	
Fever *	5 (11.4)	11 (25.00%)	16 (18.2%)	0.097
Cough *	12 (27.3)	21 (47.70%)	33 (37.5%)	0.048
COPD *	1 (2.3)	9 (20.50%)	10 (11.4%)	0.007
Chronic kidney disease *	2 (4.5)	8 (18.20%)	10 (11.4%)	0.044
WBC (K/uL) **	5.5 (4.5-7)	8.2 (5.3-10.9)	6.2 (4.9-9)	0.000
Hemoglobin, Mean ± SD, (gr/dl)	12.6±1.8	12.1±1.9	12.3±1.9	0.192
Platelet (K/uL) **	168.2 (134.5-201)	182 (139.5-257)	177(135-223.5)	0.223
Lymphocyte count (K/uL) **	1.3 (1-2.1)	0.8 (0.5-1.1)	1.1 (0.7-1.8)	0.000
Neutrophil, (K/uL) **	3.3 (2.4-4.5)	6.3 (3.9-9.1)	4.3 (2.9-6.7)	0.000
Uric acid, Mean ±SD, (mg/dl)	5.9±1.7	7.2±3.2	6.5±2.6	0.037
AS, median (U/L) **	25.5 (21.9-38.3)	41.5 (25.5-71)	31.5 (22.7-48.5)	0.008
Serum albumin, median (gr/L) **	39.9 (32.6-43)	31.5 (26.9-33.2)	33.1 (30-39.9)	0.000
LDH (U/L) **	220 (185-286)	429.5 (368-560)	310 (214.5-448.5)	0.000
Total cholesterol (mg/dl) **	169 (134-204.5)	136 (121-156)	150 (125-181)	0.008
LDL-cholesterol (mg/dl) **	114 (97.5-139.5)	85 (69-111)	103 (78-128)	0.000
HDL-cholesterol (mg/dl) **	38 (33-46)	35 (26-40)	36 (30-42)	0.037
D-Dimer (ug/L) **	386 (293.5-650)	1280 (871-2245)	774 (377.5-1540)	0.000
Troponin (ug/L) **	4.7 (1.7-9.7)	29.7 (11.7-101)	11.5 (4-40.9)	0.000
Ferritin (mcg/L) **	151 (90.7-255)	624 (296-1254)	296 (135.5-653)	0.000
C-reactive protein (mg/L) **	19.5 (6.2-68.4)	118 (65.3-167.5)	65.3 (16.5-128)	0.000
Procalcitonin (ng/mL)	0.1 (0-0.1)	0.3 (0.2-0.6)	0.1 (0.1-0.3)	0.000
Fibrinogen (mg/dL) **	337 (285-394)	409 (354-462)	376.5 (298-434)	0.003
IP-10 (pg/mL) **	21.3 (13.2-31.6)	26.6 (11.4-43.6)	23.1 (11.8-35.7)	0.406

AST: Alanine aminotransferase; COPD: Chronic obstructive pulmonary disease; CRP: C-reactive protein; IP-10: Interferon-gamma inducible protein-10; LDH: Lactate dehydrogenase; WBC: White blood cells. IQR: Interquartile range; \*: Sshown as n, (%); \*\*: Shown as IQR.

levels ( $p=0,406$ ). The mean values of D-dimer & Ferritin are dramatically different, while the difference is not prominent for IP-10.

## DISCUSSION AND CONCLUSION

In most COVID-19-positive patients, a localised, short-lived immune response is sufficient to clear the virus from the lungs, after which the immune



**Figure 1.** Comparison of survivors and non-survivors according to parameters indicating COVID-19 severity.

response subsides, and the patient recovers.<sup>1</sup> It is a hyperinflammatory condition that may lead to acute lung injury, ARDS, or multiple organ failure, with mortality of up to 15% in such patients. A more hyperinflammatory response is seen in deceased patients.<sup>9</sup> This study aimed to reveal different indicators that determine mortality in the data obtained from 88 patients. Cough, COPD, chronic kidney failure, leukocytosis, lymphopenia, low LDL, high D-dimer, high CRP, and high fibrinogen have been shown as significant predictors of determining mortality in many studies. All these high factors are associated with hyperinflammation.

Patients who died in our study had more cough complaints, more COPD history, and more chronic renal failure history. In addition, lymphopenia, increased uric acid value, low albumin, and high LDH were remarkable in our dying patients. Different researchers in different studies have demonstrated these parameters. Again, high ferritin levels are unprecedented in patients who died in D-dimer tests.<sup>10</sup> According to our findings, ferritin and D-Dimer levels are higher in patients with a mortal course associated with organ damage. Ferritin is an acute-phase protein that can be excreted from destroyed cells. Elevated ferritinemia can result from impaired liver activity or metabolic syndrome. COVID-19 patients with abnormal ferritin levels have a higher risk of liver damage and severe disease, and previous studies have shown liver damage in COVID-19 pa-

tients.<sup>11</sup>

It has been shown that proinflammatory cytokines may affect uric acid excretion or serum uric acid levels.<sup>12</sup> This study found that patients with a mortal course had a significantly higher uric acid level. Uric acid is an important antioxidant that scavenges free radicals and reactive oxygen species. Therefore, more inflammation occurs, producing more oxidants in severe COVID-19 patients. The high uric acid levels may be correlated with the anti-inflammatory effect of protecting the body. IP-10 (CXCL10) is a chemokine with multiple actions. It is important in attracting Th1 lymphocytes, monocytes, and natural killer cells. It is also involved in chemotaxis, apoptosis, and regulation of cell growth. It has a role in the immune system. It was identified as a significant biological marker mediating disease severity.<sup>13</sup> IP-10 is particularly interesting as its expression pattern in COVID-19 patients differs from that observed in traditional viral infections. It has been reported that IP-10 rises rapidly but transiently in viral infections like the common cold, while its concentrations often remain high throughout the COVID-19 course.<sup>12</sup> Different researchers have reported that IP-10 may effectively indicate the severity of COVID-19. Several studies pointed to IP-10 as a marker of COVID-19 progression.<sup>14</sup> For example, a study including 74 COVID-19 patients from China reported IP-10 and MCP-1 as parameters that may indicate mortality.<sup>1</sup> In another study from China evaluating 41 patients,

plasma levels of IL-2, IL-7, IL-10, IP-10, GSCF, MCP-1, TNF $\alpha$ , and MIP-1A were higher in ICU patients.<sup>15</sup> However, this study did not demonstrate any correlation between IP-10 and mortality. Our results showed that the IP-10 levels were 26.6 pg/mL in the non-survivors versus 21.3 pg/mL in the survivors, with no statistical difference between groups. The main reason for the difference between our study's results and other studies seems to be due to the comparison of those admitted to the ICU for more severe diseases and who were already prone to death with those who survived. In Yu Chen et al. study, they compared critically ill patients with severely ill ones in the ICU.<sup>1</sup> On the other hand, other studies compared patients admitted to the ICU with those in the wards or those with different clinical pictures.<sup>16,17</sup>

According to these results, IP-10 may be a good biomarker for predicting the progression of the COVID-19 patient newly admitted to the hospital. Still, it may not be a good biomarker for the COVID patients followed in the ICU.

Our study has some limitations. Being partially retrospective, depending on available health records, we do not have full information about the time lag between the first symptoms and application to the outpatient clinic or admission to ICU. In conclusion, comparing non-survivors and survivors of COVID-19 disease, it was determined that while ferritin, uric acid, and D-dimer were good indicators to show mortality, IP-10 could not be a marker for mortality.

**Ethics Committee Approval:** Our study was approved by the Sakarya University Faculty of Medicine Ethical Committee (Date: 28.12.2020, decision no: E-71522473-050.01.04-619). All procedures have been carried out in accordance with the Helsinki Declaration.

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

**Author Contributions:** Concept – KO, KM; Supervision – KO, DH; Materials – DH, YS, GAC, SOE; Data Collection and/or Processing –MI, AA, PM, GE; Analysis and/ or Interpretation – IM, AA, PM, GE; Writing – DH, IM.

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## Is Omalizumab Treatment Used During the COVID-19 Pandemic Effective on the Frequency and Severity of COVID-19?

### COVID-19 Pandemisi Sırasında Kullanılan Omalizumab Tedavisi COVID-19 Sıklığı ve Şiddeti Üzerine Etkili midir?

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#### Abstract

**Objective:** The effects of drugs used in chronic spontaneous urticaria (CSU) and similar chronic dermatological diseases in COVID-19 continue to be the subject of many studies. The present study aimed to reveal the frequency and severity of COVID-19 infection in CSU patients treated with omalizumab and antihistamines.

**Materials and Methods:** CSU patients who were followed up and treated with omalizumab or antihistamines were evaluated retrospectively for clinical conditions with CSU and COVID-19 during the pandemic and compared with the control group regarding the incidence and severity of COVID-19 infection. In addition, urticaria disease severity was also compared with pre-pandemic scores for the CSU group.

**Results:** Real-time reverse transcription-polymerase chain reaction test positivity rate for SARS-CoV-2 was detected in 17.4%, 30.1%, and 34.8% of the patients in omalizumab, antihistamine, and control groups, respectively (p=0.001). The disease activity scores were increased in both antihistamine and omalizumab treated compared to the pre-covid state CSU patients, while the increase was minor in patients using omalizumab.

**Conclusion:** The fact that COVID-19 infection was seen less frequent and urticaria activity scores were lower during the infection in the omalizumab group suggests that omalizumab treatment is safe and convenient to use during COVID-19 infection.

**Keywords:** Antihistamine, COVID-19, incidence, omalizumab, urticaria

#### Öz

**Amaç:** Kronik spontan ürtiker (KSÜ) ve benzeri kronik dermatolojik hastalıklarda kullanılan ilaçların COVID-19'un seyri üzerindeki etkileri halen pek çok araştırma için çalışma konusu olmaya devam etmektedir. Sunulan çalışmada omalizumab ve antihistaminikler ile tedavi edilen KSÜ hastalarında COVID-19 enfeksiyonunun sıklığını ve şiddetini ortaya koymak hedeflenmiştir.

**Materyal ve Metot:** Omalizumab veya antihistaminiklerle izlenen ve tedavi edilen KSÜ hastalarının, pandemi sırasında KSÜ ve COVID-19 ile klinik durumları retrospektif olarak değerlendirildi ve COVID-19 enfeksiyonunun insidansı ve şiddeti açısından kontrol grubu ile karşılaştırıldı. Ayrıca ürtiker hastalığının şiddeti, KSÜ grubu için pandemi öncesi skorlarla karşılaştırıldı.

**Bulgular:** SARS-CoV-2 için gerçek zamanlı ters transkripsiyon-polimeraz zincir reaksiyonu testi pozitiflik oranı omalizumab, antihistaminik ve kontrol gruplarındaki hastaların sırasıyla %17,4, %30,1 ve %34,8'inde tespit edildi (p=0,001). Hastalık aktivitesi skorları covid öncesi duruma kıyasla hem antihistaminik hem de omalizumab ile tedavi edilen KSÜ hastalarında artarken, omalizumab kullanan hastalarda artış daha düşük oranda saptanmıştır.

**Sonuç:** Omalizumab grubunda COVID-19 enfeksiyonunun daha az görülmesi ve enfeksiyon sırasında ürtiker aktivite skorlarının daha düşük olması, omalizumab tedavisinin COVID-19 enfeksiyonu sırasında kullanımının güvenli ve uygun olduğunu göstermektedir.

**Anahtar Kelimeler:** Antihistamin, COVID-19, insidans, omalizumab, ürtiker

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## INTRODUCTION

Since the first few months of 2020, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has spread rapidly around the world, causing the Coronavirus disease 2019 (COVID-19) pandemic. Worldwide, over 541 million cases of COVID-19 have been diagnosed caused by severe acute respiratory SARS-CoV-2, and more than 6 million have died in 188 countries.<sup>1</sup> COVID-19 causes various clinical symptoms, from asymptomatic cases to severe acute respiratory failure, and can affect multiple organ systems.<sup>2</sup>

The effect of chronic diseases and drugs on COVID-19 continues to be the subject of many studies, and chronic spontaneous urticaria (CSU) and medications for treating this disease are no exception. CSU is a chronic condition characterised by itchy hives, swelling, or both that persist for at least six weeks.<sup>3</sup> It is estimated to affect about 50 million people, with symptoms significantly affecting their quality of life.<sup>4</sup>

Omalizumab, a humanised monoclonal antibody that binds to the Cε3 domain of free IgE and prevents it from binding to Fc epsilon RI (FcεRI), has been approved in Europe and the United States as a treatment option for CSU in patients aged 12 and older who do not respond to high-dose H1 antihistamines.<sup>5</sup> In addition to the classical therapeutic mechanism of this molecule, it also has various effects, including potential antiviral and anticoagulant effects.<sup>6,7</sup>

During the pandemic, it was recommended to use antihistamines and omalizumab while avoiding immunosuppressive treatments such as systemic corticosteroids and cyclosporine, if possible.<sup>8,9</sup> For the possible role of mast cells in COVID-19-related lung injury, it has been reported that antihistamines and omalizumab in COVID-19 patients can decrease mortality in patients with severe to critical pulmonary disease.<sup>10,11</sup>

The present study aims to reveal the frequency and severity of COVID-19 infection in patients with CSU treated with omalizumab or antihistamine. A literature review on this subject shows a few reports regarding the use of omalizumab in patients diagnosed with CSU and COVID-19. However, this study differs from these reports in that it includes the most extensive patient series in the literature and is the only study with a control group.

## MATERIALS AND METHODS

**Ethics Committee Approval:** The research protocol was submitted to and approved by the Sakarya University Ethics Committee and was conducted according to the ethical regulations of the Declaration of Helsinki and adherence to Turkish law and regulations (E-71522473-050.01.04-136957-160).

**Design:** It is a retrospective case-control study.

**Participants:** Patients with CSU and treated with omalizumab or antihistamines in Sakarya University Training and Research Hospital, Dermatology and Venereology Department between March 2020 and July 2022 created the CSU treatment group. Individuals without CSU and any chronic disease and similar to the study group in age and sex were selected as the control group. Patients with immunosuppression, morbid obesity, incomplete file records, and who did not accept informed consent, combined therapy of omalizumab and antihistamines for the CSU group, patients who did not receive medical treatment for CSU during the pandemic, and medical history of urticaria for the control group were accepted as exclusion criteria.

**Instrumentation:** Real-time reverse transcription-polymerase chain reaction (rRT-PCR) test results for the SARS-CoV-2 between March 2020 and July 2022 were evaluated through the Public Health Management System of all of the participants, and the cases with positive rRT-PCR tests were recorded. We have done a telephone interview including standard questions with the patients who were followed up with the diagnosis of CSU and whose RT-PCR results were positive. Informed consent was obtained from all participants at the beginning of the interview. As a result of this interview, patients' COVID-19 symptoms, medical treatment methods applied to them for COVID-19, and chronic urticaria activity scores were determined. In addition, the patients were evaluated for COVID-19 disease severity as non-severe, severe, and critical diseases with the medical information retrieved from the patients and their medical information retrieved from hospital records.<sup>12</sup> The chronic urticaria activity score results of the patients evaluated in the pre-Covid period were compared with those in the Covid period.

The vaccination status of the patients was also obtained from the hospital records and compared to determine the comparability of the groups.

**Statistical Analysis:** Statistical analyses were performed using IBM SPSS version 20.0 for Windows statistical software (IBM Corporation, Armonk, New York, USA). Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed in percentage. For distribution normality analyses, Kolmogorov-Smirnov analysis was performed, and parametric and non-parametric tests were preferred according to the results of this analysis. The Independent sample t-test was used for the pairwise comparisons between groups. The Chi-square test was used for the comparison of the categorical variables. P values less than 0.05 were assigned significantly.

RESULTS

In all, 537 patients with CSU who were treated with omalizumab and/or antihistamines were reviewed for the study. However, 78 were excluded because they needed to meet the study eligibility criteria. Finally, the omalizumab group included 276 participants, of which 195 (70.7%) were female and 81 (29.3%) were male, with a mean age of 44.79 ± 14.83 years (17–84). In the antihistamine group, there were 183 patients in total, and of them, 130 (71.0%) were female, and 53 (29.0%) were male, with a mean age of 40.87 ± 15.03 years (17–78). The control group consisted of 400 participants, of which 272 (68.0%) were female, and 128 (32.0%) were male, with a mean age of 42.00 ± 15.17 years (14–90). The differences were not statistically significant

when the groups were compared regarding age and gender distribution characteristics (p= 0.670, 0.941). COVID-19 rRT-PCR test positivity rates for omalizumab, antihistamine and control groups were 17.4% (48 patients), 30.1% (55 patients), and 34.8% (139 patients), respectively. The Chi-square test showed a statistically significant difference between the groups, favouring the omalizumab group (p= 0.001). The patients were also investigated for the COVID-19 infection disease severity characteristics.12 According to the WHO classification, most patients in both groups were in the non-severe category. Only four patients were in the critical category, and six were in the severe category. When the groups were compared regarding severity characteristics, the differences were not statistically significant (p= 0.690) (Table 1).

**Table 1.** Demographics characteristics and rRT-PCR positivity rates of the groups.

		Omalizumab group (n=276)	Antihistamine group (n:183)	Control group (n=400)	p
<b>Gender</b>	Female	195(70.7%)	130(71.0%)	272 (68.0%)	0.670
	Male	81 (29.3%)	53 (29.0%)	128 (32.0%)	
<b>Age</b>		44.79 ±14.83	40.87 ±15.03	42.00 ±15.17	0.941
<b>PCR test positivity rate</b>		48 (17.4%)	55 (30.1%)	139 (34.8%)	0,001 P <sup>†-‡</sup> : <0.002 P <sup>†-§</sup> : <0.001 P <sup>‡-§</sup> : >0.212
<b>WHO Classification</b>	Mild	38 (79.2%)	41 (74.5%)	101 (72.7%)	0.690
	Moderate	8 (16.7%)	13 (23.6%)	31 (22.3%)	
	Severe	2 (4.2%)	-	4 (2.9%)	
	Critical	-	1(1.8%)	3 (2.2%)	

PCR: SARS-CoV-2 rRT – PCR test positivity rate; †: Omalizumab group; ‡: Antihistamine group; §: Control group.

The vaccination status of the CSU and control group before the COVID-19 infection was examined. Thirty-eight patients (69.1%) in the antihistamine group, thirty patients (62.5%) in the omalizumab group, and eighty patients (61.9%) in the control group were unvaccinated. The most common form of vaccination among the vaccinated was two doses of BNT162b2 mRNA (Pfizer-BioNTech) followed by two doses of

the Sinovac vaccine. Although there are rare forms of vaccination, these groups were not included in the statistical analysis because of the limited number of patients in these groups. When the groups were compared with the chi-square analysis according to the most common type of vaccination, the difference was not statistically significant (p= 0.610). These results also showed the comparability of the groups (Table 2).

