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ARAŞTIRMA / RESEARCH

Evaluation of COVID-19 clinical features and outcomes in individuals with rheumatic disease

Romatizmal hastalığı olan bireylerde COVID-19 klinik özelliklerinin ve sonuçlarının değerlendirilmesi

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Abstract

Purpose: The aim of this study was to evaluate the clinical features and course of coronavirus disease 2019 (COVID-19) in individuals with rheumatic disease.

Materials and Methods: This retrospective study was carried out at the Erciyes University rheumatology outpatient clinic from July 1 to August 1, 2021. The demographic and clinical data and summarized COVID-19 history, clinical course of COVID-19, fatigue, and pain levels of patients with rheumatic disease were obtained from our institutional electronic registration database and patient files.

Results: Recruited participants were 106 individuals (83% female, %17 male) with rheumatic disease who had been confirmed by laboratory tests to have COVID-19 and recovered from the COVID-19 infection. Their mean age and body mass index (BMI) were 48.69±11.5 years and 29.89±6.76 kg/m², respectively. Additionally, 21 (19.8%) had been hospitalized, and five (4.7%) had been admitted to the intensive care unit. The most common rheumatic diseases were axial spondyloarthritis (40; 37.7%) and rheumatoid arthritis (26 cases; 24.5%). Patients who received conventional synthetic disease-modifying drugs (csDMARDs) reportedly experienced more pain, fatigue, and headaches than those in the biologic agent and non-steroidal anti-inflammatory drug (NSAID) groups.

Conclusion: Our study results reveal similar symptoms and hospitalization rates among patients with rheumatic disease who recovered from COVID-19 and received either csDMARDs, biologic agents, or NSAIDs. However, patients in the csDMARD group reported more pain, fatigue, and headache compared to the other groups.

Keywords:. Coronavirus, COVID-19, rheumatic disease, autoimmune.

Öz

Amaç: Bu çalışmanın amacı romatizmal hastalığı olan bireylerde koronavirüs hastalığı 2019'un (COVID-19) klinik özelliklerini ve seyrini değerlendirmektir.

Gereç ve Yöntem: Bu retrospektif çalışma, 1 Temmuz-1 Ağustos 2021 tarihleri arasında Erciyes Üniversitesi Romatoloji polikliniğinde gerçekleştirildi. Hastaların demografik ve klinik verileri ile kısa COVID-19 öyküsü ve COVID-19'un klinik seyri, yorgunluk ve ağrı düzeyleri değerlendirildi. Romatizmal hastalığı olan ve COVID-19 geçirmiş olan hastaların verileri kurumsal elektronik kayıt veri tabanımızdan ve hasta dosyalarından elde edilmiştir.

Bulgular: Çalışmaya alınan katılımcılar arasında romatizmal hastalığı olan, laboratuvar testleri ile COVID-19 olduğu doğrulanan ve COVID-19 enfeksiyonundan iyileşmiş olan 106 kişi (%83 kadın, %17 erkek) yer aldı. Yaş ortalamaları 48,69±11,5 yıl ve vücut kitle indeksi (VKİ) 29,89±6,76 kg/m2 idi. Ayrıca 21'i (%19,8) hastaneye kaldırılmış ve beşi (%4,7) yoğun bakıma yatırılmıştı. En sık görülen romatizmal hastalıklar aksiyel spondiloartrit (40; %37.7) ve romatoid artrit (26 vaka; %24.5) idi. Konvansiyonel sentetik hastalık modifiye edici ilaçlar (csDMARD'lar) alan hastalar biyolojik ajan ve nonsteroidal antiinflamatuar ilaç (NSAID) gruplarına göre daha fazla ağrı, yorgunluk ve baş ağrısı yaşadıklarını bildirdi.

Sonuç: Çalışma sonuçlarımız, COVID-19'dan iyileşen ve csDMARD, biyolojik ajan veya NSAID alan romatizmal hastalığı olan hastalar arasında benzer semptomlar ve hastaneye yatış oranlarını ortaya koymaktadır. Ancak csDMARD grubundaki hastalar diğer gruplara göre daha fazla ağrı, yorgunluk ve baş ağrısı bildirdiler.

