



Effect of COVID-19 Pandemic on Anxiety in Rheumatology Patients Taking Immunosuppressive Drugs

İmmünsüpresif İlaç Kullanan Romatoloji Hastalarında COVID-19 Pandemisinin Anksiyete Üzerine Etkisi

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ABSTRACT

Objective: The purpose of this study was to determine the prevalence of anxiety due to Coronavirus disease-2019 (COVID-19) pandemic in patients with rheumatic and musculoskeletal diseases (RMDs) who used immunosuppressive drugs during the initial stage of the COVID-19 pandemic and to identify the risk and protective factors that cause anxiety.

Method: A total of 145 patients with RMDs who used regular immunosuppressive drugs and 95 healthy controls were included. An anonymous survey comprising questions regarding the COVID-19 pandemic was used, and the Beck anxiety inventory (BAI).

Results: About 42.1% patients reported that the epidemic caused concern due to the drug they were using, 33.8% rated their concerns as moderate and severe. According to the BAI scores, 16.5% patients had moderate to severe anxiety symptoms; and comparison of the groups showed that the anxiety level of the patient group was significantly higher (38.6% vs. 18.9%, $p=0.001$). Female had more anxiety symptoms in both groups ($p<0.005$). In addition, anxiety was lower in patients with higher education levels ($p=0.039$).

Conclusion: It should be ensured that patients in the high-risk group are not provided false information, the patients are individually informed, and they trust the treatment team. Providing online or smartphone-based psychoeducation and psychological interventions may be considered for these patients with high anxiety levels.

Keywords: anxiety, beck anxiety inventory, biologic drug, covid-19, immunosuppression, rheumatic and musculoskeletal diseases

ÖZ

Giriş: Bu çalışmanın amacı, Coronavirus hastalığı-2019 (COVID-19) salgınının ilk aşamasında romatizmal ve kas-iskelet sistemi hastalıkları (RMDs) olan ve immünsüpresif ilaç kullanan hastalarda COVID-19 salgınına bağlı anksiyete yaygınlığını tespit etmek ve anksiyeteye sebep olan risk ve koruyucu faktörleri tanımlamaktır.

Yöntem: 18 yaşından büyük, RMDs'i olan ve düzenli immünsüpresif ilaç kullanan 145 hasta ve 95 sağlıklı kontrol çalışmaya dahil edildi. COVID-19 salgını ile ilgili soruları içeren anonim bir anket ve katılımcıların anksiyete düzeylerini ölçmek için Beck anksiyete envanteri (BAI) kullanıldı. Demografik veriler, mevcut RMDs'i, kullandığı immünsüpresif ilaç, COVID-19 hakkında bilgi ve endişeler, COVID-19 hakkındaki bilgileri nereden öğrendiği gibi ek bilgiler toplandı.

Bulgular: Hastaların %42,1'i kullandıkları ilaç nedeniyle salgının endişe yarattığını bildirdi ve hastaların %33,8'i endişelerini orta ve şiddetli olarak derecelendirdiler. Hastaların BAI skorları 4 (0-52) ve sağlıklı kontrollerin BAI skorları 3 (0-18) olarak saptandı. BAI skorlarına göre hastaların %16,5'i orta ile şiddetli anksiyete belirtileri göstermiştir. İmmünsüpresif ilaç kullanan hastaların %38,6'sında anksiyete saptanırken kontrol grubunun %18,9'unda anksiyete mevcuttu. Gruplar karşılaştırıldığında hasta grubunun anksiyetesi anlamlı yüksek saptandı ($p=0.001$). Hasta ve kontrol gruplarında kadın cinsiyet daha fazla anksiyete belirtileri göstermektedir ($p<0.005$). Ayrıca hasta grubunda eğitim düzeyi yüksek olanlarda anksiyete daha düşük saptandı ($p=0.039$).

Sonuç: Kadın cinsiyet ve immünsüpresif ilaç kullanan hastalarda anksiyete düzeyleri daha yüksek saptanmıştır. Bu süreçte riskli grupta yer alan bu hastaların yanlış bilgilerden kaçınmasını sağlamalı, hastalar tek tek bilgilendirilerek tedavi ekibine güvenmeleri sağlanmalıdır. Anksiyeteleri yüksek olan bu hasta grubu için çevrimiçi veya akıllı telefon tabanlı psikoeğitim ve psikolojik müdahaleler sağlanması düşünülebilir.