**Table 2.** The vaccination status before COVID-19 Infection of the groups.

	Antihistamines (n:55)	Omalizumab (n:48)	Control (n:139)	Statistics
Unvaccinated	38 (69.1%)	30 (62.5%)	80 (57.6%)	p=0.610
2 dose Sinovac	5 (9.1%)	5 (10.4%)	11 (7.9%)	
2 dose BNT162b2 mRNA (Pfizer-BioNTech)	10 (18.2%)	10 (20.8%)	38 (27.3%)	Statistically non-comparable
2 dose Sinovac + 3 dose BNT162b2 mRNA (Pfizer-BioNTech)	2 (3.6%)	0	3 (2.2%)	
1 dose BNT162b2 mRNA (Pfizer-BioNTech)	0	1 (2.1%)	2 (1.4%)	
3 dose BNT162b2 mRNA (Pfizer-BioNTech)	0	2 (4.2%)	5 (3.6%)	

In the pre-pandemic period, 89.1% of the patients in the antihistamine group were well-controlled, and 10.9% were in the mild urticaria category. In the same period, 91.7% of patients in the omalizumab group were well-controlled, and 8.3% were mild urticaria. The group comparisons on this topic did not constitute a statistically significant difference (0.660). During the COVID-19 pandemic, 79.2% of the patients in the omalizumab group were well-controlled, 6.3% mild, 6.3% moderate, and 8.3% severe urticaria. In the same period, 61.8% of patients in the antihistamine group were well-controlled, 29.1% had mild

urticaria, and 9.1% had moderate urticaria. There were no severe COVID patients in the omalizumab group. The difference was statistically significant when the groups were compared (0.004). In total, 26.1% (120 patients) of the patients in CSU showed an increase in disease severity during COVID-19 infection, which is 34.5% of the patients in the antihistamine group and 20.8% in the omalizumab group. The difference was not statistically significant ( $p=0.123$ ). (Table 3)

**Table 3.** Disease activity statuses in the COVID-19 and pre-COVID-19 period.

		Omalizumab group (n=276)	Antihistamine group (n:183)	p
<b>UAS Score - prepandemic period</b>	Well-controlled	91.7%	89.1%	0.660
	Mild	8.3%	10.9%	
	Moderate	-	-	
	Severe	-	-	
<b>UAS Score -pandemic period</b>	Well-controlled	79.2%	61.8%	0.004
	Mild	6.3%	29.1%	
	Moderate	6.3%	9.1%	
	Severe	8.3%	-	
<b>Disease Worsening Rate</b>		20.8%	34.5%	0.123

UAS: Urticaria activity score.

## DISCUSSION AND CONCLUSION

Viral infections, which play a role in both triggering and exacerbating the disease in the course of CSU, may lead to T-cell activation followed by induction of inflammatory mediators (interferon, IL-1, IL-2, and TNF- $\alpha$ ). This increased cytokine environment induces degranulation of mast cells, considered the most important effector cells in chronic spontaneous urticaria and have receptors for TNF- $\alpha$  and IL-1, which cause urticaria formation<sup>13,14</sup>. Based on this basic information, Kritas and colleagues showed that coronavirus infection invades mucosal mast cells and exacerbates the inflammatory state by stimulating the secretion of pro-inflammatory cytokines (TNF -  $\alpha$ , IL - 1, IL - 6, IL - 33, and proteases).<sup>15</sup> In this clinical pro-inflammatory scenario, it can be thought that chronic spontaneous urticaria may worsen during COVID-19 disease.<sup>12-15</sup> As Kocatürk et al. state, exacerbation is observed in 36% of CSU patients, especially in severe COVID-19 patients.<sup>16</sup> The data of our study also showed an increased incidence rate for disease activity in 26.1% of the patients, similar to the literature.<sup>16</sup>

The pathophysiology of CSU is partially understood, but the excessive histamine discharge from local basophils and mast cells and the fact that anti-H1 antagonists are highly effective in the treatment indicate that histamine is the primary mediator for it.<sup>4</sup> It

provides immunomodulation by acting on T cells and may cause cytokine release and damage to tissues such as the lung by stimulating inflammation.<sup>17</sup> Dual histamine receptor blockade with the combined use of histamine-1 (H1) receptor antagonist and histamine-2 (H2) receptor antagonist is reported to be a safe and effective method to reduce progression in pulmonary symptom severity in patients with COVID-19, possibly by minimising histamine-mediated cytokine storm<sup>17</sup>. However, we did not show a similar protective effect of antihistamines for getting the COVID-19 infection and its severity.

In addition to the classical therapeutic mechanisms of omalizumab, it has anti-viral and anticoagulant effects<sup>6,7</sup>. The anti-viral effect occurs through down-regulating the high-affinity IgE receptors on plasmacytoid dendritic cells, essential for anti-viral immune responses. It also shows that it restores ex-vivo IFN- $\alpha$  responses to rhinovirus and influenza viruses.<sup>18</sup> A study by Alizadeh et al. showed that omalizumab reduced the Fc $\epsilon$ RI expression on the surface of basophils, plasmacytoid and myeloid dendritic cells in CSU patients, increasing interferon production<sup>14</sup>. The current scientific literature on COVID-19 provides the information that the levels of interferon-1, which confers anti-viral activity to host cells, were lower in severe or critical COVID-19 patients than in controls.<sup>19</sup>

Because of these reasons, we can interpret that



omalizumab treatment, which increases anti-viral immunity and interferon production, may protect against COVID-19 infection. There is a case report that supports this interpretation.<sup>7</sup> A patient under omalizumab treatment for severe asthma was presented in that report. In that report, it is stated that one of the reasons for the mild overcoming of the COVID-19 infection and the absence of asthma exacerbation as a result of the SARS-CoV-2 infection is because of the treatment of omalizumab and its antiviral effectiveness.<sup>7</sup> However, Kocatürk et al. reported that 96% (n=79) of the CSU patients showed a mild course of COVID-19 and that the severity of COVID-19 was not affected by urticaria treatment.<sup>16</sup> Similarly, Bostan et al. could not find a statistically significant relationship between the symptoms of COVID-19 and treatment types.<sup>20</sup> In the present study, the frequency of COVID-19 disease was found to be statistically significantly lower in the omalizumab group compared to both the antihistamine and control groups. This may be related to the fact that omalizumab reduces the risk of contracting COVID-19 infection, or it may be related to the fact that it causes a low-severity infection and does not cause any complaints in the patient; therefore, the PCR test is not performed. When the severity of the COVID-19 disease was examined, it was seen that the patients in the non-severe category were mostly in the omalizumab group. However, it did not create statistical significance. In addition, no critical patients were observed in this group. The discrepancy between the current literature and our study on this subject highlights the need for further research and more extensive studies to validate the findings and determine the true impact of omalizumab on the COVID-19 outcomes observed.

It is known that omalizumab inhibits inflammatory cells, such as neutrophils and coagulation, in patients with CSU.<sup>6</sup> In an experimental study, Wang et al. noted that intramuscular injection of omalizumab small peptide segment into female mice might inhibit IL-6, IL-1 $\beta$ , and TNF- $\alpha$  synthesis in bronchoalveolar lavage fluid, thereby alleviating acute inflammation.<sup>15</sup> In severe COVID-19 infection, vascular skin symptoms may occur due to multi-organ failure and hypercoagulopathy, which is associated with cytokine storm. With this mechanism of action, omalizumab treatment may promise a good prognosis during COVID-19 infection. However, the limited number of patients in the critical category did not permit the statistical analysis.

The major limitation of our study is that the possibility of different behaviours of the patients in the groups regarding the pandemic, such as wearing a mask, social isolation, etc., could not be determined. In addition, although our study included more patients than studies in the current literature, our study

group could only be expanded a little more due to the exclusion criteria used for forming the study group and the patient group being studied from rare dermatology diseases. The small sample size can limit the generalizability of the findings.

In conclusion, the fact that COVID-19 infection was less frequent in the omalizumab group and the lower urticaria severity scores during the infection make omalizumab treatment safe during the COVID-19 pandemic. Considering that COVID-19 infection may continue with different variants in the coming years, if additional studies support these data, using omalizumab in COVID-19 and similar viral diseases may be more straightforward.

**Ethics Committee Approval:** All procedures performed in studies involving human participants followed the national research committee's ethical standards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. - The research protocol was approved by the Sakarya University Non-Invasive Trial Ethics Committee (approval number: E-71522473-050.01.04-14802-82)  
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## Uniportal Video-assisted Thoracoscopic Talc Pleurodesis in the Treatment of Malignant Pleural Effusions. Is Early Phase Talc Pleurodesis More Effective?

### Malign Plevral Efüzyonların Tedavisinde Uniportal Video Yardımlı Torakoskopik Talc Plöredezis. Erken Dönem Talc Plöredezis Daha Etkili midir?

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#### ABSTRACT

**Objective:** VATS talk pleurodesis is an effective method for palliatively treating malignant pleural effusion (MPE). This study aimed to compare early and late-phase talc pleurodesis procedures and to determine the factors affecting the success of the uniportal VATS talc pleurodesis procedure.

**Materials and Methods:** The data of 58 patients who underwent uniportal VATS talc pleurodesis due to MPE were analysed retrospectively. The patients were divided into two groups as early-phase talc pleurodesis (n=23, 48.3%) and late-phase (n=25, 51.7%). Groups were compared using Pearson chi-square test and Mann-Whitney U tests.

**Results:** Complications developed in 10 patients (17.2%). No significant difference was found between the early-phase talc pleurodesis and the late-phase pleurodesis regarding complication rate (p=0.905), durations of hospitalisation (p=0.821). It was observed that the early-phase talc pleurodesis procedure had higher success than the late-phase talc pleurodesis procedure (Odds ratio=1.425, 95% CI=0.307-6.624), although not statistically significant (p=0.06). It was determined that 86% of the patients who underwent early talc pleurodesis had no hospital readmission due to MPE within the first 3 months.

**Conclusion:** Uniportal VATS talc pleurodesis is a safe and effective treatment method for malignant pleural effusion, with low complication and high success rates. Early-phase talc pleurodesis procedure significantly reduces recurrent hospitalisations.

**Keywords:** Dyspnea, malignant pleural effusion, pleurodesis, uniportal VATS

#### ÖZ

**Amaç:** VATS talk plöredezis malign plevral efüzyonun (MPE) palyatif tedavisinde etkili bir yöntemdir. Bu çalışmada erken ve geç faz talk plöredez prosedürlerinin karşılaştırılması ve uniportal VATS talk plöredez prosedürünün başarısını etkileyen faktörlerin belirlenmesi amaçlanmıştır.

**Materyal ve Metot:** MPE nedeniyle Uniportal VATS talk plöredezis uygulanan 58 hastanın verileri retrospektif olarak incelendi. Hastalar erken dönem talk plöredezis grubu (n=23, %48,3) ve geç dönem talk plöredezis grubu (n=25, %51,7) olarak ikiye ayrıldı. Gruplar Pearson ki-kare testi ve Mann-Whitney U testleri kullanılarak karşılaştırıldı.

**Bulgular:** Komplikasyon 10 hastada (17,2%) gelişti. Erken dönem Uniportal VATS talk plöredezis yapılan grup ile geç dönem Uniportal VATS plöredezis yapılan grup arasında komplikasyon oranı (p=0,905), hastanede kalış süresi (p=0,821) açısından istatistiksel fark saptanmadı (p=0,900). Erken dönemde talk plöredezis prosedürünün geç dönem talk prosedürüne göre daha yüksek başarı gösterdiği görüldü (Odds ratio=1,425, 95%CI=0,307-6,624), fakat istatistiksel olarak anlamlı değildi (p=0,060). Erken dönem talk plöredezis uygulanan hastaların % 86'sının ilk 3 ay içinde MPE nedeniyle hastaneye tekrar başvurusu olmadığı belirlendi.

**Sonuç:** Uniportal VATS talk plöredezis malign plevral efüzyonlarda komplikasyon oranı düşük, başarı oranı yüksek, güvenli ve etkili bir tedavi yöntemidir. Erken dönemde uygulanan talk plöredezis prosedürü tekrarlayan hastane yatışlarını önemli ölçüde azaltmaktadır.

**Anahtar Kelimeler:** Dispne, malign plevral efüzyon, plöredez, uniportal VATS

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**INTRODUCTION**

The presence of malignant pleural effusion (MPE) is a common complication in advanced malignant tumours.<sup>1</sup> MPE is typically accompanied by severe dyspnea that impairs patients' quality of life. The prevalence of MPE among cancer patients ranges from 15% to 39%.<sup>1,2</sup> In addition to developing from pleural metastases, MPE can also result from primary pleura tumours, such as mesothelioma.<sup>3</sup> Lung carcinoma, breast carcinoma, and lymphoma are the most common causes of MPE.<sup>1,3</sup> Survival is considered when designing treatment strategies for patients who have developed MPE. In these advanced cancer patients, where survival expectancy is generally low, the treatment approach can be palliative and aims to improve the patient's quality of life with minimally invasive interventions whenever possible. As part of MPE treatment, it is intended to drain the pleural cavity completely of fluid, to promote lung expansion as much as possible, and to apply interventions to prevent the re-accumulation of fluid. The most widely used approach is pleurodesis with sterile talcum powder.<sup>4</sup> With the advent of video-assisted thoracoscopic surgery (VATS), uniportal (U) talc insufflation, and pleurodesis are now possible.<sup>5</sup> The number of studies investigating the effects of time of application of the talc insufflation procedure and the amount of pleural effusion identified before the procedure on the success of pleurodesis is limited.<sup>5</sup> We hypothesised that the early phase UVATS talc pleurodesis procedure is more effective than the late

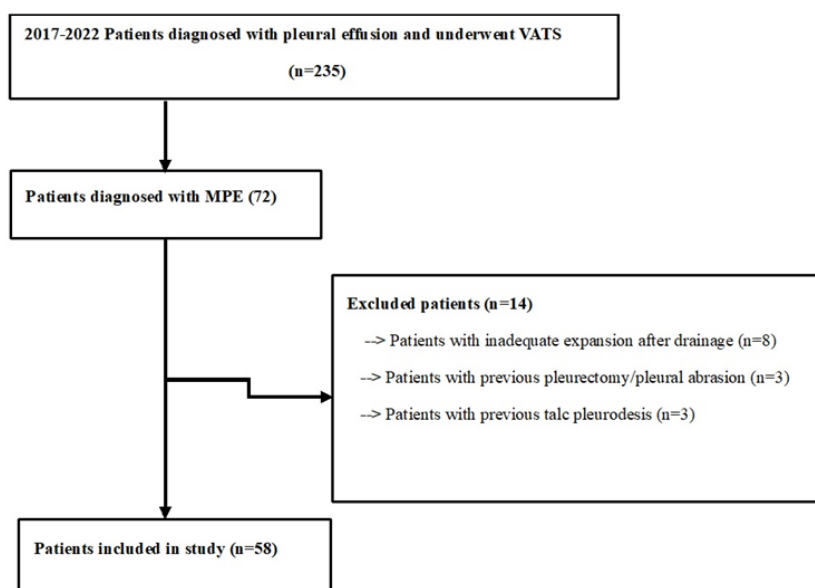
phase talc pleurodesis procedure and that the early phase talc pleurodesis procedure significantly reduces recurrent hospitalisations.

The study aimed to compare the outcomes of our patients who underwent early and late-phase talc pleurodesis and identify the factors affecting the success of the uniportal VATS (UVATS) talc pleurodesis procedure performed for MPE.

**MATERIALS AND METHODS**

**Ethics Committee Approval:** The study was approved by the Ethics Committee of Sakarya University and was conducted in accordance with the principles of the Declaration of Helsinki; (Date: 08/03/2023, decision no: 92). Informed consent was obtained from the patients.

**Patient Feature:** The records of 235 patients diagnosed with pleural effusion for any reason and who underwent diagnosis and/or treatment VATS at the Department of Thoracic Surgery between 2017 and 2022 were retrospectively analysed. It was determined found that 72 (31%) patients were diagnosed with MPE. A total of 14 patients were excluded from the study, including 8 patients for whom adequate expansion could not be achieved after drainage and three who had previously undergone pleurectomy/pleural abrasion. Patients who had previously undergone talc pleurodesis with a chest drain (n:3) were excluded from the study. Ultimately, 58 patients were included in the study (Figure 1).



**Figure 1.** Flow diagram of patient selection and algorithm. MPE: Malignant pleural effusion; VATS: video-assisted thoracoscopic surgery; n: number.

Patients with poor performance status (Karnofsky performance index  $\leq 30$ ) or a life expectancy of less than three months were excluded from the study.<sup>6</sup>

Detection of fluid filling more than two-thirds of the hemithorax on computed tomography (CT) of the thorax was considered massive MPE.<sup>7</sup> Tumours originating primarily from the pleura or lung were defined as "intrathoracic tumours".

In patients with MPE, the application of talc pleurodesis following the first diagnostic pleural procedure was defined as "early-phase talc pleurodesis". If talc pleurodesis was performed after recurrent MPE, it was defined as "late-phase talc pleurodesis". Preoperative complete blood count, coagulation tests, and biochemical tests were routinely evaluated.

**Perioperative and Postoperative Periods:** In all patients, pleurodesis was performed by UVATS and surgery was performed under general anaesthesia with double-lumen selective intubation.

The pleural cavity was evaluated after drainage with UVATS, and suspicious areas were sampled on both the visceral and parietal pleura. In patients with pleural effusion undiagnosed preoperatively, the malignant pathologic diagnosis was confirmed by intraoperative frozen-section examination. Positive pressure ventilation was used to determine whether the lung had expanded sufficiently after pleural fluid drainage. In patients with sufficient expansion, 4 mg of sterile talcum powder (Steritalc®, Novatech, France) was used for pleurodesis. Talcum powder was distributed evenly on all parenchyma and parietal pleura surfaces by insufflation using a disposable atomiser.<sup>5</sup> The procedure was terminated by placing a single 28-F thoracic drain through the UVATS incision.

In patients with a daily drainage of 100ml/24 h, the drain was terminated when the complete expansion was observed on the posterior-anterior (PA) chest radiograph, and the patients were discharged on the same or the following day.

The patients were routinely scheduled for follow-up at the postoperative day 10, month 1, and month 3 and evaluated by PA chest radiographs. Re-accumulation of pleural fluid in the patient's follow-up was considered a technique failure. The absence of fluid accumulation at subsequent 3-month outpatient clinic visits was considered the procedure's success.

**Statistical Analysis:** Data were entered into the Statistical Package for the Social Sciences software package (IBM® SPSS Statistics for Windows, version 23.0, Armonk, NY, USA). Descriptive statistics were used, quantitative variables were characterised using mean, maximum (max), and minimum (min) values, while percentages were used for qualitative variables. The normality of the distributions was

determined by Kolmogorov-Smirnov analysis. The inter-quantile range (IQR) result was also presented for the values recorded as the median. It was decided to use Student's t-test to compare continuous variables between groups. Pearson's chi-square test was used for the comparative analysis of qualitative variables, whereas Fisher's exact test was used when the sample size was small ( $\leq 5$ ). Nonparametric continuous variables were recorded as median and compared using Mann-Whitney U tests. When factors affecting the method's success were identified in the univariate analysis, logistic regression analysis was conducted with these factors.

## RESULTS

The mean age of the patients was  $62.2 \pm 10.7$  years (min=22, max=94). Most of the patients included in the study were male (n=36, 62.1%). The clinical manifestations of the patients included dyspnea (n=45, 77.6%), chest pain (n=16, 27.6%), and cough (n=2 3.4%). The cause of MPE was intrathoracic tumours in 56.9% (n=33) and extrathoracic tumours in 43.1% (n=25) of patients. The most common causes of malignant pleural effusions were primary lung cancer (n=25, 43.1%), malignant pleural mesothelioma (n=8, 13.7%), and breast cancer (n=8, 13.7%). Of the patients who underwent talc pleurodesis with UVATS, 28 (48.3%) experienced the early-phase talc pleurodesis procedure. In comparison, 30 patients (51.7%) underwent late talc pleurodesis (n=21 36.2% after the 2nd episode, n=7% after the 3rd episode and n=2 3.4% after the 4th episode). MPE was massive in most patients (n=38, 65.5%). There was no mortality among our patients after UVATS talc pleurodesis. Complications developed in 10 patients (17.2%) after UVATS talc pleurodesis. The most common complication was chest pain (n=4, 6.7%). It was followed by shortness of breath (n=2, 3.4%), arrhythmia (n=2, 3.4%), fever (n=1, 1.7%), atelectasis (n=1, 1.7%), and other complications. The mean duration of hospitalisation was 7.7 days (min=2 days, max=20), and the mean drainage duration was 7.1 days (min=2 days, max=19). The clinicopathologic and demographic characteristics of the patients are summarised in Table 1.

No significant difference was found between these two groups in terms of primary tumour location (p=0.621), complication rate (p=0.905), the success of VATS pleurodesis (p=1.000), duration of hospitalisation, and drainage duration (p=0.821, 0.900, respectively). The comparison of patients who underwent early-phase UVATS pleurodesis and patients who underwent late-phase UVATS pleurodesis is presented in Table 2.