Anahtar kelimeler: Coronavirüs, COVID-19, romatizmal hastalık, otoimmün

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INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which is the source of the coronavirus disease 2019 (COVID-19) pandemic, initially prompted strong concerns among patients with rheumatic disease (autoimmune and/or inflammatory disease) and rheumatologists. Individuals with rheumatic disease who are receiving immunosuppressant treatment and have various comorbid diseases are significantly more vulnerable to infection[1,2]. In addition, some immunosuppressant treatments that are taken by individuals with rheumatic disease are also used for patients with severe COVID-19[3,4]. Thus, there has been increased attention toward individuals with rheumatic disease.

The clinical course of COVID-19 ranges from an asymptomatic or flu-like illness or mild upper respiratory tract disease to severe and fatal acute cytokine storm syndrome or SARS-CoV-2 [5]. Generally, the most common symptoms of COVID-19 are muscle and joint pain, cough, fever, weakness and fatigue, sore throat, nasal congestion, and chest pain[5,6]. Significant risk factors associated with COVID-19 are an age of over 65 years, chronic cardiovascular or respiratory disease, diabetes, obesity, and hypertension[7,8].

Evidence indicates that the risk of COVID-19 may be slightly higher among individuals with inflammatory rheumatic disease compared to the normal population[9]. Previous studies have observed more serious cases of COVID-19 in hospitalized patients with connective tissue disease who did not previously take immunosuppressants and with inflammatory arthritis who took steroids but not in patients who took cytokine inhibitors[10]. Furthermore, being over the age of 65 and having active rheumatic disease and comorbid disease might increase the risk of developing severe COVID-19[9]. These risk factors have been linked with severe pneumonia and admission to the hospital[1]. In this regard, the COVID-19 outcomes of individuals with rheumatic disease have remained concerning. The aim of present study is to investigate the clinical characteristics and outcomes of individuals with rheumatic disease who recovered from COVID-19.

MATERIALS AND METHODS

This study was executed retrospectively at the Erciyes University rheumatology outpatient clinic from July 1 to August 1, 2021, after the Clinical Research Ethics Committee of Erciyes University approved the study protocol (28.07.2021/526). Since the study was retrospective, informed consent was not obtained from the patients. The study was conducted in accordance with the principle of the Declaration of Helsinki.

Data collection

The research included patients above the age of 18 with rheumatic disease who had a follow-up after a COVID-19 infection confirmed by laboratory tests. Patients who did not have a positive, laboratory-confirmed COVID-19 test, were pregnant, or had coexisting malignancy, psychiatric and neurological disorder were excluded. File data of 110 patients were obtained in total, but 4 patients with missing clinical findings were excluded from the study and 106 were included in the study.

The research data were collected from both the electronic registration system and patient files. The data obtained from the electronic registration system include polymerase chain reaction (PCR) diagnostic test results, laboratory and imaging findings, summaries of medications, systemic comorbidities, antirheumatic treatments received at the time of before being infected with COVID-19, hospitalization, and intensive care data. The data sourced from the patient files, which were recorded during the first post-COVID-19 visit to the rheumatology outpatient clinic, included a brief history of the patient's COVID-19 disease, their first symptoms, their recovery, the drugs they received, certain COVID-19 symptoms, hospitalization, persistent complaints (symptoms that persist after the COVID-19 infection has healed. It can be seen in patients discharged from the hospital or in patients who have recovered from COVID-19), and demographic and clinical data. In addition, the unresolved complaints and levels of fatigue and pain of the patients during COVID-19 were recorded in the institutional electronic database recording system at their post-COVID-19 visits. The fatigue and pain levels were indicated by visual analogue scale (VAS) as rating between 1 to 10. Moreover COVID-19 disease duration, duration of post-COVID-19 visit to rheumatology outpatient clinic, and vaccination status were evaluated.

The patients were divided into three groups based on received treatment. Group A consisted of patients who received biologic disease-modifying antirheumatic drugs (bDMARDs), of whom were on adalimumab (subcutaneous, 40 mg every other week), etanercept (subcutaneous, 50 mg every week), infliximab (intravenously 3 mg/kg or 5 mg/kg every 6-8 weeks), certolizumab pegol (subcutaneous, 200 mg every other week), abatacept (weekly 125mg subcutaneous), anakinra (subcutaneous 100mg/day), secukinumab (150mg subcutaneously every 4 weeks), ustekinumab (90mg subcutaneously every 12 weeks), and golimumab (50mg subcutaneously every month), as well as who received the targeted synthetic (ts) DMARDs (tofacitinib oral 5mg twice daily). Group B contained patients who received conventional synthetic (cs) DMARDs, such as methotrexate (oral or subcutaneous 15mg every week), hydroxychloroquine (orally 200mg twice daily), sulfasalazine (orally 500mg twice daily), or leflunomide (orally 20 mg daily), and other immunosuppressive drugs (e.g., azathioprine 50mg twice daily, colchicine 0.5mg orally twice a day, low-dose steroids 5-7 mg prednisolone daily in combination therapy). Patients in group C were treated with nonsteroidal anti-inflammatory drugs (NSAIDs).