Anahtar Kelimeler: anksiyete, Beck anksiyete envanteri, biyolojik ilaç, COVID-19, immünsüpresyon, romatizmal ve kas-iskelet sistemi hastalıkları

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) was first described in Wuhan, China in December 2019 due to severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) (1). Since then, the number of cases has been increasing exponentially, and the virus is spreading all over the world. COVID-19 was declared as a global health threat by the World Health Organization (WHO) on January 30, 2020, and it was recognized as a pandemic on March 11, 2020 (2,3). This pandemic is the largest outbreak of atypical pneumonia since the SARS in 2003. After the first outbreak, the total number of cases and deaths exceeded those of SARS. There is human-to-human transmission via respiratory droplets containing the virus. Patients with medical comorbidities are more likely to be infected and have worse prognosis (4). Mortality rate is estimated to be 5.7%, and this rate ranges between 0.3% and 0.6% (5,6). Since the beginning of the pandemic, strict measures have been undertaken for the prevention of infection all over the world. After the first case was detected in Turkey on March 11, 2020, these measures have increased. Social isolation has been emphasized due to the exponential increase in the number of infected cases as well as the increase in mortality rates.

During infection outbreaks, a wide range of psychosocial effects are observed in people, and people experience the fear of falling ill or the fear of death as well as the feelings of desperation (7). Anxiety is also a common negative feeling experienced by the entire population during pandemics (8). During the COVID-19 pandemic, WHO made a number of recommendations regarding mental health and psychosocial issues (9). Most studies on this pandemic have focused on determining the epidemiology and clinical characteristics of infected patients, genomic characterization of the virus, and challenges of global health management (4,10-12). During SARS and COVID-19 pandemics, studies were conducted to evaluate psychological responses of the general society (13). COVID-19 pandemic has become a stressful factor, especially because this new viral infection does not have any vaccine and can be treated only symptomatically.

The effect of anxiety caused by COVID-19 in patients with rheumatic musculoskeletal diseases (RMDs) who use immunosuppressive drugs is unknown. The European League Against Rheumatism (EULAR) has reported that patients who use immunosuppressive [e.g. biological drugs, JAK inhibitors (targeted synthetic disease modifier drugs-tsDMARD), and steroid and conventional DMARDs (csDMARDs like methotrexate, hydroxychloroquine)] drugs during the current pandemic of COVID-19 may have various issues as well as anxiety (14). However, there is no research on the psychological effect of COVID-19 in patients with RMDs who use immunosuppressive drugs. The purpose of this study is to determine the prevalence of anxiety due to COVID-19 pandemic in patients with RMDs who were using immunosuppressive drugs immediately after the first case of COVID-19 was reported in Turkey and WHO declared the pandemic and to identify the risk and protective factors that contribute to the anxiety.

MATERIALS AND METHODS

Participants

After 16 days of the first case of COVID-19 seen in Turkey at 11th of March, 2020, this study was started and patients who admitted to outpatient clinic at February 2020 was determined in hospital database. The study was approved by the local ethics committee and the Ministry of Health (Approval number: 2020/132). 45 patients aged ≥ 18 years with RMDs who were regularly using immunosuppressive drugs (biological drugs, tsDMARDs, and csDMARDs) and in remission under treatment were included. International remission criteria were used for related diseases. There was no patient under glucocorticoid treatment. Patients who did not visit outpatient clinic regularly, who did not take their medication regularly, who had active disease, who had cognitive deficit, who had difficulty understanding the questions, who did not volunteer to participate in the study, who used antidepressant drugs or depression and fibromyalgia history and who were < 18 years of age were excluded in the study. The patient group consisted of 26 familial Mediterranean fever (FMF), 33 rheumatoid arthritis (RA), 31 connective tissue disease (CTD), 25 spondyloarthritis (SpA), and 30 vasculitis, and

a total of 145 patients using immunosuppressive drugs. Further, 95 healthy individuals without a known chronic disease, depression and fibromyalgia history or regular drug use and similar to patient group were included in the control group.