**Table 1.** Demographic and clinical data of the patients.

Variables	Data
Age, years, mean±SD	62.2±14.1
Sex, n (%)	Female 22 (37.9) Male 36 (62.1)
Primary tumour location, n (%)	Intrathoracic 33 (56.9) Extrathoracic 25 (43.1)
Tumour subtype, n (%)	Primary lung cancer* 25 (43.1) Pleural mesothelioma 8 (13.7) Colorectal cancer 4 (6.8) Melanoma 1 (1.7) Breast cancer 8 (13.7) Gastric cancer 4 (6.8) Osteosarcoma 2 (3.4) Ovarian cancer 3 (5.1) Pancreatic cancer 2 (3.4) Prostate cancer 1 (1.7)
Mode of diagnosis, n (%)	Pleural biopsy 26 (44.8) Cytology 32 (55.2)
Thoracentesis / pathological diagnosis status, n (%)	No 35 (60.3) Yes 23 (39.7)
Side, n (%)	Left 39 (67.2) Right 19 (32.8)
Surgery after how many recurrences, n (%)	1 28 (48.3) 2 21 (36.2) 3 7 (12.1) 4 2 (3.4)
Amount of malignant pleural effusion, n (%)	Submassive 20 (34.5) Massive 38 (65.5)
Smoking, n (%)	No 39 (67.2) Yes 19 (32.8)
Comorbidity, n (%)	23 (39.7)
Complication, n (%)	10 (17.2)
Recurrent pleurisy status (success rate), n (%)	Successful 49 (84.5) Unsuccessful 9 (15.5)
Length of hospital stay, days, median (IQR)	6 (6.3)
Drainage time, days, median (IQR)	5 (5.3)

IQR: interquartile range; SD: standard deviation; n: number; Primary lung cancer\*: lung adenocarcinoma, lung squamous cell cancer, lung small cell cancer

**Table 2.** Comparison of those who underwent early-phase UVATS talc pleurodesis and late-phase UVATS talc pleurodesis.

Variables	Early-phase UVATS talc pleurodesis (n=28)	Late-phase UVATS talc pleurodesis (n=30)	p-value
Age, years, mean±SD	58.9±13.4	65.3±14.3	<i>0.080</i>
Sex, n (%)	Female 9 (32.1) Male 19 (67.9)	13 (43.3) 17 (56.7)	0.380
Primary tumour location, n (%)	Intrathoracic 15 (53.6) Extrathoracic 13 (46.4)	18 (60.0) 12 (40.0)	0.621
Mode of diagnosis, n (%)	Pleural biopsy 8 (28.6) Cytology 20 (71.4)	18 (60.0) 12 (40.0)	<b>0.010</b>
Thoracentesis / pathological diagnosis status, n (%)	No 16 (57.1) Yes 12 (42.9)	19 (63.3) 11 (36.7)	0.630
Side, n (%)	Left 12 (42.9) Right 16 (57.1)	23 (76.7) 7 (23.3)	0.113
Amount of malignant pleural effusion, n (%)	Submassive 11 (39.3) Massive 17 (60.7)	9 (30.0) 21 (70.0)	0.457
Smoking, n (%)	No 17 (60.7) Yes 11 (39.3)	22 (73.3) 8 (26.7)	0.306
Comorbidity, n (%)	13 (46.4)	10 (33.3)	0.308
Complication, n (%)	5 (17.9)	5 (16.7)	0.905
Recurrent pleurisy status (success rate), n (%)	Successful 24 (85.7) Unsuccessful 4 (14.3)	25 (83.3) 5 (16.7)	1.000
Length of hospital stay, days, median (IQR)	6 (6.3)	7 (6.5)	0.821
Drainage time, days, median (IQR)	5 (5.5)	6 (5.5)	0.900

The p-value in bold indicates statistical significance. The p-value in italics indicates a trend towards statistical significance. IQR: interquartile range; SD: standard deviation; UVATS: uniportal video-assisted thoracoscopic surgery

VATS talc pleurodesis was successful in 49 patients (84.5%), but not in 9 patients (15.5%), and the effusion recurred during follow-ups. It was determined that 86% of the patients who underwent talc pleurodesis in the early period had no hospital admission due to MPE within the first 3 months. It was found that the evaluated parameters did not affect the success of VATS pleurodesis (Table 3).

Logistic regression analysis of certain variables that may affect the success of VATS talc pleurodesis revealed that smoking was an independent risk factor for failure at a level close to statistical significance (Odds ratio=4.242, 95%CI=0.817-22.032, p=0.08). Early-phase VATS pleurodesis procedure increased the odds of success (Odds ratio=1.425, 95%CI=0.307-6.624, p=0.06), although not statistically significant (Table 4).

**DISCUSSION AND CONCLUSION**

Primary malignancies of the pleura and many intrathoracic or extrathoracic cancers metastasised to the pleura may cause MPE.<sup>8</sup> In Europe, approximately 100,000 patients are hospitalised annually due to MPE. In contrast, in the United States, the number is estimated to be approximately 126,000.<sup>9</sup> This leads to a dramatic increase in healthcare costs and severe economic losses. Depending on the primary disease, life expectancy ranges from 1 to 12 months on average.<sup>2,10</sup> While it has been reported that the most common cause of MPE is lung cancer, other causes include breast cancer, gastrointestinal system malignancies, hematologic malignancies, and mesothelioma, which is the primary tumour of the pleura.<sup>9,11,12</sup> As a result of our study, we found that primary lung cancer was the most common cause of MPE, followed by mesothelioma and breast cancer

**Table 3.** Grouping of patients as successful talc pleurodesis and unsuccessful talc pleurodesis according to success status and comparison of these groups.

Variables		Successful pleurodesis (n=49)	Unsuccessful pleurodesis (n=9)	p-value
Age, years, mean±SD		62.2±14.1	63.1±15.1	0.850
Sex, n (%)	Female	20 (40.8)	2 (22.2)	0.291
	Male	29 (59.2)	7 (77.8)	
Primary tumour location, n (%)	Intrathoracic	28 (57.1)	5 (55.6)	1.000
	Extrathoracic	21 (42.9)	4 (44.4)	
Side, n (%)	Left	35 (71.4)	4 (44.4)	0.113
	Right	14 (28.6)	5 (55.6)	
Timing of UVATS, n (%)	Early-phase talc pleurodesis	24 (49.0)	4 (44.4)	1.000
	Late-phase talc pleurodesis	25 (51.0)	5 (55.6)	
Amount of malignant pleural effusion, n (%)	Submassive	17 (34.7)	3 (33.3)	0.937
	Massive	32 (65.3)	6 (66.7)	
Smoking, n (%)	No	35 (71.4)	4 (44.4)	0.137
	Yes	14 (28.6)	5 (55.6)	
CT/RT after pleurodesis, n (%)	No	35 (89.8)	8 (88.9)	1.000
	Yes	5 (10.2)	1 (11.1)	
Comorbidity, n (%)		21 (42.9)	2 (22.2)	0.245
Complication, n (%)		9 (18.4)	1 (11.1)	0.596
Length of hospital stay, days, median (IQR)		6 (5.5)	4 (9.0)	0.248
Drainage time, days, median (IQR)		5 (5.5)	4 (8.0)	0.380

IQR: interquartile range; SD: standard deviation; UVATS: Uniportal video-assisted thoroscopic surgery; CT: chemotherapy; RT: radiotherapy.

**Table 4.** Logistic regression analysis of certain variables that may affect the success of pleurodesis with UVATS.

Variable	Odds ratio	95%CI	p-value
Age (for each year)	1.002	0.948-1.059	0.944
Location of the primary tumour (intrathoracic vs extrathoracic)	1.853	0.353-9.718	0.466
UVATS time (early-phase vs. late-phase)	1.425	0.307-6.624	0.651
Amount of malignant pleural effusion (Submassive vs massive)	1.329	0.258-6.842	0.734
Smoking (No vs Yes)	4.242	0.817-22.032	0.080

Vs: versus; CI: confidence interval; UVATS: Uniportal video-assisted thoroscopic surgery.

as other common causes.

Due to their short life expectancy, palliative treatment strategies are typically used in MPE patients. Evacuation of the fluid with closed-system thoracic drainages at diagnosis was accepted as the first approach. Still, after this application, it was observed that the fluid recurred in 60% of the patients within 9 days and in 90% of the patients within a month.<sup>13,14</sup>

For treating MPE, pleurodesis of the pleural cavity is recommended to prevent recurrence.<sup>15</sup> Although agents such as bleomycin, patient's blood, tetracycline, silver nitrate, and iodopovidone, as well as surgical procedures such as pleurectomy/decortication, can be used for pleurodesis, the most commonly used agent worldwide is sterile talc powder.<sup>4</sup> The aim is to provide adhesion between pleural leaves due to local irritation and inflammation.<sup>16</sup> In a systematic review and meta-analysis, talc pleurodesis with VATS was reported to be more successful than other techniques.<sup>12,17</sup> Hence, we applied the UVATS technique for talc pleurodesis in the patients included in the study. The most commonly reported complications of the technique are chest pain and fever.<sup>4,15</sup> Consistent with the findings in the literature, the most common complication we encountered was chest pain, with an incidence of 17%. There was no difference in complications between early and late-phase VATS talc pleurodesis procedures. Barbetakis et al.<sup>18</sup> demonstrated in their study that the most common complication they encountered was prolonged air leak. No prolonged air leak was observed in our series. This may be explained by the fact that decortication was not performed in patients with insufficient lung expansion, and these patients were excluded from the study. In large series, mortality of the procedure has been reported as 0.8-2%.<sup>12,18</sup> Low-performance status and delay between pleural effusion diagnosis and pleurodesis were reported to be statistically significant factors for postoperative mortality.<sup>14,18</sup> Markowiak et al.<sup>19</sup> suggested that 30-day mortality (5.8%) was not related to the procedure but to the primary disease. No early mortality was associated with the procedure in any of our patients. This may be explained by the patients with poor performance status and life expectancy of less than 3 months who were treated with therapeutic thoracentesis or pleural catheter drainage and were excluded from the study.

In the literature, the success rate in patients who underwent VATS talc pleurodesis for MPE was between 76% and 96%.<sup>19,20</sup> Cardillo et al.<sup>14</sup> argued that the early-phase VATS talc pleurodesis procedure increased the chance of success. Meanwhile, Cobanoglu et al.<sup>5</sup> suggested that talc pleurodesis is more likely to be successful when MPE is asymptomatic and a low amount of effusion is detected.

Among the patient groups included in our study, we could not see any difference in the success of the procedure between the massive and submassive patient groups. Our success rate in our UVATS talc pleurodesis cases was 84.5%, similar to the literature. Moreover, similar to the literature, when we compared the early-phase talc pleurodesis group with the late talc pleurodesis group, it was found that the early-phase talc pleurodesis procedure increased the probability of success, though not significantly. Based on our study results, the early-phase talc pleurodesis procedure significantly reduced recurrent hospitalisations, supporting our hypothesis. Nevertheless, in contrast to our expectations, there was no significant difference in efficacy between the early and late-phase UVATS talc pleurodesis groups. It was found that 86% of the patients had no hospital admission due to MPE within the first 3 months. For this reason, we think that early-phase VATS talc pleurodesis is important.

In conclusion, it is well established that UVATS talc pleurodesis is a safe and effective treatment modality for MPE, with a low complication and a high success rate. The efficacy of early and late-phase UVATS talc pleurodesis procedures was similar. Early-phase talc pleurodesis procedure significantly reduces recurrent hospitalisations. The study has some limitations. First of all, it was designed as a retrospective study. The MPE patient group is a large heterogeneous group of patients with different survival prospects. However, the fact that it was a single-centre study is a strength regarding the homogeneity of the treatment applied.

**Ethics Committee Approval:** The study approval was obtained from Sakarya University Faculty of Medicine Local Ethics Committee and was conducted in accordance with the principles of the Declaration of Helsinki; (Date: 08/03/2023, decision no: 92). Informed consent was obtained from the patients.

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

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

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## Death Anxiety in Patients with Hypertension and ST-Elevation Acute Myocardial Infarction and the Affecting Factors

### Hipertansiyon ve ST Elevasyon'lu Akut Miyokard İnfarktüsü Hastalarında Ölüm Anksiyetesi ve Etkileyen Faktörler

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#### ABSTRACT

**Objective:** Death Anxiety in Patients with Hypertension and ST-Elevation Acute Myocardial Infarction and the Affecting Factors

**Materials and Methods:** This study was conducted between February and March 2022, with 195 patients with hypertension, ST-Elevation Acute Myocardial Infarction and healthy individuals. Patients who were admitted to the city hospital's cardiology outpatient clinic and were followed up in the outpatient clinic with the diagnosis of hypertension and ST-Elevation Acute Myocardial Infarction for the last one year were included in the study. The research data were collected using a Patient Information Form and the "Abdel Khalek Death Anxiety Scale".

**Results:** The mean death anxiety scale score was 46.38±16.72 in hypertension patients, 38.27±12.84 in patients with ST-Elevation Acute Myocardial Infarction, and 48.93±16.83 in healthy individuals. A significant difference was found between the death anxiety scores of patients with hypertension compared to patients with ST-Elevation Acute Myocardial Infarction (p=0.007). Death anxiety scores of the groups were found to be correlated with some sociodemographic characteristics (p<0.05).

**Conclusions:** It was determined that death anxiety was significantly higher in hypertension patients compared to ST-Elevation Acute Myocardial Infarction patients.

**Keywords:** Death anxiety, hypertension, myocardial infarction, ST-elevation

#### ÖZ

**Amaç:** Bu araştırma, Hipertansiyon ve ST Elevasyon'lu Akut Miyokard İnfarktüsü hastalarında ölüm anksiyetesi ve etkileyen faktörleri belirlemek amacıyla yapıldı.

**Materyal ve Metot:** Bu çalışma Şubat-Mart 2022 tarihleri arasında hipertansiyonu olan, ST elevasyonlu Akut Miyokard İnfarktüsü geçirmiş hasta ve sağlıklı bireylerden oluşan toplam 195 kişi ile gerçekleştirildi. Çalışmaya şehir hastanesi kardiyoloji polikliniğine başvuran, son 1 yıldır hipertansiyon ve ST Elevasyon'lu Akut Miyokard İnfarktüsü tanısı ile poliklinikte izlenen hastalar dahil edildi. Araştırmanın verileri; Hasta Bilgi Formu ve "Abdel Khalek Ölüm Kaygısı Ölçeği" kullanılarak toplandı.

**Bulgular:** Ölüm anksiyetesi ölçeği puan ortalaması Hipertansiyon hastalarında 46,38±16,72, ST Elevasyon'lu Akut Miyokard İnfarktüsü 38,27±12,84, sağlıklı bireylerde ise 48,93±16,83 olarak bulundu. Hipertansiyon hastalarının ST Elevasyon'lu Akut Miyokard İnfarktüsü'lü hastalara göre ölüm anksiyete puanları arasında farklılık belirlendi (p=0,007). Grupların ölüm kaygısı puanlarının bazı sosyodemografik özelliklerle ilişkili olduğu belirlendi (p<0,05).

**Sonuç:** Araştırmada hipertansiyon hastalarında ölüm anksiyetesinin ST Elevasyon'lu Akut Miyokard İnfarktüsü hastalarına göre anlamlı derecede daha yüksek olduğu belirlendi.

**Anahtar Kelimeler:** Ölüm anksiyetesi, hipertansiyon, miyokard enfarktüsü, ST-elevasyonu

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## INTRODUCTION

Death is the end of life due to the irreversible cessation of vital functions of a living thing.<sup>1</sup> Diagnosed with a chronic disease causes individuals to reconsider their lives by remembering death.<sup>2,3</sup> Hypertension (HT) and Myocardial Infarction (MI) are among the most common causes of death worldwide.<sup>4</sup> It is reported that more than 17.9 million people die yearly due to Cardiovascular Diseases (CVD) in the world.<sup>5</sup> In Türkiye, circulatory system diseases rank first among the causes of death with a rate of 35.4% in 2022. When deaths due to circulatory system diseases are examined according to sub-death causes, it was observed that 42.3% of the deaths were due to ischemic heart diseases.<sup>6</sup> Among CVD, MI is a significant health problem due to its high mortality rate, severe complications, and infarction recurrence.<sup>7,8</sup> It is stated that one in every six men and one in every seven women in Europe had MI, and 12.0% of patients died within six months following the infarction due to ST-Elevation Acute Myocardial Infarction (STEMI).<sup>9</sup> While worrying about death is normal, for some people, thinking about their death or the process of dying can cause intense anxiety and fear.<sup>10</sup> Death anxiety encompasses many emotions, such as fear, grief, and restlessness.<sup>11,12</sup> One of the factors that cause death anxiety is the presence of a chronic disease.<sup>11,13,14</sup> The most important reason for death anxiety and depression in STEMI patients is the high mortality rate.<sup>15-19</sup> When literature is examined, it is stated that there are a limited number of studies examining the death anxiety of heart patients, and these patients experience moderate to severe death anxiety<sup>19,20</sup>. In contrast, patients with MI generally experience moderate and severe death anxiety.<sup>14,19,21</sup> Hypertension is a chronic disease that progresses insidiously and can cause rhythm disorders, angina pectoris, myocardial infarction, and sudden deaths due to heart failure.<sup>22,23</sup> Hypertension patients are more likely to experience negative emotions such as anxiety and depression, and there are a limited number of studies showing that death anxiety is high in HT patients.<sup>24</sup>

Death anxiety affects the risky disease group and may negatively affect the life and quality of life of individuals of all ages. This study aimed to determine the death anxiety levels and related factors in patients with STEMI, patients with chronic diseases such as HT, and healthy volunteers.

## MATERIALS AND METHODS

**Ethical Approval:** Ethics committee approval was obtained from the Ethics Committee of Non-Interventional Clinical Studies of Selçuk University (Date:03.02.2022 decision no: 2022/60). Permission was obtained from the Director's Office of the hospi-

tal. Written consent of the patients who participated in the study was obtained after reading an informed consent. The principles in the Declaration of Helsinki were complied with in the study.

**Study Design:** It was conducted as a randomized-controlled research.

**Setting and Sample:** The study population consisted of patients admitted to Tekirdağ City Hospital Cardiology outpatient clinic. The sample of the study included patients who were admitted to the cardiology outpatient clinic at least one year ago, who were diagnosed with hypertension and had STEMI at least once, who were using antihypertensive/cardiac medications, who were aged 18 or over, who volunteered to participate in the study, and who met the inclusion criteria of the study. It was determined that at least 55 participants in each group should have at least a 5% significant difference in the 95% confidence interval for 80% power, including the control group, hypertension patients, and STEMI patients. The research was completed with 195 participants who met the inclusion criteria, 65 people in each group.

In this study, the names of the patients who were admitted to Tekirdağ City Hospital Cardiology Outpatient Clinic between 01.02.2022 and 01.03.2022 were written on paper by a person who was not included in the study, they were placed in a black bag, and the groups were determined by simple randomisation method. Individuals aged over 18 who had no communication problems, were literate and were not diagnosed with HT or STEMI constituted healthy volunteers.

**Data Collection:** The data were collected with the data collection form prepared by the researchers in the scope of literature review and the "Abdel-Khalek Death Anxiety Scale (ASDA)".<sup>3,19</sup> The data were collected by face-to-face interview technique (in a private room, wearing the three-layer mask, considering hand hygiene and social distance rules). Before implementing the questionnaire, written and verbal consent was obtained after the patients were informed about the purpose of the study and the questionnaire form. Patients who could fill out the scales were given questionnaires and asked to complete them. The implementation of the data collection forms took approximately 20-25 minutes.

**Patient Information Form:** This form consists of two parts. The first part includes socio-demographic data and information about hypertension and STEMI disease; the second has "ASDA".

**Abdel-Khalek Death Anxiety Scale (ASDA):** It was developed by Abdel-Khalek<sup>25</sup>, considering the cultural differences of Muslim societies. It consists of 20 items.<sup>26</sup> In the validity and reliability study, Cronbach's alpha coefficients were between 0.88 and 0.93. The scale was adapted to Turkish by Ay-

dogan et al.<sup>27</sup>. Cronbach's alpha value was calculated as 0.86. In this study, the Cronbach Alpha reliability coefficient was 0.91.