Statistical analysis

The study data were analyzed with the IBM SPSS statistics V26 package program. Whether the distribution of the data was normal or not was determined by the Shapiro–Wilk test. Comparisons of normally distributed more than two groups were conducted by one-way analysis of variance. The Kruskal–Wallis test was used in the comparisons of more than two groups that did not show normal distribution. The Mann–Whitney U test was used for pairwise comparison, and Bonferroni's correction was employed to adjust multiple comparisons. The adjusted critical significant p-value according to the Bonferroni correction was accepted as $p<0.017$ for the three groups. Categorical variables were compared by Pearson Chi-square test or Fisher's exact test and expressed in terms of frequency and percentage, while continuous variables were expressed as mean ± standard deviation and median and minimum-maximum. Spearman's rank correlation test was used for correlation between continuous data. The sample size of the study was calculated as 21 patients for each of patients group (the minimum significant clinical difference for pain variable between patient's groups calculated as 1.6, alpha error 0.05, beta error 0.80) and power was calculated as 0.80. A total of 106 patients were included in the study and it was sufficient according to the calculated sample size. A p-value of less than 0.05 was recognized as statistically significant.

RESULTS

A total of 106 individuals (88 female and 18 male) with rheumatic disease were included in this study. The mean age and BMI of the patients were 48.69±11.51 years and 29.89±6.76 kg/m^2, respectively (see Table 1). Among all patients, only 7 (6.6%) were vaccinated with one or 2 doses (see Table1). In order of prevalence, the rheumatic diseases were axial spondyloarthritis (ax-SpA) with 40 cases (37.7%), rheumatoid arthritis (RA) with 26 cases (24.5%), Sjogren's syndrome (SS) with 11 cases (10.4%), systemic lupus erythematosus (SLE) with six cases (5.7%), psoriatic arthritis (PsA) with six cases (5.7%), systemic scleroderma (SSC) with six cases (5.7%), Behçet's disease (BD) with five cases (4.7%), familial Mediterranean fever (FMF) with four cases (3.8%), and adult Still's disease (ASD) with two cases (1.9%), as illustrated in Table 2.

The most frequently reported first symptoms of COVID-19 in patients with rheumatic disease were arthralgia and myalgia (47; 44.3%), sore throat (21; 19.8%), and fatigue (11; 10.4%), while the most common unresolved complaints were arthralgia, fatigue, and back pain, respectively (see Table 2).

Tables 3 and 4 present the patients' demographic and clinical data based on the received medical treatment. Group A contained 24 (22.6%) patients, who received biologic agents of whom four were on adalimumab, four were on etanercept, five were on infliximab, three were on certolizumab pegol, three were on abatacept, and one each was on anakinra, secukinumab, ustekinumab, and golimumab, as well as one patient who received the tsDMARD (tofacitinib). Group B consisted of 59 (55.7%) patients, who received csDMARDs (46; 43.4%), colchicine (11; 10.4%), and azathioprine (2; 1.9%). Group C was comprised of 23 (21.7%) patients, who received NSAIDs.

Table 1. Demographic and clinical characteristics of patients with rheumatic diseases recovered from COVID-19.

Variable		
Age, years, (mean±SD)	48.69 ± 11.51	
BMI, kg/m² (mean±SD)	29.89±6.76	
RDD, years (mean±SD)	12.57±7.79	
	n	%
Gender/Female	88	83
Unvaccinated	99	93.4
Vaccinated (one or two doses)	7	6.6
Mild/moderate disease	85	80.2
Hospitalization	21	19.8
Needing O_2	17	16
ICU (severe disease)	5	4.7
Sepsis	2	1.9
Thrombosis	1	0.9
Arthralgia-myalgia	95	89.6
Sore throat	80	75.5
Cough	77	72.6
Headache	74	69.8
Anorexia	74	69.8
Sweating	72	67.9
Anosmia	68	64.2
Chest pain	64	60.4
Fever	59	55.7
Dyspnea	57	53.8
Abdominal pain	54	50.9
Diarrhea	44	41.5
Pneumonia	44	41.5
Comorbidities		
none	48	45.3
Diabetes	19	17.9
Hypertension	16	15.1
Cardiovascular disease	4	3.8
Thyroid disease	7	6.6
others	12	11.3

SD: Standard Deviation, Min-max: minimum-maximum, BMI: Body Mass Index, RDD: Rheumatic Disease Duration, ICU: Intensive care unit.