Study Design

In this observational and cross-sectional clinical study, self-reported questionnaires were used. Previous studies on the psychological effects of SARS and influenza outbreaks were reviewed (15, 16). Accordingly, an anonymous survey was developed that included additional questions about the COVID-19 pandemic. The structured survey comprised questions covering several areas as follows: (1) demographic data; (2) information and concerns about COVID-19; (3) where the information about COVID-19 was obtained; (4) knowledge of current number of COVID-19 cases; (5) anxiety due to the immunosuppressive drugs used by the participant; and (6) diagnosis of COVID-19 in the participant or someone they knew. Anxiety was measured using a clinical survey and scoring system which was conducted the Turkish validity and reliability study by Ulusoy et al (17). The questionnaire was filled with the patients one to one and the data were collected. The questionnaire was filled anonymously by answering all questions by 145 patients and 95 healthy controls.

Demographic Data and Social Characteristics

The demographic data and social characteristics of the study participants included age, gender, education and marital status, and the number of children they had. The professional and business data included titles and information regarding the institutions they worked for. In addition, existing chronic diseases of patients and immunosuppressive drugs used were recorded.

Beck Anxiety Inventory (BAI)

The BAI was developed by Beck et al. to assess the degree of anxiety symptoms in an individual (18). BAI is a self-reporting questionnaire comprising 21 items; each item is rated between 0 and 3 points and gives a total score of 0 to 63 points.

The total score from the scale indicates the degree of anxiety of the individual. Those with BAI scores of 0-7, 8-15, 16-25, and 26-63 are classified to have “no anxiety symptoms,” “mild symptoms,” “medium symptoms”, and “severe symptoms,” respectively and were grouped into no anxiety symptoms (0–7 points) and the presence of anxiety symptoms (8–63 points) based on the BAI scores (18).

Statistical Analysis

The Statistical Package for Social Sciences version 22.0 software was used to evaluate the data. Descriptive statistical data are expressed as frequency (percentage), number and mean \pm standard deviation, or median (min-max). The distribution properties of the numeric variables were evaluated by Kolmogorov–Smirnov test. Independent-samples t-test was used for intergroup comparisons of numeric variables with normal distribution, and Mann–Whitney’s U test was used for variables without normal distribution. The estimates of the strengths of associations were demonstrated by the odds ratio (OR) with a 95% confidence interval (CI). Factors affecting anxiety were analyzed using the Backward LR selection method and Binary logistic regression analysis. Variables that were statistically significant as a result of univariate analyzes were included in the binary logistic regression analysis. Relationships between risk factors and outcomes are presented as odds ratios (ORs) and 95% CI. Categorical data were evaluated using chi-square test. A P-value of <0.05 was considered statistically significant.

RESULTS

A total of 240 individuals, including 145 patients and 95 healthy controls, meeting the study criteria were included in the study by filling the survey. Mean age of the patient and control groups were 40.41 ± 13.51 and 42.34 ± 10.07 years, respectively. No difference was observed between the groups in terms of age and gender ($p=0.209$ and $p=0.183$). No patient was diagnosed with COVID-19 in both groups. The demographic and clinical characteristics are shown in Table 1.