**Statistical Analysis:** IBM SPSS 24.0 and SigmaStat 3.5 statistical software were used to evaluate the data. A normality test evaluated the distribution of numerical variables. The t-test and Mann-Whitney U test were used to compare the two groups. One-way ANOVA and Kruskal Wallis tests were used to compare three or more groups. Pearson correlation analysis was used to compare the scales used with each other. p<0.05 was accepted as significant in the study.

**RESULTS**

The mean age of HT patients was 55.63±11.81 years. Of them, 63.1% were male, 84.6% were married, and 52.3% were primary school graduates. The

mean age of the STEMI group was 61.00±11.10 years. Of them, 80.0% were male, 89.2% were married, and 50.8% were primary school graduates. The mean age of healthy individuals was 37.64±17.43 years. Of them, 55.4% were female, 46.2% were married, and 72.3% were university graduates (Table 1).

It was determined that 58.5% of the patients in the HT group had a disease duration of 1-5 years, 73.8% had a family history of HT, 86.2% developed HT-related complications, and 70.8% did not have HT-related death anxiety. Of the STEMI patients, 61.5% had a heart disease duration of 1-5 years, 63.1% had a family history of heart disease, 86.2% had a STEMI history, 60.0% were afraid of having recurrent STEMI, 33.8% had STEMI-related death anxiety (Table 2).

**Table 1.** Distribution of HT, STEMI and healthy individuals by sociodemographic characteristics.

Sociodemographic Characteristics		HT (n=65) X̄±SD	STEMI (n=65) X̄±SD	Control (n=65) X̄±SD
<b>Age</b> (Min-Max)		55.63±11.81 34-82	61.00±11.10 37-87	37.64±17.43 30-82
<b>Sociodemographic Characteristics</b>		<b>n (%)</b>	<b>n (%)</b>	<b>n (%)</b>
<b>Gender</b>	Female	24 (36.9)	13 (20.0)	36 (55.4)
	Male	41 (63.1)	52 (80.0)	29 (44.6)
<b>Marital status</b>	Married	55 (84.6)	58 (89.2)	30 (46.2)
	Single	10 (15.4)	7 (10.8)	35 (53.8)
<b>Place of residence</b>	Province	48 (73.8)	38 (58.5)	33 (50.8)
	District	14 (21.5)	19 (29.2)	30 (46.2)
	Village/town	3 (4.7)	8 (12.3)	2 (3.0)
<b>Educational status</b>	Primary education	34 (52.3)	33 (50.8)	4 (6.2)
	Secondary education	7 (10.8)	12 (18.5)	8 (12.3)
	High school	12 (18.5)	15 (23.1)	6 (9.2)
	University	12 (18.4)	5 (7.6)	47 (72.3)
<b>Income status</b>	Income less than expenses	9 (13.8)	9 (13.8)	20 (30.8)
	Income equal to expenses	50 (76.9)	53 (81.5)	37 (56.9)
	Income more than expenses	6 (9.3)	3 (4.7)	8 (12.3)
<b>Smoking abuse</b>	Yes	22 (33.8)	16 (24.6)	15 (23.1)
	No	33 (50.8)	39 (60.0)	49 (75.4)
<b>Alcohol abuse</b>	Quit	10 (15.4)	10 (15.4)	1 (1.5)
	Yes	46 (70.8)	50 (76.9)	49 (75.4)
	No	1 (1.5)	3 (4.6)	2 (3.1)
	Quit	18 (27.7)	12 (18.5)	14 (21.5)

X̄: Mean; SD: Standard Deviation; Min: Minimum; Max: Maximum

**Table 2.** Distribution of HT and STEMI patients by disease-related characteristics.

Distribution of HT Patients by Disease Characteristics (n=65)	n (%)	
<b>HT Duration of illness</b>	1-5 years	38 (58.5)
	6-10 years	11 (16.9)
	11-15 years	8 (12.3)
	16 years and above	8 (12.3)
<b>Presence of HT in the family history</b>	Yes	48 (73.8)
	No	17 (26.2)
<b>HT-related complication development status</b>	Yes	9 (13.8)
	No	56 (86.2)
<b>Status of getting information about HT</b>	Yes	26 (40.0)
	No	39 (60.0)

**Table 2.** Continue.

<b>The need for information about their illness</b>	Yes	24 (36.9)
	No	41 (63.1)
<b>HT-related death anxiety</b>	Yes	19 (29.2)
	No	46 (70.8)
<b>COVID status</b>	Yes	16 (24.6)
	No	49 (75.4)
<b>Treatment for COVID</b>	Yes	13 (81.3)
	No	3 (18.7)
<b>Distribution of Patients with STEMI by Disease Characteristics (n=65)</b>		n (%)
<b>Heart disease duration</b>	1-5 years	40 (61.5)
	6-10 years	12 (18.5)
	11-15 years	6 (9.2)
	16 years and above	7 (10.8)
<b>Presence of heart disease in the family history</b>	Yes	41 (63.1)
	No	24 (36.9)
<b>The need for information about their illness</b>	Yes	14 (21.5)
	No	51 (78.5)
<b>Number of previous STEMI</b>	1 time	56 (86.2)
	2 times	7 (10.8)
	3 times	2 (3.1)
<b>STEMI-related death anxiety</b>	Yes	22 (33.8)
	No	43 (66.2)
<b>Status of getting information about coronary angiography</b>	Yes	38 (58.5)
	No	27 (41.5)
<b>Coronary angiography status</b>	Yes	41 (63.1)
	No	24 (36.9)
<b>Pre-coronary angiography death anxiety status</b>	Yes	21 (32.3)
	No	44 (67.7)
<b>Post-coronary angiography death anxiety status</b>	Yes	13 (20.0)
	No	52 (80.0)
<b>COVID status</b>	Yes	15 (23.1)
	No	50 (76.9)
<b>Treatment for COVID</b>	Yes	10 (62.5)
	No	5 (37.5)

The mean death anxiety scores of the groups were 46.38±16.72 in the HT group, 38.27±12.84 in the STEMI group, and 48.93±16.83 in the control group. There was a significant difference between the mean scores of intergroup death anxiety (F= 8.302, p=

0.000). It was found that the individuals in the HT group experienced death anxiety significantly more than the STEMI group and the control group (p=0.009, p=0.000) (Table 3).

**Table 3.** Comparison of average ASDA of HT, STEMI, and healthy individuals.

	<b>HT (n=65)</b>	<b>STEMI (n=65)</b>	<b>Control (n=65)</b>
	Min-Max	Min-Max	Min-Max
	$\bar{X} \pm SD$	$\bar{X} \pm SD$	$\bar{X} \pm SD$
	20-92	20-75	20-92
<b>ASDA</b>	46.38±16.72 <sup>a</sup>	38.27±12.84 <sup>b</sup>	48.93±16.83 <sup>c</sup>
Tukey HSD Test	<b>p= 0.009**</b> , a>b		
The difference between the groups	F= 8.186, <b>p=0.000**</b> , c>b		
	F=8.302, <b>p=0.000**</b>		

$\bar{X}$ : Mean; SD: Standard Deviation; "One-way ANOVA Test" was used in comparisons of 3 or more normally distributed groups; Tukey HSD Test was used to determine the group that caused the difference; \*\*p<0.01, a,b,c: shows the difference between groups.

When Table 4 is examined, a significant relationship was found between the death anxiety scale averages with gender, the status of experiencing death anxiety due to disease, income status, and alcohol abuse in the HT group patients. In the STEMI group, a significant relationship was found between the death anxiety

scale averages and age, the status of experiencing death anxiety, information about heart disease and recurrent STEMI. It was found that there was a significant relationship between the death anxiety scale averages of the individuals in the control group and their age, gender and income status (Table 4).

**Table 4.** Correlation of HT, STEMI and healthy individuals ASDA averages.

Some characteristics of individuals		HT (n=65) ASDA	STEMI (n=65) ASDA	Control (n=65) ASDA
Age	r	-0.132	-0.316	-0.496
	p	0.293	<b>0.010**</b>	<b>0.000**</b>
Gender	r	-0.388	-0.240	-0.399
	p	<b>0.001**</b>	0.055	<b>0.001**</b>
Experiencing death anxiety due to disease	r	<b>-0.605</b>	-0.444	-
	p	<b>0.000**</b>	<b>0.000**</b>	-
Income status	r	-0.325	0.013	-0.321
	p	<b>0.008**</b>	0.916	<b>0.009**</b>
Alcohol abuse	r	0.250	0.143	0.021
	p	<b>0.045*</b>	0.256	0.871
Information about heart disease	r	-	-0.420**	-
	p	-	<b>0.000</b>	-
Recurrent STEMI	r	-	-0.491	-
	p	-	<b>0.000**</b>	-

r = Pearson Correlation Coefficient; \*p < 0.05; \*\*p < 0.01.

**DISCUSSION AND CONCLUSION**

In this study, HT patients had higher levels of death anxiety than patients with STEMI. In general, death anxiety was found to be associated with age, gender, disease status, income status, and STEMI history. Since it is important to address the individual in all aspects (physiological, psychological, and sociological) in holistic care, it is thought that it is important to provide a good counselling service and psychotherapy support by healthcare professionals at certain intervals to reduce death anxiety in both healthy individuals and patients with HT and STEMI.

Death is an inevitable and irreversible event experienced by the individual. Death, an important and real part of human life, creates much anxiety in some individuals.<sup>10</sup> In another study, there is strong evidence that increased anxiety negatively affects the prognosis of MI.<sup>3</sup> It is believed that cardiovascular diseases are high on the list of diseases, cause death worldwide, and cause numerous complications that remind people of death, generate emotional issues such as anxiety, and enhance people's fear of death.<sup>16,21</sup> Therefore, in this study, the death anxiety of patients with STEMI, HT, and healthy individuals was discussed in line with the literature.

In our study, it was found that the mean death anxiety scale score of the HT group was at a moderate level (46.38±16.72). ASDA mean score was significantly higher than the STEMI group's (Table 3). It is

stated in the literature that hypertension, anxiety and depression occur together to a great extent. On the other hand, cognitive dysfunction leads to inadequacies in the control of hypertension.<sup>24</sup> Since there are limited studies in the literature examining the death anxiety of HT patients, these results and our study suggest that evaluating the death anxiety status of HT patients, taking the necessary precautions, and making interventions are important in preventing death anxiety and the occurrence of disease-related complications.

In our study, the mean ASDA score of the patients in the STEMI group was found to be at the lowest level (38.27±12.84) than the other groups (Table 3). In the study by Yıldırım and Kocatepe<sup>19</sup> examining the death anxiety of 300 patients with MI, it was stated that the death anxiety score of the patients was 12.50 ±2.91. They experienced severe death anxiety, and these anxiety levels were at panic levels. Our findings were consistent with the limited number of literature findings.<sup>12,14,15,20</sup> It is emphasised in the literature that severe symptoms and recurrent MIs experienced by patients with heart disease may cause death anxiety.<sup>16,20</sup> At the same time, it is stated that psychosocial problems such as depression and anxiety disorder may occur when death anxiety experienced by patients is not prevented.<sup>14,26</sup> Based on the results of this study, although different death anxiety scales are used in the studies, it is thought

that STEMI patients experience death anxiety at different levels (moderate, severe, and panic). Therefore, it will be important to determine the death anxiety of the patients in the early period and make the necessary interventions to reduce the complications and mortality rates.

It was determined that the ASDA levels of the healthy control group were significantly higher than the STEMI group and the HT group (Table 3). These results suggest that the death anxiety levels of patients with different chronic diseases are lower than those of healthy individuals because they may have thought about death more. In this case, they may have reduced their sensitivity to death and denied it. In other words, it may be because healthy individuals fear facing death suddenly and unexpectedly. Literature states that thinking about death and accepting it may have improved individuals' ability to cope with death anxiety.<sup>9,21</sup>

The study found that the death anxiety of the HT group patients was correlated with gender, the status of experiencing death anxiety due to disease, income status, and alcohol abuse. In the STEMI group, death anxiety was associated with age, experiencing death anxiety, information about heart disease, and recurrent STEMI. It was found that there was a significant relationship between the death anxiety level of the individuals in the control group and their age, gender, and income status (Table 4). When the literature is examined, it is stated that there are similar findings: MI frequency,<sup>26</sup> age and gender are associated with anxiety and death anxiety.<sup>14,26</sup> In their study examining the death anxiety of MI patients, Soleimani et al.<sup>14</sup> found that the predictors of death anxiety were age, economic status, religious belief, and self-esteem.

In conclusion, it is thought that it is important to provide individual training on disease symptoms and treatments, consider the variables affecting death anxiety, and develop problem-oriented positive coping strategies to reduce the death anxiety of HT and STEMI patients. This study does not reflect the generality of HT and STEMI patients. It is limited to individuals with HT and STEMI who comply with the research limitations and participated in the study in the hospital where it was conducted. The weaknesses of our study were that the rate of male patients in the STEMI and HT groups was higher than that of female patients. Although the patients were randomly selected, the fact that these diseases were more common in males made this difference. Similarly, the healthy control group individuals were younger than the patient group because the incidence of disease increases as they get older. The strengths of our study are that there are two important groups of cardiovascular diseases, including HT and STEMI diseases and a control group.

**Ethics Committee Approval:** Before data collection, Ethics committee approval was obtained from the Ethics Committee of Non-Interventional Clinical Studies of Selcuk University (Date:03.02.2022 decision no: 2022/60). Written permission was obtained from the Director's Office of the Hospital. Written consent of the patients who participated in the study was obtained after reading an informed consent. The principles in the Declaration of Helsinki were complied with in the study.

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

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

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## Nurses' Fear of COVID-19 and Job Motivation Levels: A Cross-Sectional Study

### Hemşirelerin COVID-19 Korkusu ve İş Motivasyon Düzeyleri: Kesitsel Çalışma

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#### ABSTRACT

**Objective:** This study determined nurses' fear of COVID-19 and job motivation levels.

**Materials and Methods:** The study was conducted cross-sectionally with 147 nurses working in a public hospital between April 1 and April 30, 2022. Data were collected using the Personal Information Form, COVID-19 Fear Scale, and Nurse Job Motivation Scale. Data were evaluated using number, percentage, mean, and nonparametric tests.

**Results:** The mean age of the nurses was 29.95±6.12 years (min=22, max=51); 89.1% were female, 59.2% were married, and 68.7% were undergraduate graduates. The total score on the COVID-19 Fear Scale was 15.85±5.73 (min=7, max=35), and the total score on the Nurse Job Motivation Scale was 60.70±8.66 (min=37, max=75). There was a significant difference between the total scores of the Nurse Job Motivation Scale and educational status, willingly choosing the unit where the nurses work, being satisfied with the unit where they job, and finding the nursing profession suitable for themselves (p<0.05). In addition, female nurses' mean COVID-19 Fear Scale scores were higher than male nurses (p<0.05).

**Conclusion:** The study's results showed that nurses' fear of COVID-19 was close to average, and their work motivation was above average.

**Keywords:** Fear of COVID-19, motivation for job, nurse

#### ÖZ

**Amac:** Bu çalışma hemşirelerin COVID-19 korkusunu ve iş motivasyon düzeylerini belirlemek amacıyla yapıldı.

**Materyal ve Metot:** Çalışma bir kamu hastanesinde 1 Nisan-30 Nisan 2022 tarihleri arasında görev yapan 147 hemşire ile kesitsel olarak yapıldı. Kişisel Bilgi Formu, COVID-19 Korkusu Ölçeği ve Hemşire İş Motivasyonu Ölçeği kullanılarak veriler toplandı. Veriler sayı, yüzde, ortalama ve nonparametrik testler kullanılarak değerlendirildi.

**Bulgular:** Hemşirelerin yaş ortalaması 29.95±6.12 (min=22, max=51) olup, %89.1'i kadın, %59.2'i evli ve %68.7'si lisans mezunudur. Hemşirelerin COVID-19 Korkusu Ölçeği toplam puanı 15.85±5.73 (min=7, max=35) ve Hemşire İş Motivasyonu Ölçeği toplam puanı 60.70±8.66 (min=37, max=75) bulundu. Hemşire İş Motivasyonu Ölçeği toplam puanları ile eğitim durumu, hemşirelerin çalıştığı birimi isteyerek seçme, çalıştığı birimden memnun olma ve hemşirelik mesleğini kendisi için uygun bulma değişkenleri arasında anlamlı bir fark vardır (p<0.05). Ayrıca kadın hemşirelerin COVID-19 Korkusu Ölçeği puan ortalamaları erkeklerden anlamlı bir biçimde yüksektir (p<0.05)

**Sonuç:** Çalışmanın sonuçları hemşirelerin COVID-19 korkusunun orta düzeye yakın ve iş motivasyonlarının ortalamasının üzerinde olduğunu gösterdi.

**Anahtar Kelimeler:** COVID-19 Korkusu, hemşire, iş motivasyonu

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## INTRODUCTION

Motivation, the force that influences or directs behavior, effectively initiates behaviors to achieve intended goals.<sup>1,2</sup> Motivation can be an internal drive that creates behaviors and inspiration to fulfil responsibilities without external influence. Motivation can also consist of rewards, bonuses, payments, and benefits by guiding individuals to fulfil their responsibilities using coercion or instruction to receive rewards in return.<sup>2</sup>

Work motivation is one of the main factors determining an organisation's success.<sup>2,3</sup> The main thing in ensuring work motivation is that employees do their jobs willingly, and as a result, their productivity increases.<sup>3</sup> Work motivation in the healthcare organisation is considered an important measure of the response of the healthcare professional to increasing challenges and demands.<sup>2</sup> Motivation, which has a critical place in every profession, is important for nurses, who constitute a large part of healthcare organizations.<sup>4</sup>

Many factors affect the motivation of nurses.<sup>1,4</sup> Factors such as loving their profession, being valued and respected, being appreciated, participating in decisions, fair discipline, job security, and social security affect the motivation of nurses.<sup>1</sup> The level of motivation has a positive or negative effect on the health service.<sup>4,5</sup> The service provided by nurses with increased motivation can reflect positively on patients and the health institution.<sup>4</sup> Motivation levels can change very quickly because nurses work in a stressful environment.<sup>5</sup> Changes in the direction of decreasing motivation negatively affect the performance of nurses and may lead to a decrease in the quality of patient care and an increase in mistakes.<sup>5,6</sup>

The COVID-19 pandemic is an extraordinary situation that causes fear in many people. Evaluating this fear is important in taking measures against psychological problems that may arise.<sup>7</sup> Determining and evaluating the fear levels of nurses in high-risk groups during the COVID-19 pandemic is necessary for managing COVID-19 fear and the continuity of psychological well-being.<sup>8</sup> When the literature is examined, it is stated that nurses have a high level of fear of COVID-19.<sup>9-11</sup> Studies have been conducted in the world and in Türkiye to determine nurses' fear of COVID-19,<sup>8-12</sup> and their motivation<sup>4-6,8,12</sup> but no study was found to examine the level of fear of COVID-19 and work motivation in the same group of nurses.

This study was conducted to determine the fear of COVID-19 and the job motivation levels of nurses.

## MATERIALS AND METHODS

**Ethical Considerations:** This study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee of a

university (Decision date:24.02.2022, decision no:45-03). In addition, institutional permission was obtained from the Provincial Directorate of Health, and written informed consent from the nurses participating in the study.

**Type of Study:** This study was cross-sectional.

**Place and Time of the Study:** This study was conducted in a public hospital in the Eastern Black Sea Region of Türkiye between April 1 and April 30, 2022.

**Population and Sample of the Study:** No sample selection was made in the study, and it was aimed to reach the entire population with the complete census method. Out of a total of 185 nurses working in the hospital, 147 nurses who had been working as a nurse for more than one year, were not on leave or reported on the study dates, and agreed to participate were included.

**Data Collection Tools:** Personal Information Form, COVID-19 Fear Scale, and Nurse Job Motivation Scale were used as data collection tools.