Table 2. Name of rheumatic diseases, first symptoms and unresolved complaints of COVID-19 in patients with rheumatic diseases

Rheumatic disease	**n**	**%**	**First Symptoms**	**n**	**%**	**Unresolved complaints**	**n**	**%**
Ax-SpA	40	37.5	Arthralgia-myalgia	47	44.3	Fatigue	17	16.0
RA	26	24.5	Sore throat	21	19.8	Arthralgia-myalgia	5	4.7
SJS	11	10.4	Fatigue	11	10.4	Back pain	4	3.8
SLE	6	5.7	Back pain	9	8.5	Dyspnea	3	2.8
SSC	6	5.7	Fever	4	3.8	Insomnia	3	2.8
PsA	6	5.7	Cough	5	4.7	Cough	2	1.9
BD	5	4.7	Headache	4	3.8	Headache	2	1.9
FMF	4	3.4	Nausea	3	2.8	Anosmia	2	1.9
ASD	2	1.9	Dyspnea	1	0.9	Poor mental	2	1.9
			Runny nose	1	0.9	Dysrhythmias	2	1.9

Ax-SpA: Axial Spondyloarthritis, RA: Rheumatoid arthritis, SJS: Sjogren's Syndrome, SLE: Systemic Lupus Erythematosus, SSC: Systemic Scleroderma, PsA Psoriatic Arthritis, BD: Behçet's Disease, FMF: Familial Mediterranean Fever, ASD: Adult Still's Disease

In terms of age, BMI, rheumatic disease duration, COVID-19 disease duration, post-COVID-19 visit duration, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), the three groups were similar (all p>0.05). However, there was a statistically significant difference between the three groups in VAS-pain and VAS-fatigue (p<0.007 and p<0.013, respectively). After performing the Bonferroni adjusted post-hoc analyses, there was a statistically significant higher pain level in group B compared to group C (p=0.022). Group B also had a higher pain level than group A, though this was not significant to statistically. Group A and group C had similar pain levels (p=0.053 and p>0.05, respectively). On the other hand, fatigue scores of the three groups were statistically significant (p=0.013). After conducting post-hoc analyses, VAS-fatigue was higher in group B than in group C to a statistically significant extent (p=0.012).

Table 3. Demographic and clinical characteristics of rheumatic disease patients with COVID-19

		Group A, n=24	**Group B, n=59**	**Group C, n=23**	**p**
Age, years	Mean±SD	47.21±13.93	50.19±10.93	46.39±10.06	0.291§
BMI, kg/m^2	Mean±SD	28.91±5.69	30.81±7.68	28.54±4.83	0.286¶
	Median (Min-max)	29 (15.-38)	29 (19-55)	28 (19-41)	
CDD, days	Mean±SD	9.42±2.93	9.85±4.49	11.57±4.46	0.127¶
	Median (Min-max	7.5 (7-15)	10 (3-30)	12 (3-20)	
PCVD, months	Mean±SD	4.23±2.27	5.17±3.07	5.46±2.15	0.172¶
	Median (Min-max	4.25 (1-9)	6 (1-11)	6 (1-8)	
RDD, years	Mean±SD	13.08±7.92	13.08±7.83	10.70±7.61	0.389¶
	Median (Min-max)	10.5 (5-40)	10 (1-35)	10 (1-30)	
VAS-p	Mean±SD	6.50±1.96	5.37±1.97	6.57±1.38	**0.007¶**
	Median (Min-max)	6.5 (3-10)	5 (1-10)	7 (4-9)	
VAS-f	Mean±SD	6.08±2.13	5.19±2.22	6.61±1.59	**0.013¶**
	Median (Min-max)	6(3-10)	5(1-10)	6(3-10)	
ESR, mm/h	Mean±SD	16.47±14.74	16.34±12.62	17.39±15.81	0.925¶
	Median (Min-max)	12.5 (2-59)	12 (2-55)	13 (2-62)	
CRP	Mean±SD	7.74±8.53	7.17±9.23	4.38±5.68	0.482¶
	Median (Min-max)	3.8 (0.11-29)	4.4 (0-48)	1.7 (0-22)	