Study Parameters		Patient Group (n=145)		Control Group (n=95)	
		n	%	n	%
Gender	Female	85		47	
	Male	60		48	
Age, mean \pm standard deviation		40,41 \pm 13,51		42,34 \pm 10,07	
Marital status	Married	102	70.3	81	85.3
	Single	43	29.7	14	14.7
Status as a parent	Has	105	72.4	75	78.9
	No children	40	27.6	20	21.1
Number of children	0	40	27.6	20	21.1
	1	18	12.4	23	24.2
	2	44	30.3	38	40.0
	3	35	24.1	7	7.4
	>3	8	5.5	7	7.4
Educational attainment	Lower secondary school	77	53.1	24	25.3
	Upper secondary school	41	28.3	17	17.9
	University-Bachelors	27	18.6	34	35.8
	University- Masters/ Doctorate	-	-	20	21.1
Occupation	Officer	19	13.1	29	30.5
	Worker	34	23.4	11	11.6
	Manager	3	2.1	15	15.8
	Retired	17	11.7	18	18.9
	Student	17	11.7	1	1.1
	Unemployed	55	37.9	21	22.1
Working institution	Private sector	31	21.4	20	21.1
	Public	23	15.9	29	30.5
	Self-employment	5	3.4	6	6.3
	Retired	14	9.7	18	18.9
	Unemployed	72	49.7	22	23.2
Medication used	Anti TF	39	26.9	-	-
	Tocilizumab	6	4.1	-	-
	Tofacitinib	7	4.8	-	-
	Anti IL-1	26	17.9	-	-
	Cyclophosphamide	3	2.1	-	-
	Rituximab	2	1.4	-	-
	csDMARD	60	41.4	-	-
Anti IL-17	2	1.4	-	-	

RA: Rheumatoid Arthritis; SpA: Spondyloarthropathy; FMF: Familal Mediterranean fever; CTD: Connective Tissue Disease; COVID-19: Coronavirus disease 2019, Anti TNF: Anti tumor necrosis factor; Anti IL-1: Anti interleukin-1; Anti IL-17: Anti interleukin 17; csDMARD: Conventional Disease Modifying Anti-Rheumatic Drugs;

Overall, 76.6% patients reported that they were up-to-date with the current number of COVID-19 cases, and 63.4% reported that their knowledge levels about COVID-19 were intermediate. Patients stated that they learned COVID-19 information on television (82.8%) and the internet (13.1%); 42.1% reported that the pandemic caused concern due to the drug they used; and 33.8% rated their concerns as moderate and severe. Anxiety was found in 38.6% patients. The prevalence of anxiety in patients with RA, SpA, vasculitis, FMF, and connective tissue disease were 39.4%, 16%, 36.7%,

65.4%, and 35.5%, respectively. The BAI scores of the patients and healthy controls were 4 (0-52) and 3 (0-18), respectively. According to the BAI scores, 16.5% patients had moderate to severe anxiety symptoms. The concern levels and BAI scores of both groups are shown in Table 2.

Disease duration was median (min-max): 5 (0.5-40) years. There was no significant difference in the duration of illness between the group with anxiety and the patients without anxiety ($p = 0.450$).

Study Parameters		Patient Group (n=145)			Control Group (n=95)		P
		n	%	n	%		
COVID-19 case information	Yes	111	76.6	88	92.6	<0.001	
	No	34	23.4	7	7.4		
COVID-19 knowledge level	No knowledge	8	5.5	2	2.1	<0.001	
	Intermediate	92	63.4	39	41.1		
	Totally dominated	45	31.0	54	56.8		
The main source of COVID-19 information	Television	120	82.8	58	61.1	<0.001	
	Internet	19	13.1	26	27.4		
	Newspaper	4	2.8	11	11.6		
	No Information	2	1.4	-	-		
Does the medicine you use cause concern	Yes	61	42.1	-	-	N/A	
	No	72	49.7	-	-		
	Undecided	12	8.3	-	-		
How much do you worry about medication	No worries	79	54.5	-	-	N/A	
	Mild	17	11.7	-	-		
	Moderate	30	20.7	-	-		
	Severe	19	13.1	-	-		
Beck Anxiety Inventory score		median	min	max	median	-	0.039
		4	0	52	3	-	
Anxiety symptoms level	No anxiety symptoms	89	61.4	77	81.1	<0.001	
	Mild	32	22.1	17	17.9		
	Moderate	17	11.7	1	1.1		
	Severe	7	4.8	-	-		
Anxiety symptom status	No	89	61.4	77	81.1	0.001	
	Yes	56	38.6	18	18.9		

RA: Rheumatoid Arthritis; SpA: Spondyloarthropathy; FMF: Familial Mediterranean fever; CTD: Connective Tissue Disease; COVID-19: Coronavirus disease 2019.