**Personal Information Form:** A 12-question form including questions such as age, gender, educational status, physical and psychiatric illness, having COVID-19, and nursing profession was created by the researchers.

**COVID-19 Fear Scale:** The scale was developed by Ahorsu et al.,<sup>13</sup> and a Turkish validity and reliability study was conducted by Ladikli et al.<sup>14</sup> The 7-item scale with a single sub-dimension is a 5-point Likert type. The increase in the participants' mean score on the scale indicates an increased fear of COVID-19. The Cronbach's alpha coefficient of the scale adapted to Turkish is 0.86.<sup>14</sup> In our study, the Cronbach's alpha coefficient was 0.85.

**Nurse Job Motivation Scale:** The validity and reliability scale performed by Engin and Çam<sup>15</sup> is a 25-item scale in a 3-point Likert type. According to the answers given by the nurses to the items of the scale, 1 point is given to "strongly disagree," 2 points to "partially agree," and 3 points to "agree." The maximum score that can be obtained from the scale is 75, and the minimum score is 25. Higher scores indicate higher levels of job motivation. Cronbach's alpha coefficient of the scale is 0.84.<sup>15</sup> In our study, Cronbach's alpha coefficient of the scale was 0.89.

**Data Collection:** The study's data were collected through face-to-face interviews conducted by the researchers by going to the fields where the nurses worked. The nurses took approximately 15 minutes to complete the data collection tool.

**Statistical Analysis:** Data were analysed using the IBM SPSS 25 package program. The statistical significance level was accepted as  $p < 0.05$ . Whether the data were normally distributed was evaluated by the Kolmogorov-Smirnov normality test. Descriptive statistics were shown as a number, percentage, mean,

standard deviation, minimum, and maximum values. Since the data were not normally distributed, the Mann-Whitney U test was used to compare scale scores and two variables, and the Kruskal-Wallis H test was used to compare three or more variables.

## RESULTS

The mean age of the nurses in the study was  $29.95 \pm 6.12$  years (min=22, max=51). 89.1% of the nurses were female, 59.2% were married, 68.7% had a bachelor's degree, 66.0% had middle income and

expense status. 8.2% of the nurses had a physical illness, 5.4% had a psychiatric illness, and COVID-19 positive rate of nurses was 60.5%. The proportion of nurses who willingly chose the unit where they work is 63.3%, those who are satisfied with the unit where they work is 80.3%, those who find the nursing profession suitable for them is 63.3%, and those who are satisfied with the prestige of the nursing profession in the society is 8.2% (Table 1).

**Table 1.** Descriptive characteristics of nurses.

Variable		n (%)
Age	$\bar{X}=29.95 \pm 6.12$ (min=22, max=51)	
Gender	Female	131 (89.1)
	Male	16 (10.9)
Marital status	Married	87 (59.2)
	Single	60 (40.8)
Educational status	High school graduate	18 (12.2)
	Associate degree	14 (9.5)
	Bachelor's degree	101 (68.7)
	Higher graduate	14 (9.5)
Income status	Bad	36 (24.5)
	Middle	97 (66.0)
	Good	14 (9.5)
Physical illness	There is	12 (8.2)
	None	135 (91.8)
Psychiatric illness	There is	8 (5.4)
	None	139 (94.6)
Being COVID-19 positive	Yes	89 (60.5)
	No	58 (39.5)
Willingly chose the unit where they work	Yes	93 (63.3)
	No	54 (36.7)
Satisfied with the unit where they work	Yes	118 (80.3)
	No	29 (19.7)
Finding the nursing profession suitable for you	Yes	93 (63.3)
	No	54 (36.7)
Satisfaction with the prestige of the nursing profession in society	Yes	12 (8.2)
	No	135 (91.8)
Total		147 (100)

The mean score of the COVID-19 Fear Scale was  $15.85 \pm 5.73$  (min=7, max=35), and the mean score of

the Nurse Job Motivation Scale was  $60.70 \pm 8.66$  (min=37, max=75) (Table 2).

**Table 2.** Nurses' scores on the COVID-19 Fear Scale and the Nurse Job Motivation Scale.

Variable	Min-Max	Mean $\pm$ SD
COVID-19 Fear Scale	7-35	$15.85 \pm 5.73$
Nurse Job Motivation Scale	37-75	$60.70 \pm 8.66$

In this study, no statistical difference was found between the distribution of nurses' education, income status, current disease, and occupational characteristics and the total score of the Fear of COVID-19 Scale ( $p>0.05$ ). In the study, a significant difference was found between gender and COVID-19 Fear Scale total scores ( $p<0.05$ ), and the mean COVID-19 Fear Scale scores of female nurses were significantly higher than those of males ( $p<0.05$ ). There is a significant difference between the total scores of the Nurse

Job Motivation Scale and the variables of educational status, willingly choosing the unit where the nurses work, being satisfied with the unit where they work, and finding the nursing profession suitable for themselves ( $p<0.05$ ). There is no significant difference between the total scores of the Nurse Job Motivation Scale and those who are satisfied with the prestige of the nursing profession in society ( $p>0.05$ ) (Table 3).

**Table 3.** Comparison of nurses' characteristics with COVID-19 Fear and Nurse Job Motivation Scale Scores.

Variable		COVID-19 Fear	Nurse Job Motivation
<b>Gender</b>	Female	15.00	63.00
	Male	12.00	61.50
	U	670.00	975.00
<b>Marital status</b>	p	0.018	0.649
	Married	16.00	63.00
	Single	14.00	63.00
<b>Educational status</b>	U	2180.50	2551.00
	p	0.090	0.816
	High school graduate	13.50	59.00
	Associate degree	15.00	57.00
	Bachelor's degree	14.00	64.00
<b>Income status</b>	Higher graduate	20.00	57.50
	KW	6.630	8.578
	p	0.085	0.035
	Bad	14.50	63,50
	Middle	14.00	62,00
<b>Physical illness</b>	Good	17.00	63,17
	KW	0.400	1.843
	p	0.819	0.398
	There is	11.50	58.50
	None	15.00	63.00
<b>Psychiatric illness</b>	U	710.00	646.50
	p	0.478	0.247
	There is	11.50	59.00
	None	15.00	63.00
	U	337.50	437.50
<b>Being COVID-19 positive</b>	p	0.61	0.311
	Yes	16.00	63.00
	No	14.00	62.00
	U	2118.50	2453.00
	p	0.114	0.611
<b>Willingly chose the unit where they work</b>	Yes	15.00	65.00
	No	15.50	56.00
	U	2453.00	1473.50
	p	0.611	0.001
	Yes	15.00	65.00
<b>Satisfied with the unit where they work</b>	No	14.00	50.00
	U	1697.00	412.00
	p	0.946	0.001
	Yes	15.00	65.00
	No	15.00	55.00
<b>Finding the nursing profession suitable for you</b>	U	2385.50	1100.00
	p	0.613	0.001
	Yes	16.00	66.00
	No	15.00	63.00
	U	714.00	583.50
<b>Satisfaction with the prestige of the nursing profession in society</b>	p	0.496	0.108

U: Mann-Whitney U test; KW: Kruskal-Wallis H test;  $p<0.05$ .

## DISCUSSION AND CONCLUSION

The total score that can be obtained from the Fear of COVID-19 Scale is in the range of 7-35, and according to the mean total score of the Fear of COVID-19 Scale ( $15.85 \pm 5.73$ ) of the nurses in this study, their fear of COVID-19 is close to moderate. The COVID-19 pandemic is the leading cause of stress and fear for nurses who are important in health services (10). In a study, nurses' total COVID-19 Fear Scale score was reported to be 20.01.<sup>11</sup> The COVID-19 Fear Scale score of intensive care nurses (22.7) was moderate.<sup>10</sup> In a study conducted on nurses working in 5 hospitals in the Philippines, it was reported that the mean COVID-19 Fear Scale scores of nurses who did not participate in COVID-19-related training were higher than those who participated in such training.<sup>16</sup> Compared to the periods when the pandemic was widespread, it can be said that nurses' fear of COVID-19 was not high in this study due to situations such as increased vaccination rates, decreased case and mortality rates, and the information about COVID-19.

Emotional distress experienced by nurses due to stress decreases their motivation.<sup>15</sup> In a study conducted on intensive care nurses in 2017, the mean total score of the Motivation scale was  $69.22 \pm 7.95$  (min=29, max=87).<sup>12</sup> In a 2015 study conducted on nurses working in the internal medicine service, it was reported that the motivation of nurses was at a moderate level.<sup>17</sup> In the literature, studies conducted before the pandemic reported that nurses' work motivation was moderate and above average.<sup>12,17</sup> In this study, the work motivation level of nurses was  $60.70 \pm 8.66$  (min=37, max=75), which is above the average. According to this result, we can say that the pandemic did not decrease the work motivation level of nurses in our study.

In this study, female nurses' mean COVID-19 Fear Scale scores were significantly higher than male nurses. The results of our study are similar to the literature.<sup>11,18,19</sup> In a study, it was reported that there was no significant difference between nurses' age, education, marital status, having children, the clinic they worked in, total working hours and working hours in the present clinic, and COVID-19 Fear Scale scores. In the same study, a significant difference was found between gender and COVID-19 Fear Scale scores, and it was reported that the level of fear of COVID-19 was higher in female nurses than in male nurses.<sup>11</sup> In another study, it was reported that female health-care workers' mean COVID-19 fear scores were significantly higher than male nurses.<sup>18</sup> In a systematic review, it was revealed that being a nurse and being a woman poses a greater risk for fear of COVID-19.<sup>19</sup> In terms of evaluating fears, it is important to know whether different groups need education and prevention programs according to some socio-demographic

characteristics such as age, gender, and education.<sup>7</sup>

This study showed no significant difference between the total Nurse Job Motivation Scale score and nurses' gender, marital status, income status, current illness, and COVID-19 positive status. No study was found in the literature to determine the level of nurse work motivation during the COVID-19 pandemic. A study conducted in 2018 with nurses working in 12 hospitals in Istanbul reported no statistical difference between nurses' gender, education, marital status, and mean scores of work motivation.<sup>17</sup> In a 2017 study, it was reported that there was no significant relationship between intensive care nurses' age, education, working time, having a certificate and finding the facilities of the institution they work in sufficient and their motivation scores and that the motivation scores of female nurses were higher than male nurses.<sup>12</sup> In this study, which was conducted towards the end of the pandemic, the mean scores of nurses' work motivation did not differ according to gender.

In this study, the Nurse Job Motivation Scale scores were higher in nurses with higher educational status, who willingly chose the unit where they worked, who were satisfied with the unit where they worked, and who found the nursing profession suitable for themselves. According to a study, the motivation scores of nurses who see their profession as valuable and are satisfied with being in the institution where they work are higher.<sup>12</sup> In another study, it was reported that nurses' quality of work life positively affected their work motivation, and it was stated that nurses' work motivation levels could be positively affected by increasing their perception levels of quality of work life.<sup>3</sup> A study in Ethiopia reported that 60.8% of nurses were satisfied with their jobs.<sup>21</sup> In a study conducted to determine how nurses perceive work motivation, it was reported that most nurses (64.1%) perceived cause as motivating. The same study also reported that nurses defined motivation as prospective, recognition, and financial incentives.<sup>22</sup> Our study was found to be consistent with the literature.

In conclusion, according to the study results, the COVID-19 fear of nurses working in the hospital is close to average, and their work motivation is above average. The Nurse Job Motivation Scale scores are higher in nurses with higher educational status, who willingly choose the unit they work in, who are satisfied with the unit they work in, and who find the nursing profession suitable for themselves. In addition, female nurses had higher COVID-19 fears than male nurses. It is predicted that nurses' fears will decrease as their knowledge about COVID-19 increases, and their work motivation will decrease with the improvement of the conditions in which they work. A similar study examining the fear of COVID-19 and work motivation level in the same group of nurses was not found in the literature. The following are recommen-

ded: 1- Further studies examining nurses' fear of COVID-19 and work motivation, 2- Determination of nurses' COVID-19 fear levels, 3- Implementation of prevention programs based on counselling and psychological support, 4- Strengthening the human resource management system and practices to improve the overall motivation of nurses. It was found in the study that the fear of COVID-19 among the nurses was close to moderate, and their work motivation was above average. Since our data reflect the nurses participating in the study in a hospital, it cannot be generalised to the entire nurse population.

**Ethics Committee Approval:** This study was planned following the Helsinki Principles, and ethical approval was obtained from the XXX University Ethics Committee (Date 24.02.2022, decision no: 45-03).

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

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

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## Rare factor deficiencies in children: A review of 23 cases from a single center

### Çocuklarda nadir faktör eksiklikleri: Tek merkezden 23 vakanın gözden geçirilmesi

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Rare factor deficiencies in children: A review of 23 cases from a single center

#### ABSTRACT

**Objective:** The prevalence of rare factor deficiency (RFD) is one in 500.000-2.000.000 in the general population. Different symptoms may occur from mild or moderate bleeding to severe and life-threatening bleeding. This study aimed to evaluate children with RFD in a single Turkish center.

**Materials and Methods:** The records of children with RFD (Factor I, V, VII, X, XIII deficiency) were evaluated retrospectively.

**Results:** Twenty-three cases (70% female) were reviewed. The mean age of patients was 9.52 years at review, and mean follow-up was 66.3 months. The most common factor (F) deficiencies were FVII (35%) and FX (35%). Parental consanguinity was present in 65%. The most common symptoms were mucocutaneous bleeding and epistaxis. Regarding treatment, fresh frozen plasma (FFP) was given to two patients, FXIII concentrate was given to one patient, and prothrombin complex concentrate (PCC) was given to two patients. Prophylaxis was started in patients with recurrent bleeding. Of the 16 receiving prophylaxis, three received FFP, seven received recombinant coagulation factor VIIa, and six received PCC.

**Conclusion:** Treatment was given to a fifth of patients while nearly three-quarters received prophylaxis. As parental consanguinity was present in most of these patients, obtaining a detailed family history may aid in diagnosis.

**Keywords:** Child, factor, hemorrhage, rare factor deficiencies

#### ÖZ

**Amaç:** Nadir faktör eksikliğinin (NFE) prevalansı genel popülasyonda 500,000-2,000,000'de birdir. Hafif veya orta dereceli kanamalardan şiddetli ve hayatı tehdit eden kanamalara kadar farklı semptomlar ortaya çıkabilir. Bu çalışmanın amacı tek bir Türk merkezinde RFD'li çocukları değerlendirmektir.

**Materyal ve Metot:** Nadir faktör eksikliği (Faktör I, V, VII, X, XIII eksikliği) olan çocukların kayıtları retrospektif olarak değerlendirildi.

**Bulgular:** Yirmi üç olgu (%70 kadın) retrospektif olarak incelendi. İnceleme sırasında hastaların ortalama yaşı 9.52 idi ve ortalama takip süresi 66.3 aydı. En yaygın faktör (F) eksiklikleri FVII (%35) ve FX (%35) idi. Anne baba akrabalığı %65 oranında mevcuttu. En sık görülen semptomlar mukokutanöz kanama ve epistaksis idi. Tedavi açısından iki hastaya taze donmuş plazma (TDP), bir hastaya FXIII konsantresi, iki hastaya protrombin kompleks konsantresi (PCC) verildi. Tekrarlayan kanaması olan hastalara profilaksi başlandı. Profilaksi alan 16 kişiden üçü TDP, yedisi rekombinant pıhtılaşma faktörü VIIa ve altısı PCC aldı.

**Sonuç:** Hastaların beşte birine tedavi verilirken, yaklaşık dörtte üçüne profilaksi uygulandı. Bu hastaların büyük çoğunluğunda anne baba akrabalığı mevcut olduğundan ayrıntılı aile öyküsünün alınması tanıya yardımcı olabilir.

**Anahtar Kelimeler:** Çocuk, faktör, kanama, nadir faktör eksiklikleri

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## INTRODUCTION

Rare factor deficiency (RFD) encompasses the deficiencies of clotting factors in the blood clotting cascade and includes factor I (FI; fibrinogen), FII, FV, FVII, FX, FXI, FXII, and FXIII. RFD constitutes only 3-5% of hereditary factor deficiencies,<sup>1</sup> and the prevalence is between 1:500,000 and 1:2,000,000.<sup>2</sup> The inheritance of RFD is usually autosomal recessive and thus affects both boys and girls.

RFD presents a heterogeneous clinical picture in affected patients, regardless of the degree of factor deficiency. Symptoms can range from mild or moderate bleeding to severe and life-threatening bleeding.<sup>3</sup> The most typical symptoms of RFDs involve the mucosal tissues or unexpected bleeding during invasive procedures. However, the most serious manifestations include intracranial hemorrhage. Prophylaxis may be considered in patients with recurrent severe bleeding. Information about the epidemiology and clinical consequences of RFD in children is limited due to the condition's rarity.<sup>4</sup> In 2004 and 2007, data from the World Federation of Hemophilia and the European Rare Diseases Group were published and reported on RFD epidemiology, clinical and laboratory diagnosis, classification, and treatment options. It was reported that diagnosis of hereditary RFD can be made by prenatal amniocentesis and chorionic villus sampling. This early prenatal diagnosis will provide a decision about the continuation of the pregnancy and, if it is decided to continue, an opportunity for early intervention.<sup>5</sup>

Factor concentrates, fresh frozen plasma (FFP), and prothrombin complex concentrate (PCC) are used when bleeding occurs. Prophylaxis approaches for FI, FVII, FX, and FXIII deficiencies exist. In addition to factor replacement therapy, antifibrinolytic agents can be given to prevent bleeding, especially mucosal bleeding.<sup>4</sup>

The aim of this study was to evaluate the clinical and laboratory findings of children diagnosed with a rare coagulation defect in a single Turkish center.

## MATERIALS AND METHODS

**Ethics Committee Approval:** This study was approved by the Sağlık Bilimleri University, Bakırköy Dr. Sadi Konuk, Training and Research Hospital Ethics Committee (Date: 03.05.2023, decision no: 2023-09-06). All procedures for studies involving human participants were carried out in accordance with the 1964 Declaration of Helsinki.

**Patient Selection:** All patients, aged between 0-18 years who were followed up because of a diagnosis of deficiency in any of the clotting factors (I, II, V, VII, X, XI, XII, XIII) in the Pediatric Hematology and Oncology Clinic of Sanliurfa Training and Research Hospital were identified. Of the total of 36 cases with a clotting factor deficiency, only those

with an RFD, defined as a deficiency in any of FI, FII, FV, FVII, FX, FXI, FXII, and FXIII were included in the study. The data were extracted from patient follow-up files. Demographic features, age at presentation, family history, medical history of bleeding, laboratory assessments and prophylactic treatments of the patients were recorded. In RFDs detection of plasma factor activity below 50% was considered diagnostic. Patients whose fibrinogen levels could not be measured were diagnosed with afibrinogenemia. Abnormal tests were repeated on two occasions to confirm the diagnosis. Mutation analysis of the cases was not performed.

**Statistical Analysis:** Statistical Packages for Social Sciences, version 25, was used for data analysis (IBM Inc., Armonk, NY, USA). Descriptive statistical data are presented. As individual factor deficiency sub-group sizes were small, no comparative data analysis was attempted.

## RESULTS

RFD was diagnosed in 23 patients and of these, 16 (70%) were female. At the time of data extraction, the mean age of the patients was 9.52 years the mean/median follow-up period was 66.3 months. Consanguineous marriage was present in 15 (65%) families. Twenty-two patients had a history of bleeding diathesis (95.6%). Factor deficiencies diagnosed were FVII (n=8, 35%), FX (n=8, 35%), FXIII (n=5, 22%) and one each with FI and FV deficiency (Table 1).