Group A: Patients received biologic and targeted synthetic DMARDs.
Group B: Patients received conventional synthetic DMARDs and other immunosuppressive treatments.
Group C: Patients receive nonsteroidal anti-inflammatory drugs
SD: Standard Deviation, Min-max: minimum-maximum, BMI: Body Mass Index, CDD: COVID-19 Disease Duration, PCVD: Post-COVID-19 Visit Duration, RDD: Rheumatic Disease Duration, VAS-p: Visual analogue scale-pain, f: fatigue, ESR, mm/h: Erythrocyte sedimentation rate/ millimeters per hour, CRP:C-reactive protein.
VAS-p and VAS-f groups were compared by Kruskal Wallis test, and post-hoc Bonferroni correction implemented, p<0.05 accepted as statistically significant. §: One-Way Analysis of Variance (ANOVA), ¶: Kruskal-Wallis test.

Table 4. Demographic and clinical characteristics of rheumatic disease patients with COVID-19

	Group A, n=24	**Group B, n=59**	**Group C, n=23**	**p**
	N (%)	N (%)	N (%)	
Gender, female	15 (17)	52 (59.1)	21 (23.9)	**0.009****
Arthralgia-myalgia	19 (20)	54 (56.8)	22 (23.2)	0.139**
Fever	14 (23.7)	28(47.5)	17 (28.8)	0.091*
Sore throat	17 (21.3)	46 (57.5)	17 (21.3)	0.776*
Cough	15 (29.5)	44 (57.1)	18 (23.4)	0.423*
Dyspnea	11 (19.3)	33 (57.9)	13 (22.8)	0.674*
Chest pain	13 (20.3)	36 (56.3)	15 (23.4)	0.733*
Anosmia	15 (22.1)	35 (51.5)	18 (26.5)	0.270*
Headache	12 (16.2(	42 (62.2)	16 (21.6)	**0.042***
Abdominal pain	12 (22.2)	29 (53.7)	13 (24.1)	0.831*
Diarrhea	8 (18.2)	25 (56.8)	11(25.0)	0.590*
Anorexia	15 (20.3)	42 (56.8)	17 (23.0)	0.655*
Sweating	14 (19.4)	40 (55.6)	18 (25.0)	0.343*
Pneumonia	8 (18.2)	27 (61.4)	9 (20.5)	0.562*
Hospitalization	2 (9.5)	13 (61.9)	6 (28.6)	0.254**
Needing O_2	2 (11.8)	11 (64.7)	4 (23.5)	0.500**
ICU	1 (20.0)	3 (60.0)	1 (20.0)	0.980**
Chest CT scan	9 (14.5)	41 (66.1)	12 (19.4)	**0.039***
Chest x-ray	12 (18.5)	39 (60.0)	14 (21.5)	0.393*
Comorbities				
None	14 (28.6)	21 (42.9)	14 (28.6)	0.173**
DM	3 (16.7)	13 (72.2)	2 (11.1)	
HT and CVD	4 (18.2)	16 (72.7)	2 (9.1)	
Others	3 (17.6)	9 (55.7)	5 (21.7)	

ICU: Intensive Care Unit, CT: Computerized Tomography,
DM: Diabetes mellitus, HT: Hypertension, CVD: Cardiovascular disease, *: Pearson Chi-square test, **: Fisher's exact test.

Regarding female gender, chest CT imaging, and headache there was a statistically significant difference between the three groups (p=0.009, p=0.042, and p=0.039, respectively). Bonferroni's adjustment post-hoc pairwise comparisons were performed using an X^2 test and Fisher's exact test. There were statistically significant higher proportions of female patients, headache symptoms, and chest CT imaging in group A than in group B (p=0.022, p=0.035, and p=0.033, respectively). In terms of arthralgia, fever, sore throat, cough, dyspnea, chest pain, anosmia, abdominal pain, diarrhea, anorexia, sweating, pneumonia, hospitalization, need for O_2, need for ICU treatment, chest radiography, and comorbidities, the three groups of patients were similar (p>0.05). Of the patients who had been hospitalized in the ICU, three received csDMARDs, one received a biologic agent, and one received NSAID treatment. Moreover, three had RA, and two had ax-SpA. Of those patients, two had diabetes, one had CVH, and one had HT as a comorbid disease. Two of the patients were also 65 years of age or older. Only one patient in the entire study was a smoker. There were weak, positive correlations between age and BMI (r=0.240, p=0.013) between age and ESR (r=0.272, p<0.005), a moderate, positive, significant correlation between age and disease duration (r=0.435, p<0.001), and weak positive correlations between BMI and ESR (r=0.342, P<0.001) and between BMI and CRP (r=0.332, p<0.001). A strong, positive, and significant correlation was found between VAS-pain and VAS-fatigue (r=0.866, p<0.001), whereas the correlation among ESR and CRP was average, and positive (r=0.454, p<0.001).