Table 3: Comparison of Factors Affecting Anxiety in Patient and Control Groups															
		Patient Group						Control Group							
		Anxiety Status						Anxiety Status							
		Presence			Absence			p	Presence			Absence			p
		n	%		n	%			n	%		n	%		
Gender	Female	39	45.9		46	54.1	0.033	15	31.9		32	68.1	0.001		
	Male	17	28.3		43	71.7		3	6.3		45	93.8			
Age		median	min	max	median	min	max	0.480	median	min	max	median	min	max	0.890
		38	20	82	43	18	70		43	26	60	42	28	62	
Marital status	Married	38	37.3		64	62.7	0.603	17	21		64	79	0.294		
	Single	18	41.9		25	58.1		1	7.1		13	92.9			
Status as a parent	Has	38	36.2		67	63.8	0.330	14	18.7		61	81.3	1.00		
	No children	18	45		22	55		4	20		16	80			
Number of children	0	18	45		22	55	0.717	4	20		16	80	0.054		
	1	6	33.3		12	66.7		1	4.3		22	95.7			
	2	17	38.6		27	61.4		10	26.3		28	73.7			
	3	11	31.4		24	68.6		3	42.9		4	57.1			
	>3	4	50		4	50		0	0		7	100			
Educational attainment	Lower secondary school	31	40.3		46	59.7	0.039	9	37.5		15	62.5	0.053		
	Upper secondary school	20	48.8		21	51.2		2	11.8		15	88.2			
	University-Bachelors	5	18.5		22	81.5		3	8.8		31	91.2			
	University-Masters/Doctorate	-	5		-	-		4	20		16	80			
Occupation	Officer	5	26.3		14	73.7	0.505	4	13.8		25	86.2	0.240		
	Worker	13	38.2		21	61.8		2	18.2		9	81.8			
	Manager	0	0		3	100		1	6.7		14	93.3			
	Retired	7	41.2		10	58.8		4	22.2		14	77.8			
	Student	6	35.3		11	64.7		1	100		0	0			
	Unemployed	25	38.6		30	54.5		6	28.6		15	71.4			
Working institution	Private sector	12	38.7		19	61.3	0.730	1	5		19	95	0.140		
	Public	7	30.4		16	69.6		4	13.8		25	86.2			
	Self-employment	1	20		4	80		2	33.3		4	66.7			
	Retired	5	35.7		9	64.3		4	22.2		14	77.8			
	Unemployed	31	43.1		41	56.9		7	31.8		15	68.2			
COVID-19 case information	Yes	41	36.9		70	63.1	0.452	17	19.3		71	80.7	1.00		
	No	15	44.1		19	55.9		1	14.3		6	85.7			
Drug	Biologic drug + tsDMARD	38	44.7		47	55.3	0.073	-	-		-	-	-		
	csDMARD	18	30		42	70		-	-		-	-			
The main source of COVID-19 information	Television	47	39.2		73	60.8	0.361	14	24.6		43	75.4	0.231		
	Newspaper	0	0		4	100		1	10		9	90			
	Internet	8	42.1		11	57.9		3	10.7		25	89.3			

RA: Rheumatoid Arthritis; SpA: Spondyloarthritis; FMF: Familial Mediterranean fever; CTD: Connective Tissue Disease; COVID-19: Coronavirus disease 2019, csDMARD: Conventional Disease Modifying Anti-Rheumatic Drugs; tsDMARD: Targeted Synthetic Disease Modifying Anti-Rheumatic Drugs

Both groups were evaluated in terms of the factors affecting anxiety states within the groups. Upon examining the affecting factors such as gender, age, marital status, number of children, occupation, institution, biological medicine used, and DMARDs, female were found to have more anxiety symptoms in both the groups. In addition, anxiety symptoms was lower in patients with higher education levels ($p=0.039$). When comparing COVID-19 knowledge in terms of communication tools and occupational groups between the two groups, no significant difference was observed. Factors affecting anxiety in both groups are shown in Table 3.

Multivariate logistic regression analysis includes the level of education and gender factor found significant in univariate analysis. In this analysis, it was determined that male gender (OR = 0.460, 95% CI = 0.221 – 0.958, $p = 0.038$) and university graduation (OR = 0.234, 95% CI = 0.073 – 0.749, $p = 0.014$) are protective factors for anxiety in the patient group (Table 4).