**Table 1.** The demographic features of our patients.

Variable	Result	n (%)
Age		9.52 years
Follow period		66.3 months
Gender	Female	16 (70)
	Male	7 (30)
Consanguinity	Present	15 (65)
	Absent	8 (35)
Bleeding symptoms	Symptomatic	22 (96)
	Asymptomatic	1 (4)
Factor (F) deficiency	FI (Fibrinogen deficiency)	1 (4)
	FV deficiency	1 (4)
	FVII deficiency	8 (35)
	FX deficiency	8 (35)
	FXIII deficiency	5 (22)

Abnormal bleeding had occurred in all but one of the patients, including mucodermal bleeding in eight patients (35%), epistaxis in seven patients (30%), hematoma in the knee in four patients (17%), gluteal bleeding in three patients (13%), umbilical cord bleeding in three patients (13%), hematuria in three (13%), anal bleeding in two patients (8.7%), hematoma in the elbow in two patients (8.7%), hematoma in the ankle in two patients (8.7%), abnormal menstrual bleeding in two (8.7%) and conjunctival bleeding in one patient (4.3%). The patient with FV deficiency

had no history of abnormal bleeding. Sites of bleeding by factor deficiency are shown in Table 2. Factor activity was  $\leq 5\%$  in eight (35%) patients. Factor activity was 5-10% in 13 (56.5%), and activity in

the remaining two patients was 10-20%. Factor activity (%) by factor deficiency is shown in Table 3.

**Table 2.** The distribution of sites of bleeding symptoms by factor deficiency.

Bleeding	Factor Deficiency				
	F I Deficiency	F V Deficiency	F VII Deficiency	F X Deficiency	F XIII Deficiency
	n	n	n	n	n
Mucodermal	-	-	4	3	1
Umbilical cord	-	-	2	-	1
Epistaxis	-	-	2	4	1
Anus	-	-	1	1	-
Hematuria	-	-	-	3	-
Hematoma/knee	1	-	1	1	1
Hematoma/elbow	-	-	-	2	-
Gluteal	-	-	1	-	2
Hematoma/ankle	-	-	2	-	-
Conjunctival	-	-	1	-	-
Menstrual	-	-	-	1	1
Asymptomatic	-	1	-	-	-

F: Factor; n: Number of patients.

**Table 3.** Factor activity (%) by factor deficiency in 23 patients with rare factor deficiency.

Factors	Factor activity (%)		
	$\leq 5$	5-10	10-20
FI (Fibrinogen) deficiency	-	1	-
FV deficiency	-	-	1
FVII deficiency	2	6	-
FX deficiency	3	5	-
FXIII deficiency	3	2	-

Regarding treatment, fresh frozen plasma (FFP) was given to three patients, factor XIII concentrate was given to one patient, and prothrombin complex concentrate (PCC) was given to two patients. Of the patients receiving prophylaxis, three received FFP, seven received recombinant coagulation factor VIIa, and

six received PCC. In addition to factor replacement therapy, two patients were given antifibrinolytic drugs to prevent bleeding (Table 4).

**Table 4.** The distribution of patients according to factor deficiency.

Factor deficiency	Treatment	Prophylaxis
F I deficiency	FFP	-
F V deficiency	-	-
F VII deficiency	FFP, recombinant coagulation factor VIIa	FFP, recombinant coagulation factor VIIa
F X deficiency	PCC	PCC, antifibrinolytic drugs
F XIII deficiency	FFP, factor XIII concentrate	FFP

FFP: Fresh Frozen Plasma; PCC: Prothrombin Complex Concentrate.

Prophylaxis was started in patients with recurrent bleeding. Seven patients had not received prophylaxis. The distribution of factor activity and bleeding

symptoms in patients receiving prophylaxis are shown in Table 5.

**Table 5.** Factor activity (%) and distribution of sites of bleeding symptoms in patients receiving prophylaxis.

Factor Deficiency	n	Factor activity (%)	Bleeding
F VII deficiency	7	7 (range 5-8)	Mucodermal, umbilical cord, epistaxis, anus, hematoma/ankle, conjunctival
F X deficiency	6	7 (range 5-12)	Mucodermal, anus, hematuria, menstrual, hematoma/elbow
F XIII deficiency	3	5 (range 4-5)	Mucodermal, hematoma/knee, gluteal, menstrual

F: Factor; n: Number of patients.

## DISCUSSION AND CONCLUSION

Due to the rarity, information on the epidemiology and clinical outcomes of RFD is limited. Hereditary bleeding diseases with autosomal recessive inheritance are more prevalent in regions with common consanguineous marriages.<sup>6-8</sup> The rate of consanguineous marriage in the parents of patients with RFD was reported to be 48.6% to 49.5% in Turkey.<sup>9,10</sup> In the present study, a consanguineous marriage rate of 65% was found in the parents of our patients. In our case series, consanguineous marriage rate was higher than in other studies. This may be because there is a high proportion of consanguineous marriage in the catchment population of the study center. The rate of consanguineous marriage in Sanliurfa is 18.4%.<sup>11</sup> However, Elhadi et al. reported a consanguineous marriage rate of 93.6% in their study of 43 RFDs in Sudan.<sup>12</sup> Consanguinity marriage is common in Africa, and the estimates range from 29 to 49% of all marriages in Africa.<sup>13</sup> Hemarthrosis and intramuscular bleeding are the most common symptoms in patients with hemophilia, while mucocutaneous bleeding is more common in RFDs. It has been reported that the most common type of bleeding in RFD patients was mucosal bleeding, affecting 40% to 67.7%.<sup>14,16</sup> In the study of Akdeniz et al., most bleeds were of mucosal origin (67.7%).<sup>14</sup> Park et al. reported that the most frequent symptoms were mucosal tract bleeding (40%) similarly.<sup>15</sup> In the study of Gelen et al., this rate is 53%.<sup>16</sup> In keeping with these reports, the most common site of bleeding in the present study was the mucosa (35%), followed by epistaxis (30%), although seven (30%) had also had hemarthrosis. The two most reported deficiencies among the RFDs are FVII and/or FXI deficiency.<sup>3,17-19</sup> In the present study, FX and FVII deficiency (35% and 35%) were the most common RFD. In the past, prediction of the severity of bleeding was based on factor activity levels in RFD.<sup>3</sup> However, studies have shown that factor activity levels and clinical manifestation of bleeding are not always compatible. In FI, FII, FX,

and FXIII deficiency, the correlation between factor activity level and the severity of bleeding was strong, but this does not hold for FV, FVII, and FXI deficiency.<sup>3</sup> Khudhair et al. reported that clinical manifestations of FVII deficiency are variable and not necessarily correlated to the FVII level.<sup>18</sup> In the study, five out of 10 patients with FVII level < 1% have either mild to moderate disease without complications, while six out of 14 patients with FVII > 1% had at least one episode of severe bleeding.<sup>18</sup> Of note, no serious bleeding was observed in any of the patients in the present study, despite 3/8 of the patients with FX deficiency having activity <5% and 3/5 with FXIII deficiency also having <5% activity. In addition, the factor activity of patients with recurrent bleeding was found in the 4-12% range.

There is no accepted therapeutic strategy for RFDs. Management of RFDs is mainly based on expert consensus rather than evidence-based guidelines. Patients with RFD may have a broad spectrum of clinical symptoms, ranging from mucocutaneous bleeding to life-threatening hemorrhages, such as those occurring in the central nervous system. Early diagnosis and treatment prevent mortality and morbidity, and prophylactic procedures in required cases significantly increase patients' quality of life. FFP, PCC, and activated recombinant factor VII (rFVIIa) can be given to treat/prophylaxis bleeding in affected patients.<sup>4,20,21</sup> In our study, prophylaxis with FFP, PCC, or rFVIIa was applied to sixteen patients with FVII, FX, and FXIII deficiency because of recurrent bleeding. No complications or bleeding were observed in our patients, and they were followed up without any problems at the time of writing; due to this, we think that prophylaxis is appropriate after recurrent bleeding.

In conclusion, RFDs are rare autosomal recessive conditions. However, in regions with a high degree of consanguineous marriage, the prevalence of RFD may be higher, and it becomes a significant clinical problem. There must be awareness of bleeding diathesis in the general population, especially in re-

gions with an increased incidence of consanguineous marriage. It should also be remembered that there may not be a direct relationship between the factor activity level and the severity of bleeding experienced by affected patients. This study had some limitations. These include the study's retrospective nature, the small size of the longitudinal cohort, and the fact that genetic mutation analysis was not performed in any patient.

**Ethics Committee Approval:** Our study was approved by the Sağlık Bilimleri University Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee (Date:03.05.2023, decision no: 2023-09-06)

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## Does Hemostasis with Controlled Arterial Hypertension Before Surgical Wound Closure in Total Knee Arthroplasty Affect the Amount of Bleeding and Transfusion Need?

### Total Diz Artroplastisinde Cerrahi Yara Kapatılması Öncesinde Kontrollü Arteriyel Hipertansiyon ile Yapılan Hemostazis Kanama Miktarını ve Transfüzyon İhtiyacını Etkiler mi?

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#### ABSTRACT

**Objective:** We aimed to assess the efficacy of hemostasis while controlled augmentation of arterial blood pressure before surgical closure after total knee arthroplasty (TKA).

**Materials and Methods:** This retrospective cohort involved data collected from the medical files of 87 patients (62 women, 25 men) who underwent TKA using hypotensive epidural anesthesia (HEA). Patients were allocated into two groups. Group I (n=44) received HEA, while Group II (n=43) had controlled arterial hypertension before surgical closure. Perioperative hemoglobin and hematocrit levels, systolic and diastolic blood pressure, and the amount of erythrocyte suspension transfusion were compared between the two groups.

**Results:** The average age of our series was  $66.41 \pm 6.17$  (range: 57-78) years. Notably, the amount of bleeding on postoperative 1st, 2nd, 4th, 12th, and 24th (p=0.031, 0.032, 0.001, 0.001, 0.001, respectively) hours was significantly less in Group II. There were no significant differences between the two groups for complications, operative duration, perioperative bleeding, duration of follow-up and hospitalisation, and compared descriptives.

**Conclusion:** Our data indicated that controlled elevation of mean arterial pressure before surgical closure might allow the achievement of meticulous hemostasis after TKA. Further prospective, randomised, controlled trials on more extensive series are warranted to verify our preliminary results.

**Keywords:** Bleeding, controlled hypertension, hypotensive epidural anesthesia, hemostasis, total knee arthroplasty

#### ÖZ

**Amaç:** Total diz artroplastisinde (TDA) cerrahi yaranın kapatılmasından önce kontrollü olarak artırılan arteriyel kan basıncı ile yapılan hemostazisin etkinliğinin değerlendirilmesi amaçlanmıştır.

**Materyal ve Metot:** Veriler hipotansif epidural anestezi (HEA) ile TDA ameliyatı olmuş 87 hastanın (65 kadın, 25 erkek) tıbbi kayıtlarından retrospektif olarak toplanmıştır. Hastalar cerrahi yaranın kapatılmasından önce kontrollü arteriyel hipertansiyon uygulanmasına göre iki gruba ayrılmıştır. Grup I (n:44) HEA uygulanan hastaları, grup II (n:43) cerrahi yara kapatılmasından önce kontrollü arteriyel hipertansiyon (operasyon öncesindeki ortalama arteriyel kan basıncından daha yüksek) uygulanan hastaları içermektedir. Temel tanımlayıcılar olarak peroperatif hemoglobin ve hematokrit seviyeleri, sistolik ve diastolik kan basıncı, transfüze edilen eritrosit süspansiyonu miktarları iki grup arasında kıyaslanmıştır.

**Bulgular:** Gruplardaki ortalama yaş  $66,41 \pm 6,17$  (57-78) dir. Operasyon sonrası 1.(p=0,031), 2.(p=0,032), 4. (p=0,001), 12.(p=0,001), 24.(p=0,001) saatlerdeki kanama miktarı grup II de anlamlı olarak daha düşüktü (Sırasıyla, p=0.031, 0.032, 0.001, 0.001, 0.001). Komplikasyon, cerrahi süre, peroperatif kanama, hastanede yatış ve takip süresi, peroperatif hemoglobin değeri, transfüze edilen eritrosit süspansiyonu miktarı ile peroperatif sistolik-diastolik kan basıncı değerleri açısından gruplar arasında istatistiksel bir fark yoktu.

**Sonuç:** Bulgularımız TDA'da cerrahi yara kapatılması öncesinde ortalama arteriyel kan basıncının kontrollü olarak yükseltilmesinin daha ayrıntılı bir şekilde kanama kontrolü yapılmasına olanak verdiğini göstermektedir. Bizim bu şekildeki ilk bulgularımızı daha büyük vaka serilerinde yapılan prospektif, randomize, kontrollü çalışmalar destekleyecektir.

**Anahtar Kelimeler:** Kanama, hemostazis, hipotansif epidural anestezi, kontrollü hipertansiyon, total diz artroplastisi

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## INTRODUCTION

Many orthopedic surgeries are associated with remarkable and unpredictable blood loss. This condition is attributed to the texture of bony and soft tissues that impedes effective hemostasis.<sup>1</sup> Total knee arthroplasty (TKA) is an efficient therapeutic procedure for severe knee osteoarthritis (OA) with good long-term outcomes. Despite improvement in techniques, blood loss after TKA constitutes a concern of surgeons. Up to 70% of patients who underwent total joint arthroplasty may receive a blood transfusion.<sup>2</sup>

Blood transfusion has substantial risks, such as prolonged hospitalisation, transmission of infectious diseases, immunologic, hemolytic and anaphylactic reactions, and increased mortality. Thus, preoperative red blood cell mass expansion, autologous blood transfusion, and reduction of perioperative blood loss using careful hemostasis, drugs, and controlled hypotension have been described to avoid unnecessary blood transfusions. Each of these methods possesses advantages and disadvantages. There is a seek for an effective, practical, and safe method to omit unnecessary allogeneic blood transfusion.<sup>1,3</sup> Patients with a low baseline hemoglobin level are more likely to receive a blood transfusion.<sup>4</sup>

Hypotensive epidural anesthesia (HEA) is a technique to diminish blood loss. It involves the concomitant use of an extensive epidural block and an intravenous infusion of low-dose epinephrine. This approach provides hemodynamic stability, reduces intraoperative blood loss, and allows a dry surgical field.<sup>5</sup> Epidural anesthesia has been shown to decrease blood loss during TKA without applying a tourniquet.<sup>6</sup>

Parameters influencing blood loss associated with TKA are hypertensive patients, prolonged duration of surgery, and lower preoperative hemoglobin levels. To reduce the use of allogeneic blood transfusion, arterial blood pressure must be adjusted preoperatively in hypertensive patients, and lower preoperative hemoglobin levels must be restored.<sup>7</sup>

Prediction of blood loss also involves intraoperative and postoperative aspects as well. Applying novel and effective management strategies may aid surgeons in diminishing blood loss and transfusion risk.<sup>3</sup> Controlled hypotension is frequently utilised during total joint arthroplasties, and the quantity of hemorrhage monitored the blood pressure from the surgical field. Controlled intraoperative hypotension can provide a diminution of intraoperative and postoperative blood loss. Post-operative hypertension is supposed to be linked with an increased risk of transfusions.<sup>8</sup>

Identifying factors is a critical step for establishing an adequate blood management strategy. We aimed

to assess the efficacy of hemostasis performed by controlled augmentation of arterial blood pressure before surgical closure after TKA in patients receiving hypotensive anesthesia.

## MATERIALS AND METHODS

**Ethics Committee Approval:** The study was approved by the Memorial Sisli Hospital Ethics Committee (Date: 03.06.2023, decision no: 003). The study was planned under the Helsinki Principles. Written informed consent was obtained from all patients.

**Design:** This retrospective cohort was performed in our tertiary care centre's orthopedics and traumatology department.

**Participants:** Our target population was the patients who underwent elective unilateral TKA and received HEA without a tourniquet between February 2016 and January 2019.

**Procedure:** Data were derived from the medical files of 87 patients (62 women, 25 men) with an average age of  $66.41 \pm 6.17$  (range: 57-78). Patients were allocated into two groups to administer controlled arterial hypertension before surgical closure. Group I (n=44) received HEA, while Group II (n=43) had controlled arterial hypertension (up to preoperative mean arterial blood pressure) before surgical closure.

Inclusion criteria were a history of unilateral TKA without tourniquet and administration of HEA. Exclusion criteria were history of bleeding disorders, refractory hypertension, previous history of myocardial infarction, valvular heart disease, unstable angina, stroke, thrombocytopenia, hematological disease, malignant disease, abnormal liver function, acute infection, use of anticoagulants, a refusal for blood transfusion, or need for revision arthroplasty.

All patients were routinely hospitalised a day before surgery. Preoperative American Society of Anaesthesiologists (ASA) scores<sup>9</sup> and baseline descriptive data, including sex, age, side of knee osteoarthritis, comorbidity, and complications were recorded. Blood pressure was monitored, and the mean arterial pressure was recorded every 6 hours. Routine anti-hypertensive treatment was maintained for hypertensive patients.

Perioperative mean arterial blood pressure was measured immediately after surgery and on 1, 2, 4, 8, 12, 16, 20, and 24 hours postoperatively. The operative duration and the average mean arterial pressure at 12 and 24 hours were noted.

The amount of intraoperative blood loss was measured using the blood collected in suction. The quantity of irrigation fluid and the weight of gauze sponges were considered when calculating the amount of blood loss. The drain was removed after

24 hours, and the collection amount was measured on 1, 2, 4, 12, and 24 hours. For this purpose, we have noted the additional amount of blood accumulated over the preceding quantity.

Patients in this study were monitored intraoperatively by the anesthetist and were evaluated in the postoperative period clinically and with a complete blood count. Hemoglobin levels were evaluated preoperatively and 1, 24, and 48 hours after surgery. Blood was transfused based on the clinical assessment. Criteria for blood transfusion were either Hb level <9 g/dL, hematocrit <28, or Hb level <10 g/dL or hematocrit <30 presenting with symptoms of acute anemia such as tachycardia, fatigue, pallor of lips, dizziness, shortness of breath, or lightheadedness. The amount of erythrocyte suspension transfusion was recorded.

All patients received 1 g of 10% tranexamic acid injectable solution (*Transamine*<sup>®</sup>, *Teva Pharmaceuticals, Istanbul, Türkiye*) through the intravenous route. The injections were performed 30 minutes before and after surgery and 3 hours after. All patients underwent HEA, and body temperature was kept above 36.0 °C.

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is commonly used to evaluate treatment effects in OA.<sup>10</sup> The Knee Society Score (KSS) is a measure of which higher scores indicate less severity. The KSS is comprised of the Knee Society Knee Score (KSKS) and the Knee Society Function score (KSFS).<sup>11</sup>

Standard surgical methods were employed in all patients, and the operations were performed in a supine position by the same surgical team. Midline anterior incision and medial parapatellar approach were routinely adopted. Cephalosporins were routinely applied for 24 hours after operation for infection prophylaxis.

In all cases, a total knee prosthesis (*Genesis II*<sup>®</sup>, *Smith Nephew, Memphis, USA*) that allows posterior cruciate ligament retention was used and fixed with cement. The femoral milling orifice was occluded with a bone plug. The patellar replacement was not performed in any of our TKA procedures. All patients received periarticular injections. The preoperative blood pressure was controlled for hypertensive patients to below 140/90 mmHg.

In Group I, surgical closure was performed after meticulous hemostasis and placement of a drain. In Group II, systolic blood pressure was restored to the preoperative levels and hemostasis was achieved under these conditions. Surgical closure and drainage tube placement were performed after hemostasis was completed. All perioperative transfusions were recorded. Hypotensive epidural anesthesia was maintained two days postoperatively, and 0.2% ropivacaine (2 mg/ml) was administered. Analgesia after

discontinuation of HEA was provided by acetaminophen 1 g and tramadol 75 mg. Low-molecular-weight heparin, enoxaparin (*Clexane*<sup>®</sup>, *Sanofi, Istanbul, Turkey*) was initiated on the 12<sup>th</sup> hour postoperatively. After removing the drainage tube on the first postoperative day, patients were mobilised with Canadian walking sticks.

**Outcome Measures:** Baseline descriptive data, including age, sex, and body-mass index, were recorded. The side of involvement, ASA scores, preoperative and postoperative hemoglobin and hematocrit levels, amount of erythrocyte suspension transfusion, WOMAC, KSKS, and KSFS values were compared between the two groups under investigation.