Covariate	OR (95% CI)	p
Gender (Male)	0.460(0.221 – 0.958)	0.035
University graduation	0.234(0.073 – 0.749)	0.014

A total of 38.6% patients taking immunosuppressive drugs had anxiety and 18.9% in the control group had anxiety. Compared to the control group, anxiety in the patient group was significantly higher ($p=0.001$). Although there was no significant difference in the anxiety levels and anxiety conditions of patients receiving biological drugs + tsDMARDs and csDMARDs as immunosuppressive drugs, patients taking biological drugs + tsDMARDs had more anxiety ($p>0.05$) (Table 5).

Table 5: Comparison of csDMARD Group and Biologic Drug + tsDMARD Group

		csDMARD		Biologic Drug + tsDMARD		P
		n	%	n	%	
Anxiety Level	No anxiety	42	47.2	47	52.8	0.056
	Mild	13	40.6	19	59.4	
	Moderate	5	8.3	12	70.6	
	Severe	-	-	7	100	
Anxiety	Yes	18	32.1	38	67.9	0.073
	No	42	47.2	47	52.8	

csDMARD: Conventional Disease Modifying Anti-Rheumatic Drugs; tsDMARD: Targeted Synthetic Disease Modifying Anti-Rheumatic Drugs

DISCUSSION

In this study, the prevalence of anxiety caused by COVID-19 pandemic and the risk and protective factors contributing to psychological stress in patients with RMDs who were using immunosuppressive drugs were investigated. Female sex was a risk factor for anxiety in the patients taking immunosuppressive drugs as well as in the control group. In addition, anxiety levels of patients who took immunosuppressive drugs were significantly higher than the control group, whereas anxiety was lower in those with higher education levels. Based on the BAI scores, 16.5% patients showed moderate to severe anxiety symptoms.

COVID-2019 is a pandemic and pandemics have various psychological effects on humans, including anxiety (19). During the influenza epidemic (influenza A H1N1v), approximately 10% and 30% of the population had high or severe anxiety (15). In a study conducted on the general population on the COVID-19 pandemic in China, 53.8% participants rated the psychological effect of the pandemic as moderate or severe, and 28.8% reported moderate to severe anxiety symptoms (13).

Sensational popular media titles, lack of information, and incorrect information have shown to increase the health concerns and phobias (20). Television (82.8%) and the Internet (13.1%) were the primary information channels during the initial stage of the COVID-19 pandemic. Most participants (76.6%) were aware about the number of cases, advice on prevention, and warnings for those with chronic diseases. However, it is believed that this information, the accuracy of which is controversial, can lead to an increase in patient anxiety levels.

A guideline has stated that it is important to medically and psychologically prepare the health systems and general public if widespread transmission occurs during a pandemic (21), and it is recommended to identify high-risk groups based on the sociodemographic information for early psychological intervention (13). The sociodemographic data in this study have shown that women who take immunosuppressive drugs have a higher level of anxiety. This result supports the extensive epidemiological studies reporting that women are at a higher risk of anxiety (22,23).

In a study conducted on the general population in China, it was found that students experienced a higher level of anxiety and psychological impact due to the pandemic (13). Schools of all levels have been indefinitely closed in Turkey as well as the rest of the world. In this study, there were no significant differences in terms of anxiety based on occupational groups including students. During pandemics, educational authorities should develop online portals and web-based applications for courses and other teaching activities (24). Although schools are closed in Turkey, many teaching activities continue online. As the younger population is more familiar with smartphone applications (25), they are able to continue their education. It is believed that this may be the reason why high levels of anxiety have not been detected in the younger individuals.

A recent study in China found that the general population without formal education was more likely to be depressed during the pandemic (13). In another study that evaluated population-based psychological morbidity after the SARS epidemic,

there was a significant correlation between education level and psychiatric morbidity, and it was recommended to divide the population into sections based on the level of education to increase crisis communication (8). In this study, anxiety was lower in those with higher education levels. Therefore, it may be recommended to provide audio-visual information with simple language, when required, to support patients based on their education levels during the pandemic.

In this study, anxiety was found in 38.6% patients. The prevalence of anxiety in patients with RA, SpA, vasculitis, FMF, and connective tissue disease were 39.4%, 16%, 36.7%, 65.4%, and 35.5%, respectively. A study that evaluated anxiety disorder in patients with rheumatic disease, anxiety was reported in 44.4% patients. The prevalence of anxiety in patients with RA, primary Sjögren syndrome, systemic lupus erythematosus, and Behçet syndrome were reported to be 52%, 50%, 41%, and 38%, respectively (26). The prevalence of anxiety in the SpA group was similar to the previous study (27), whereas the prevalence of anxiety in the FMF patient group was higher than the other groups. This suggests that FMF patient group may have been more affected by social isolation caused by the quarantine process due to younger age and being more active. Similarly, in studies that compared patients with inflammatory rheumatic diseases with healthy controls, anxiety was higher in the patient group (28-30).

In this study, the prevalence of anxiety was 18.9% in the control group, and there was a significant difference in anxiety levels between the patient and controls groups. In pre-pandemic studies, the prevalence of anxiety in healthy controls is significantly lower than that found in this study (6.6%-9.6%) (28,29). Although the control group had increased anxiety levels, the difference was significant, suggesting that our patients had high anxiety. It may be recommended that health authorities consider providing online or smartphone-based psychoeducation and psychological interventions to reduce the risk of virus infection via face-to-face treatment. In addition, they should be informed individually by

the clinic where they are followed, and it should be ensured that they trust the treatment team.

This study has several limitations. Given the inability to meet face-to-face and time sensitivity of the COVID-19 pandemic, data were collected by contacting patients on the phone. The reported anxiety levels may not always correspond to the assessment by mental health professionals. Similarly, patients may have given socially desirable responses regarding their anxiety levels. Other limitations are that each patient does not use the same immunosuppressive drugs and the control group consists of healthy individuals rather than rheumatological diseases that do not use drugs. Finally, a patient was diagnosed with COVID-19 and had no relatives around her/him. Therefore, surveys may have been conducted early. Despite the above limitations, this study, which was conducted on patients with inflammatory RMDs who were using immunosuppressive drugs 2 weeks after the appearance of COVID-19 in Turkey, was considered to be the first that evaluated the effects of pandemic on anxiety. As the COVID-19 pandemic continues to spread, our results are expected to provide recommendations on the development of psychological support for patients in the risk group who are taking immunosuppressive drugs and in priority areas in Turkey and in other countries affected by the pandemic.

Conclusion

This observational cross-sectional study evaluated anxiety caused by immunosuppressive drugs used by patients diagnosed with RMDs during the COVID-19 pandemic in Turkey. Neither the participants nor their relatives encountered COVID-19 infection; however, a high level of anxiety was found in patients. Anxiety in female patients and patients who were using immunosuppressive drugs was higher. In this process, it should be ensured that these patients in the high-risk group are not provided false information, the patients are informed individually, and they trust the treatment team. If the anxiety of the patients cannot be controlled, it may cause them to discontinue their medication and exacerbate

their existing rheumatological diseases. Providing online or smartphone-based psychoeducation and psychological interventions may be considered for these patients with high anxiety.

Learning Points

- Covid-19 pandemic increases the anxiety of healthy people and patients with RMDs using immunosuppressive drugs.
- Female patients have higher anxiety.
- Male gender and being a university graduate were found to be protective factors for anxiety.

Conflict of Interest

No conflict of interest.

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Ethics Committee Approval

This study was conducted in accordance with the Helsinki Declaration. All participants were informed and their consent was obtained. The study was approved by the local ethics committee and the Ministry of Health (Approval number: 2020/132).

Contributions

Concept and design: TID, SBA, CG, AU, GY, MO. material preparation and data collection: TID, SBA, CG, AU, GY., analysis: TID, SBA. writing: TID, SBA, CG, AU, GY MO.

Consent for publication

Written informed consent for the publication of the data and details relating to the participants has been obtained from the participants.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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