**Statistical Analysis:** Our data were analysed with Statistical Package for Social Sciences version 21.0 for Windows software (*SPSS Inc., Chicago, Illinois, USA*). Descriptive data were presented as counts and percentages. The p-value was accepted as <0.05. Normality was tested using the Shapiro-Wilks test. A Chi-square test was utilised for categorical variables. Quantitative variables with normal distribution were tested with a parametric and independent variables t-test. Quantitative variables without normal distribution were analysed using a non-parametric Mann-Whitney U test.

## RESULTS

Retrospective analysis of data derived from the medical files of 87 patients (62 women, 25 men). Patients were allocated into two groups to administer controlled arterial hypertension before surgical closure. Group I (n=44) received HEA, while Group II (n=43) had controlled arterial hypertension (up to preoperative mean arterial blood pressure) before surgical closure. Group I consisted of 31 women and 13 men with an average age of 66.82 ± 5.96 (58-76). Group II (n=43) was comprised of 31 women and 12 men with an average age of 66.00 ± 6.42 (57 to 78). In Group II, perioperative surgical closure systolic pressure was 122.35 ± 10.44 mmHg (range: 108-142), and perioperative surgical closure diastolic pressure was 80.21 ± 12.16 (range: 65-106). Two groups exhibited similar features for age (p=0.894), sex distribution (p=0.927), side of involvement (p=0.326), comorbidities (p=0.911), ASA scores (p=0.826), and complications (p=0.987) (Table 1).

The survey of 2 groups in terms of operative duration, perioperative bleeding and bleeding in the postoperative 2<sup>nd</sup> hour were compared. Groups I and II exhibited similar outcomes for operative duration (p=0.167) and perioperative bleeding (p=0.888); however, the amount of bleeding in the postoperative 2<sup>nd</sup> hour was significantly less in Group II (p=0.032) (Table 2).



Table 1.

Variable	Groups		p-value
	I (n=44)	II (n=43)	
Age (years)	66.82 ± 5.96	66.01 ± 6.42	0.894
Sex	Female	31	0.927
	Male	13	
Side of involvement	Right	22	0.326
	Left	22	
Comorbidity	Diabetes mellitus	3	0.911
	Hypertension	8	
	DM & HT	1	
ASA Score	No	32	
	I	31	0.826
	II	12	
Complication	III	1	
	Wound infection	1	0.987
	No	43	

DM: Diabetes mellitus; HT: Hypertension; ASA: American Society of Anaesthesiologists.

Table 2. A survey of quantitative variables in 2 groups (Independent Samples T-test).

Variable	Groups		p-value
	I (n=44)	II (n=43)	
Operative duration (minutes)	64.09 ± 6.27	70.16 ± 5.26	0.167
Perioperative bleeding (mL)	256.25 ± 31.12	270.35 ± 29.12	0.888
Postoperative 2 <sup>nd</sup> hour bleeding (mL)	110.57 ± 16.47	95.58 ± 21.61	<b>0.032*</b>

\*: Statistically significant.

Two groups were similar for the duration of follow-up (p=0.821), body-mass index (p=0.786), duration of hospitalisation (p=0.770), hemoglobin levels preoperatively (p=0.200), postoperatively 1<sup>st</sup> hour (p=0.865), postoperatively 1<sup>st</sup> day (p=0.528), and postoperatively 2<sup>nd</sup> day (p=0.296). The amount of erythrocyte suspension transfusion (p=0.203), preoperative systolic (p=0.848) and diastolic pressures (p=0.878), peroperative systolic (p=0.956) and diastolic pressures (p=0.878), postoperative 1<sup>st</sup> hour sys-

tolic (p=0.808) and diastolic pressures (p=0.983), postoperative 2<sup>nd</sup> hour systolic (p=0.838) and diastolic pressures (p=0.892), postoperative 4<sup>th</sup> hour systolic (p=0.852) and diastolic pressures (p=0.848), postoperative 12<sup>th</sup> hour systolic (p=0.983) and diastolic pressures (p=0.882), postoperative 24<sup>th</sup> hour systolic (p=0.683) and diastolic pressures (p=0.969). In Group II, postoperative bleeding was significantly less than in Group I on 1<sup>st</sup> (p=0.031), 4<sup>th</sup> (p=0.001), 12<sup>th</sup> (p=0.001), and 24<sup>th</sup> hours (p=0.001) (Table 3).

Table 3. The survey of quantitative variables in 2 groups.

Variable	Group	Mean rank	Total rank	Mann-Whitney U test	Z	p-value
Duration of follow-up (months)	I	43.40	1909.50	919.500	-0.226	0.821
	II	44.62	1918.50			
Body-mass index (kg/m <sup>2</sup> )	I	43.28	1904.50	914.500	-0.272	0.786
	II	44.73	1923.50			
Duration of hospitalisation	I	43.33	1906.50	916.500	-0.293	0.770
	II	44.69	1921.50			
Preoperative Hb level (g/dL)	I	47.27	2080.00	802.000	-1.282	0.200
	II	40.65	1748.00			
Postoperative 1 <sup>st</sup> hour Hb level (g/dL)	I	43.57	1917.00	927.000	-0.170	0.865
	II	44.44	1911.00			
Postoperative 1 <sup>st</sup> day Hb level (g/dL)	I	41.86	1800.00	854.000	-0.631	0.528
	II	45.14	1941.00			
Erythrocyte suspension transfusion (units)	I	47.07	2071.00	811.000	-1.274	0.203
	II	40.86	1757.00			

Table 3. Continue.

Postoperative 2 <sup>nd</sup> day Hb level (g/dL)	I	46.49	2045.50	836.500	-1.046	0.296
	II	41.45	1782.50			
Postoperative 1 <sup>st</sup> hour amount of bleeding (mL)	I	49.75	2189.00	693.000	-2.153	<b>0.031*</b>
	II	38.12	1639.00			
Postoperative 4 <sup>th</sup> hour amount of bleeding (mL)	I	52.63	2315.50	566.500	-3.235	<b>0.001*</b>
	II	35.17	1512.50			
Postoperative 12 <sup>th</sup> hour amount of bleeding (mL)	I	53.09	2336.00	546.000	-3.425	<b>0.001*</b>
	II	34.70	1492.00			
Postoperative 24 <sup>th</sup> hour amount of bleeding (mL)	I	54.14	2382.00	500.000	-3.788	<b>0.001*</b>
	II	33.63	1446.00			
Preoperative systolic blood pressure	I	43.49	1913.50	923.500	-0.191	0.848
	II	44.52	1914.50			
Preoperative diastolic blood pressure	I	43.59	1918.00	928.000	-0.153	0.878
	II	44.42	1910.00			
Peroperative systolic blood pressure	I	44.15	1942.50	939.500	-0.055	0.956
	II	43.85	1885.50			
Peroperative diastolic blood pressure	I	43.59	1918.00	928.000	-0.153	0.878
	II	44.42	1910.00			
Postoperative 1 <sup>st</sup> hour systolic blood pressure	I	43.35	1907.50	917.500	-0.242	0.808
	II	44.66	1920.50			
Postoperative 1 <sup>st</sup> hour diastolic blood pressure	I	43.94	1933.50	943.500	-0.021	0.983
	II	44.06	1894.50			
Postoperative 2 <sup>nd</sup> hour systolic blood pressure	I	44.55	1960.00	922.000	-0.204	0.838
	II	43.44	1868.00			
Postoperative 2 <sup>nd</sup> hour diastolic blood pressure	I	44.36	1952.00	930.000	-0.136	0.892
	II	43.63	1876.00			
Postoperative 4 <sup>th</sup> hour systolic blood pressure	I	44.50	1958.00	924.000	-0.187	0.852
	II	43.49	1870.00			
Postoperative 4 <sup>th</sup> hour diastolic blood pressure	I	44.51	1958.50	923.500	-0.191	0.848
	II	43.48	1869.50			
Postoperative 12 <sup>th</sup> hour systolic blood pressure	I	44.06	1938.50	928.500	-0.021	0.983
	II	43.94	1889.50			
Postoperative 12 <sup>th</sup> hour diastolic blood pressure	I	44.40	1953.50	928.500	-0.149	0.882
	II	43.59	1874.50			
Postoperative 24 <sup>th</sup> hour systolic blood pressure	I	42.91	1888.00	898.000	-0.408	0.683
	II	45.12	1940.00			
Postoperative 24 <sup>th</sup> hour diastolic blood pressure	I	44.10	1940.50	941.500	-0.038	0.969
	II	43.90	1887.50			

Hb: Hemoglobin; \*: Statistically significant.

Two groups did not display any significant differences for preoperative (p=0.714) and postoperative (p=0.330) WOMAC, preoperative (p=0.748) and

postoperative (p=0.282) KSKS, as well as preoperative (p=0.653) and postoperative KSFS (p=0.890) (Table 4).

Table 4. The survey of Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee

Variable	Group	Mean	Total rank	Mann-Whitney U test	Z	p-value
Preoperative WOMAC	I	44.98	1979.00	903.000	-0.366	0.714
	II	43.00	1849.00			
Postoperative WOMAC	I	41.45	1824.00	834.000	-0.974	0.330
	II	46.60	2004.00			
Preoperative KSKS	I	43.15	1898.50	908.500	-0.321	0.748
	II	44.87	1929.50			
Postoperative KSKS	I	41.17	1811.50	821.500	-1.076	0.282
	II	46.90	2016.50			
Preoperative KSFS	I	42.82	1884.00	894.000	-0.440	0.653
	II	45.21	1944.00			
Postoperative KSFS	I	43.65	1920.50	930.500	-0.139	0.890
	II	44.36	1907.50			

WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; KSKS: Knee Society Knee Score; KSFS: Knee Society Function Score.

## DISCUSSION AND CONCLUSION

Total knee arthroplasty is usually performed with a bloodless field, and blood loss after TKA can occur in obvious or hidden forms.<sup>12</sup> Hypotensive epidural anesthesia can be preferred for TKA, and diminished intraoperative blood loss during HEA allows clear vision without a tourniquet.<sup>13</sup>

We noted that postoperative bleeding was significantly less in Group II at all postoperative intervals. We did not encounter any rebound bleeding in the recovery room; these findings were consistent with relevant publications.<sup>14,15</sup> This may be due to the prolonged hypotensive state stabilising the intravascular clotting in the operated knee before the mean arterial pressure was increased. Our data support that controlled elevation of the systolic blood pressure and performance of hemostasis in this setting before surgical closure can be helpful for adequate hemostasis.

Total knee arthroplasty without a tourniquet allows the surgeon to achieve more effective intraoperative hemostasis and abate the postoperative bleeding. The remarkably diminished blood loss leads to a lesser need for transfusion. Tourniquet use is associated with the augmentation of postoperative blood loss. Avoiding tourniquet use offers benefits like decreased postoperative pain and early mobilisation if surgeons abstain from using a tourniquet.<sup>16,17</sup> Using a tourniquet is linked with altering thrombotic and fibrinolytic activities.<sup>18</sup> The incidence of embolic events is increased<sup>19</sup>, and releasing the inflated tourniquet may have adverse metabolic consequences.<sup>20</sup> Further trials are encouraged to unveil the impacts of HEA and various methods conducted to diminish intraoperative blood loss during TKA.<sup>21</sup>

The risk for bleeding and blood transfusions is complex and multifactorial, and adequate preoperative preparation is essential.<sup>3</sup> During TKA, there is considerable blood loss, which increases morbidity and mortality rates. Specific methods, such as using pneumatic cuffs, minimally invasive surgery, and anti-fibrinolytic agents, aid in the reduction of hemorrhage.<sup>22</sup> Hu et al. suggested that possible influential factors of total blood loss included gender, type of prosthesis, and drainage.<sup>2</sup> We sought a method that would minimise blood loss in patients who underwent TKA. Our novel method yielded that it can be easily applicable with minimal risk. Since postoperative blood loss in the drains is unpredictable and varies over a wide range, surgeons should take additional measures to keep hemoglobin and hematocrit levels within the safe range. Our data imply that controlled elevation of arterial blood pressure and performance of hemostasis under these conditions before surgical closure may yield a practical, safe, reliable, and effective way to reduce blood loss and the need for blood transfusion after TKA, an elective

major surgery. This approach must be performed in close collaboration with the anesthesiology team, and hemodynamic stability must be preserved during the controlled elevation of mean arterial pressure before hemostasis. We encountered no significant complications in both groups, including hemodynamic instability and thromboembolic events.

In conjunction with Kourtzis et al.,<sup>1</sup> it is desirable for every surgeon to avoid risk when applying a novel method and to keep in the safe zone with sufficient options. Since postoperative blood loss cannot be predicted, every technique must be administered safely. Preserving the mean arterial blood pressure within normal limits is essential in reducing blood loss via the drains.<sup>1</sup>

Marked blood loss during TKA may cause higher rates of transfusion, which may negatively influence surgical outcomes and lead to more excellent rates of complication. It is, therefore, essential to develop novel methods to decrease postoperative blood loss. Every patient must be evaluated concerning demographic and clinical features, and the hemostatic approach must be tailored individually to diminish risks implicated with TKA, like thromboembolic events and hemodynamic instability. In other words, recognition of patient-specific risk factors linked with blood loss may allow clinicians to prepare for perioperative hazardous outcomes and take proper measures.<sup>3</sup>

In conclusion, our data indicate that controlled elevation of mean arterial pressure before surgical closure may allow the achievement of meticulous hemostasis after TKA. Therefore, our results are promising to protect candidates of TKA against unpredictable or substantial blood loss. However, further prospective, randomised, controlled trials on more extensive series are warranted to verify our preliminary results. Some limitations must be considered during the interpretation of our results. This study reflects the experience of a single center and a surgical team. Retrospective design, relatively small sample size, and possible confounding factors such as ethnicity and socio-economical aspect may restrict the extrapolation of our results to larger populations.

**Ethics Committee Approval:** This study was approved by the Memorial Sisli Hospital Ethics Committee (Date: 03.06.2023, decision no: 003). The study was conducted in accordance with the principles of the Helsinki Declaration.

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

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## Anesthesia Management in A Case with Prader-Willi Syndrome

### Prader Willi Sendromlu Bir Olguda Anestezi Yönetimi

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#### ABSTRACT

Prader Willi (PWS) is the most common and rare genetic cause of obesity. Airway problems associated with obesity and hypotonia, increased risk of aspiration due to gastrointestinal (GI) motility and hyperphagia, obstructive sleep apnea syndrome (OSAS), difficult airway management, and postoperative respiratory failure risk due to narrow airway are the factors that complicate anesthesia management. It should be noted that there are many anatomical and physiological factors that may adversely affect perioperative anesthesia management in patients with PWS. For this reason, preoperative anesthesia evaluation and all preparations should be performed completely.

**Keywords:** Anesthesia management, difficult airway, prader-willi syndrome

#### ÖZ

Prader Willi (PWS), obezitenin en yaygın ve nadir görülen genetik nedenidir. Obezite ve hipotoni ile ilişkili hava yolu sorunları, gastrointestinal (GI) motilite ve hiperfaji nedeniyle artan aspirasyon riski, obstrüktif uyku apne sendromu (OUAS), zor hava yolu yönetimi, dar hava yoluna bağlı postoperatif solunum yetmezliği riski anestezi yönetimini zorlaştıran faktörlerdir. PWS'li hastalarda perioperatif anestezi yönetimini olumsuz etkileyebilecek birçok anatomik ve fizyolojik faktör olduğu unutulmamalıdır. Bu nedenle ameliyat öncesi anestezi değerlendirmesi ve tüm hazırlıklar eksiksiz yapılmalıdır.

**Anahtar Kelimeler:** Anestezi yönetimi, prader-willi sendromu, zor havayolu

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#### INTRODUCTION

Prader-Willi syndrome (PWS) was first described in 1956 and is a genetic disease caused by loss of gene expression (15q 11-13) occurring in the proximal long arm of paternal chromosome 15. Its incidence is approximately 1/15000. PWS is the most common and rare genetic cause of obesity.<sup>1,2</sup>

In this syndrome, craniofacial anomalies (dolichocephaly, narrow bifrontal diameter, strabismus, thin upper lip, small upturned nose and downturned corners of the mouth, enamel hypoplasia), mental retardation, infantile hypotonia, growth and other hormone deficiencies, hypogonadism/hypogonitalism, behavioural problems in early child-

hood play a role in clinical manifestations. It is a neurodevelopmental disorder with hyperphagia that leads to obesity if not controlled.<sup>1</sup>

Airway problems associated with obesity and hypotonia, increased risk of aspiration due to gastrointestinal (GI) motility and hyperphagia, obstructive sleep apnea syndrome (OSAS), risk of postoperative respiratory failure due to narrow airway, and difficulty in providing intravenous access are factors that complicate anesthesia management. It should be noted that many anatomical and physiological factors may adversely affect perioperative anesthesia management in patients with PWS. For this reason, preoperative anesthesia evaluation and all preparati-

ons should be performed completely.

In this case report, we aimed to present the anesthesia management of a 9-year-old male patient who presented to the emergency department of our hospital due to foreign body obstruction in the esophagus.

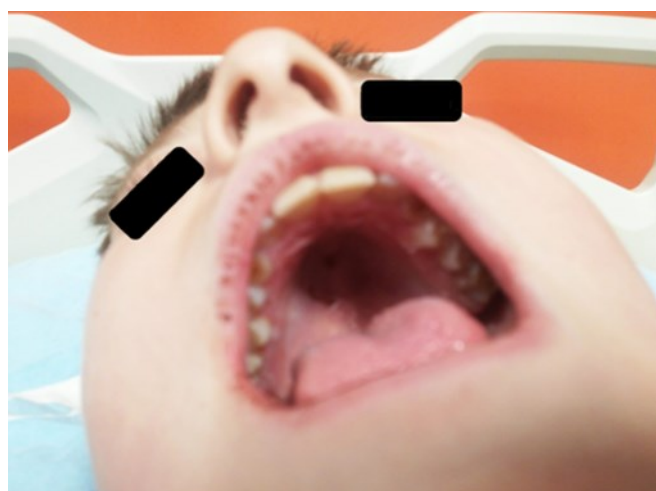
### CASE REPORT

A 9-year-old male patient diagnosed with PWS by genetic analysis and followed-up in an outer center, with a height of 131 cm, weight of 55 kilograms, and body mass index of 32 kg/m<sup>2</sup>, was consulted by our pediatric surgeon for emergency esophagoscopy under general anesthesia due to foreign body obstruction (coin) in the esophagus. When the patient was evaluated preoperatively, it was observed that he had mental retardation, hyperphagia, and OSAS findings. It was learned that he had growth retardation and thyroid hormone deficiency and had used 1 mg/day recombinant human growth hormone and 12.5 mcg/day levothyroxine for treatment. In the physical examination, craniofacial anomalies such as a thin upper lip, downward curved corners of the mouth, and high palate were detected. The patient had adequate mouth opening and a Mallampati score of III. The patient was clinically euthyroid, and there was no anomaly in other laboratory parameters. The preoperative fasting period of the patient was 8 hours. Considering that there may be a risk of postoperative respiratory failure and reintubation, pharyngeal hypotonia and stenosis in the patient with OSAS, preparations were made with the necessary equipment (ETT and LMA in different diameters and sizes, Videolaryngoscope etc.). The patient had peripheral vascular access, which was controlled. The patient was taken to the operating table without any premedication, and standard monitoring was performed with electrocardiography (ECG), peripheral oxygen saturation (SpO<sub>2</sub>) and non-invasive blood pressure (NIBP) measurement. Case baseline measu-

rement values were heart rate: 87/min, NIBP: 121/75 mmHg, and SpO<sub>2</sub>: 97%. Preoxygenation was provided with 5 L/min 100% O<sub>2</sub> in spontaneous respiration. In the induction of anesthesia, 1 mg/kg IV lidocaine, 2 mg/kg IV propofol and 3 mcg/kg IV remifentanyl were administered. Neuromuscular blocker administration was avoided in the patient. Before esophagoscopy, the laryngeal and esophageal entrance part of the patient was visualised with the help of a C-MAC videosyngoscope, and it was observed that the coin was inserted into the first stenosis of the esophagus, and the foreign body was successfully removed by the pediatric surgeon using magell forceps. Esophagoscopy was performed to control the esophagus, and no other foreign body was found. The patient, whose hemodynamic data were within normal limits and no additional medication was administered during the procedure, was ventilated with a mask until spontaneous breathing returned. In the case that lasted 20 minutes in total, no complications developed, and the patient's spontaneous breathing returned to normal. He obeyed verbal commands, and after the patient woke up, he was interned in the postanesthetic care unit (PACU). The patient, who was kept under observation for 30 minutes in PACU, was transferred to the pediatric surgery service without any problem, with a Modified Aldreate Score of 10.

### DISCUSSION AND CONCLUSION

PWS is a genetic disease with a clinical course consisting of 2 stages. The hypotonic infantile stage is the first stage, which is characterised by difficulty in sucking, muscle hypotonia, weakness in the cough reflex, and growth retardation. The hyperphagic obese stage is the second stage that follows the first stage and starts with the recovery of muscle activity between the ages of 2-4 and causes the development of mental retardation, behavioral disorders, hyperp-



**Figure 1.** Craniofacial anomalies such as a thin upper lip, downward curved corners of the mouth, and high palate.

hagia and obesity.<sup>3</sup>

In studies conducted with PWS patients, it has been reported that morbid obesity, central hypotonia and OSAS are the most common and important factors of perioperative complications. In these patients, general and regional anesthesia may be more risky than normal due to the perioperative risks arising from hypotonia and morbid obesity, especially in general anesthesia.<sup>4</sup>

If access to food and weight gain are not adequately controlled in PWS, diabetes mellitus, right heart failure, hypoventilation, obstructive sleep apnea (OSAS), and narrow airway, GI dysmotility, esophageal dysmotility, delayed gastric emptying may accompany the clinical picture associated with hyperphagia and obesity. The presence of conditions such as water intoxication may make anesthesia management more difficult.<sup>1</sup> In these patients, the difficulty in maintaining hunger control before the procedure due to hyperphagia should be considered, and the last food intake period should be followed closely. It is stated that the risk of aspiration is high due to preoperatively uncontrolled food intake. In patients with OSAS, close follow-up should be applied after the procedure because of the risk of postoperative respiratory failure. (4) In addition, venous access difficulties, thermoregulation disorders and metabolic problems are also common.<sup>2</sup>

Tseng et al. presented a 5-year-old, 50 kg male PWS patient who was admitted with OSAS and underwent general anesthesia with IV propofol and face mask and sevoflurane induction for bilateral tonsillectomy and uvulopalatopharyngoplasty. The patient was intubated endotracheally without the use of muscle relaxants. It has been reported that the patient, who was extubated when fully awakened, was reintubated and sent to the pediatric intensive care unit when the O<sub>2</sub> saturation (SpO<sub>2</sub>) decreased to 70%, and the respiratory rate increased to 70/min within a few minutes after the follow-up in the post-anesthesia care unit (PACU).<sup>5</sup>

In our case, the patient with OSAS, growth retardation and thyroid hormone deficiency, hyperphagia, mental retardation and behavioral disorder; to eliminate the foreign body obstruction developed in the esophagus as a result of coin ingestion, the procedure was performed without any problem with the help of a videaryngoscope under general anesthesia by avoiding the use of neuromuscular blocking agents. The patient was followed closely in the PACU in the postoperative period. The patient, who did not develop any complications during the follow-up, was transferred to the pediatric surgery service.

In conclusion, it should not be forgotten that many anatomical and physiological factors may adversely affect the perioperative process in patients with PWS. Therefore, the preoperative anesthesia evalua-

tion should be detailed, and all preparations should be made completely. Necessary equipment (laryngeal mask, videaryngoscope, flexible bronchoscopy, tracheostomy materials, etc.) that may be needed should be readily available and easily accessible in the operating room, taking into account possible difficult airway in the patient, and respiratory complications that may arise intraoperatively and postoperatively. Using long-acting muscle relaxants should be avoided, especially in cases with severe OSAS. In this patient group, individualised and well-planned anesthesia management before the procedure can provide uneventful anesthesia.

**Ethics Committee Approval:** Ethics committee approval was not required for the case report. The patient /relatives have signed an informed consent/ consent form, and the study was conducted in accordance with international declarations, guidelines, etc.

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

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

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## Did the Covid 19 Pandemic Affect the Diagnosis of Pediatric Solid Tumors?

### Covid 19 Pandemisi Çocuk Solid Tümörlerinin Tanısını Etkiler mi?

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#### ABSTRACT

During the Covid-19 pandemic, hospital admissions have decreased due to non-coronavirus diseases in our country. Therefore, the treatment processes of children with many serious and important diseases have been affected. In this study, the delays in diagnosis and treatment of children with solid tumors due to the delay in admission to the hospital during the Coronavirus Disease 2019 (Covid-19) pandemic period, and the results are presented. It was aimed to draw attention to the delays in diagnosis and treatment of diseases other than Covid-19 by presenting three children (two 17-year-old girls and an 11-year-old boy) with three solid tumors whose diagnosis was delayed due to the Covid-19 pandemic.

In conclusion, patients with non-pandemic complaints should be informed and encouraged to apply to the hospital during all pandemic periods, as in the Covid-19 pandemic.

**Keywords:** Covid-19, children, solid tumors

#### ÖZ

Covid-19 pandemisi döneminde ülkemizde de koronavirüs dışı hastalıklar nedeniyle hastaneye başvurular azalmıştır. Bundan dolayı pek çok ağır ve önemli hastalıkları olan çocukların tedavi süreçleri etkilenmiştir. Bu çalışmada, Koronavirüs Hastalığı 2019 (Covid-19) pandemi döneminde solid tümörlü çocukların hastaneye başvuru gecikmesinden dolayı tanı ve tedavisindeki gecikmeler ve sonuçları sunuldu. Covid-19 pandemisi nedeniyle tanısı geciken solid tümörü olan 3 çocuk hasta (17 yaşında iki kız ve 11 yaşında bir erkek) sunularak Covid-19 dışındaki hastalıkların tanı ve tedavi gecikmelerine dikkat çekilmesi amaçlandı.

Sonuç olarak, Covid-19 pandemisinde olduğu gibi tüm pandemi dönemlerinde, pandemik hastalık dışı şikayetleri olan hastaların da hastaneye başvurma konusunda bilgilendirilmeleri ve teşvik edilmeleri gereklidir.

**Anahtar Kelimeler:** Covid 19, çocuk, solid tümörler

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#### INTRODUCTION

Coronavirus Disease-2019 (Covid-19), which first appeared in Wuhan, China, in December 2019, has spread rapidly worldwide.<sup>1,2</sup> Each country has taken its precautions in health care. Measures were taken both to prevent the increase in cases and to meet this burden on health services. These changes in the healthcare system have also affected people with diseases other than Covid-19. Admissions to hospi-

tals have decreased, especially due to measures such as the weekend curfew taken on a societal basis, and people's fears about the risk of Covid-19 transmission. This led to decreased hospital admissions if Covid-19 was negative in diseases requiring urgent treatment, such as appendicitis and tumors.<sup>3</sup>

Here, 3 cases with solid abdominal tumors who did not have Covid-19 but were affected by delayed diagnosis due to the Covid-19 pandemic were

shared; and to draw attention to the fact that the pandemic affects the treatment of patients not infected with Covid-19 in a life-threatening way were wanted.

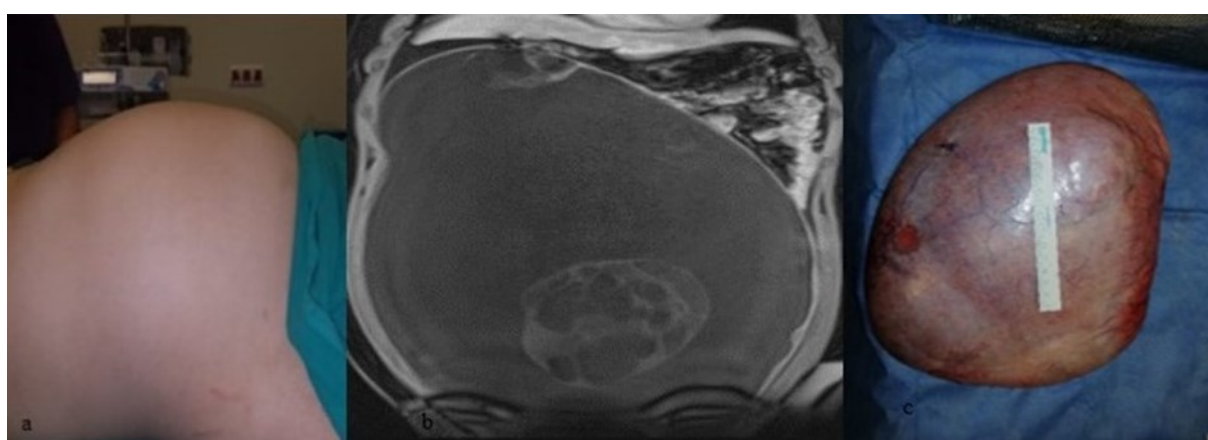
## CASE REPORT

### Case 1.

A 17-year-old girl was admitted to our emergency department with a complaint of restlessness that developed in the last weeks. In her first anamnesis, she stated that she complained of abdominal distention and weight gain for the last 3 months. The fami-

ly related these complaints to changes in social and personnel life. Especially due to the quarantine imposed on the pandemic, it was also learned during the interview, we understood that the family did not want to come to the hospital due to fear of the Covid-19 pandemic.

On inspection, the abdomen was extremely swollen, and there was a pronounced abdominal enlargement that gave the impression of 36 weeks of gestation by age. On palpation, the abdominal mass extending from pubis to xiphoid (Figure 1a).



**Figure 1.** 1a: The appearance of the abdomen before the operation in the first case by inspection; 1b: MRI of a huge mass filling the entire abdomen; 1c: The postoperative appearance of the huge, smooth surface cystic mass.

Abdominal ultrasound (US) and abdominal magnetic resonance (MRI) were performed. A huge mass of 38x26x19 cm in size, predominantly cystic, containing heterogeneous components with cystic-solid areas, was observed (Figure 1b).

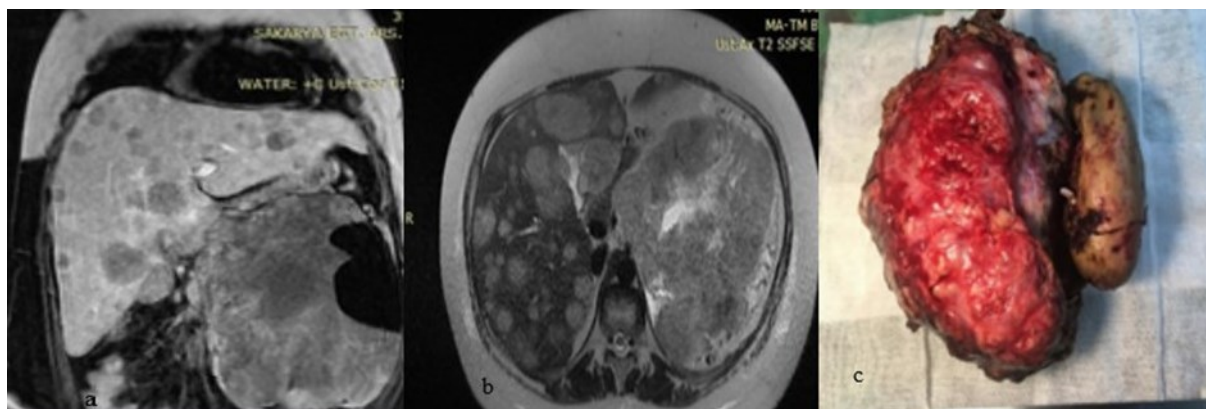
The patient was operated on, and the mass was totally removed by right salpingo-oophorectomy (Figure 1c). In surgery, frozen could not be sent due to the official holiday. There was no ovarian tissue that could be separated from the mass. Samples of tissues from the left ovary, peritoneum and omentum were taken, and the sample of intra-abdominal fluid was taken for cytology. The entire abdomen, including the liver and appendix, was evaluated. No other pathology was detected. The histopathologic examination revealed as a mucinous borderline tumor. The patient, who has no problems with follow-up, is in the 19th postoperative month.

### Case 2.

An 11-year-old male patient applied to the emergency department due to a convulsion that started after a

fall of about 1 meter. The patient was 90 kg and 155 cm tall at admission. It was above the 97th percentile in terms of weight. It was learned from his medical history that he had low back pain for the last three months and gained 30 kilos during the Covid-19 pandemic. However, the situation was attributed to changes in their social and personal life due to the quarantine applied by his family during the Covid-19 pandemic. Orthopedic consultation was requested due to the patient's low back pain. Vertebral tomography revealed several nodules, the largest of which was 1 cm in diameter in both lungs, metastasis, lesions compatible with metastasis in the liver, and a 15 cm mass in the left kidney. We performed MRI of the abdomen (Figure 2a, 2b).

On exploration, an excessive vascular mass that filled the left side of the abdomen up to the midline was encountered. While dissecting the mass from all areas, mass could not separate it from the renal pelvis, and we observed that it was highly fixed and included the pelvis and ureter. The frozen evaluation of mass sample was stated that it could be an aggres-



**Figure 2.** 2a and 2b: MRI imaging revealed the mass and metastasis to the liver in second case; 2c: the postoperative appearance of the mass with a diameter of 15 cm including the renal pelvis and ureter.

sive tumor of mesenchyme origin. The mass was removed with the left nephrectomy, considering it might be a pelvic-derived mesenchymal tumor (Figure 2c). The patient's deteriorated gradually. The patient's histopathology was reported as adrenocortical carcinoma. The patient died 20 days after the first admission due to multiple organ failure.

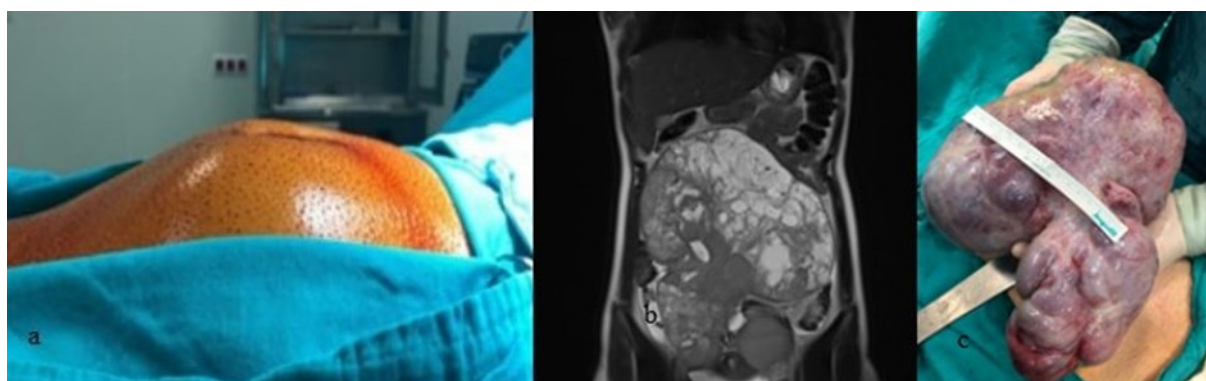
### Case 3.

A 17-year-old female patient applied to the emergency room with her mother for a Covid-19 test because her father was Covid-19 positive. The emergency physician noticed abdominal swelling compatible with six months of pregnancy (Figure 3a). The patient and her family insisted that she gained weight due to the Covid-19 pandemic and that her abdomen was normal. Then USG was performed. A mass covering the entire abdomen was detected in the patient. An intra-abdominal mass extending from

the symphysis pubis to the xiphoid process was detected on MRI (Figure 3b). In the exploration performed, a mass covering the entire abdomen originating from the right ovary was detected. The right ovary frozen result was evaluated as dysgerminoma. No tumor was found in the left ovarian tissue. The mass was removed by performing a right salpingo-oophorectomy (Figure 3c). The mass compatible with metastasis was excised behind the uterus. Omentectomy, peritoneal biopsies and cytology were performed. They reported that the pathology of the patient was as dysgerminoma stage 2C.

### DISCUSSION AND CONCLUSION

In studies conducted in various countries, it has been shown that during the pandemic period, admissions to pediatric emergency departments decreased, and the operations performed by pediatric surgery decreased.<sup>1,3,4</sup> It has been argued that pediatric surgery



**Figure 3.** 3a: the appearance of the abdomen before the operation by inspection in the third case; 3b: MRI imaging; intra-abdominal mass extending from symphysis pubis to xiphoid process; 3c: The postoperative appearance of the mass, with a diameter of 30 cm semisolid mass.

has mostly turned into emergency surgery, elective cases are neglected, and the results are unknown. A study conducted in China argued that the operations performed during the pandemic period decreased by more than 50%. The reason for this was interpreted as the curfews imposed by the countries, the concerns of families to encounter the Covid-19 virus when they applied to the hospital, and the postponement of elective cases by healthcare professionals.<sup>5</sup> During the pandemic period, after the measures taken in our country, it was observed that the number of applications to the pediatric emergency department was decreased in our 3rd step hospital. In the early stages of the pandemic, the pediatric surgery service was closed and transformed into a Covid-19 service. Approximately three months after the start of the pandemic, pediatric surgery service was opened, and elective cases were started to be operated on again, but we still observe that the number of elective cases is lower than before the pandemic due to the low number of referrals to the outpatient clinic.

There is a delay in diagnosis in oncology patients. In most hospitals, the number of new pediatric oncology patients has decreased significantly compared to before the pandemic. In a study conducted in Turkey, the number of newly admitted pediatric oncology patients and oncological surgeries performed significantly decreased compared to before the pandemic. However, interestingly, no significant change was found when the delay in the presentation of pre-pandemic and pandemic oncological patients was compared. It was thought that there might be patients who have not been diagnosed as the reason for the decrease in admission and that they may be diagnosed in the future, or that admission to other hospitals may have increased. Considering the effect of delay in diagnosis on prognosis in oncology patients, it is recommended that these patients should not be overlooked and the society should be informed so that they do not turn into a disaster after Covid-19.<sup>6,7</sup> In a study conducted in Italy; it was argued that in the period of curfew, childhood solid tumors decreased by 45.7% compared to the previous years. It was argued that the Covid-19 pandemic caused a delay in the diagnosis of tumor cases that could be cured.<sup>8</sup>

As in the literature, late presentation in our cases during the pandemic period draws attention. Although Covid-19 has brought an additional burden to the health system. We made no delay in this process in tumors in our hospital. All the patients who applied were evaluated and treated as before the pandemic. However, our patients were diagnosed late because they attributed their tumor-related complaints to staying at home due to the pandemic and that their complaints were not important enough to go to the hospital during the pandemic period. Alt-

hough our patients started their treatment immediately after admission and underwent surgery, we lost our patient with adrenocortical carcinoma due to late admission. In our patient with dysgerminoma, pelvic metastasis was present at the time of diagnosis. Except for our case with borderline mucinous cystadenoma, the prognosis of our patients was adversely affected due to late admission.

In conclusion, the Covid-19 pandemic has affected not only patients with this disease but also the diagnosis and treatment of solid masses in children. Admissions to the hospital are delayed because families do not consider the possibility of their child having a disease as serious as Covid-19. Families should be informed that they should not hesitate to apply to the hospital with the fear of Covid-19 transmission, and they should be encouraged to apply to the hospital in their children's non-Covid-19 complaints.

**Ethics Committee Approval:** The patient/relatives have signed an informed consent/consent form, and the study was conducted following the international declaration, guidelines, etc.

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

**Author Contributions:** Concept-ZAY, Zİ; Supervision-Zİ; Materials-ZAY, ST; Data Collection and/or Processing-ZAY; Analysis and/or Interpretation-ZAY, ST; Writing-ZAY, Zİ.

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