Table 5. Spearman correlation of continuous variables of patients with rheumatic diseases who recovered from COVID-19.

	Age	BMI	RDD	VAS-p	VAS-f	ESR	CRP
Age	1						
rho		0.240*	0.435**	0.040	0.077	0.272**	0.187
p		0.013	0.001	0.687	0.433	0.005	0.055
BMI							
rho	0.240*	1	0.079	0.083	0.105	0.342**	0.332**
p	0.013		0.422	0.395	0.286	0.001	0.001
RDD							
rho	0.435**	0.079	1	-0.019	-0.021	-0.040	0.077
p	0.001	0.422		0.847	0.830	0.685	0.430
VAS-p							
rho	0.040	0.083	-0.019	1	0.866**	0.174	0.147
p	0.687	0.395	0.847		0.001	0.074	0.133
VAS-f							
rho	0.077	0.105	-0.021	0.866**	1	0.149	0.115
p	0.433	0.286	0.830	0.001		0.127	0.239
ESR							
rho	0.272**	0.342**	-0.040	0.174	0.149	1	0.454**
p	0.005	0.001	0.685	0.074	0.127		0.001
CRP							
rho	0.187	0.332**	0.077	0.147	0.115	0.454**	1
p	0.055	0.001	0.430	0.133	0.239	0.001	

Correlation is significant at the 0.01 level (2-tailed). **
Correlation is significant at the 0.05 level (2-tailed). *
BMI: Body Mass Index, RDD: Rheumatic Disease Duration, VAS-p: Visual analogue scale-pain, f: fatigue, ESR, mm/h: Erythrocyte sedimentation rate/ millimeters per hour, CRP:C-reactive protein.

DISCUSSION

In this retrospective study of patients with rheumatic disease (autoimmune and/or inflammatory) who recovered from COVID-19, more patients received csDMARD therapy than biologic agent or NSAID therapies. A high proportion of the patients were female. The hospitalization rate was 19.8%, and five patients were admitted to the ICU for severe COVID-19. Comorbidities were detected in more than half of patients. The most prevalent rheumatic diseases were ax-SpA and RA. The most common symptoms of COVID-19 were arthralgia and myalgia, followed by sore throat, cough, and headache. The most frequently unresolved complaints were fatigue and arthralgia. The group who received csDMARDs and other immunosuppressant treatment reported higher pain levels and fatigue scores and more headache symptoms. Moreover, they exhibited a higher rate of chest CT scans. Also, this study reveals a significant association among VAS-pain and VAS-fatigue in patients with rheumatic disease with COVID-19.

In the light of the information we have obtained, this study is the first comprehensive, a single center study in our country in patients with rheumatic disease who recovered from COVID-19 according to the course and clinical signs and symptoms of COVID-19.

In this study, the majority of individuals were female. This result is consistent with previous studies[11] and the widely known fact that rheumatic disease is naturally more prevalent in females than in males[12]. Furthermore, the common COVID-19 symptoms of patients and the most frequent comorbidities were similar to those noted in previous studies[11,13-15].

Prior studies of patients with rheumatic disease and COVID-19 have reported that the use of DMARDs and NSAIDs was not associated with severe COVID-19 or hospitalization[16], and the use of DMARDs, steroids, and biologic agents did not contribute to mortality [17]. Our study reveals similar results between the csDMARD, biologic agent, and NSAID groups in terms of hospitalization rate, which is associated with serious COVID-19. Although age is a strong risk factor for severe COVID-19 and poor outcomes, the mean age of the

study patients was below 65, which may be a reason for the similarity in hospitalization rates between the three groups of patients. Of the five (4.7%) patients who were admitted to the ICU, three had RA. Of those three patients, one received a biologic agent, and two received csDMARDs. The other two ICU patients had ax-SpA and received NSAIDs. Two ICU patients were above the age of 65 years and had diabetes mellitus (DM), and one had cardiovascular disease (CVD). The proportion of patients who required the ICU was comparable to that in existing research [18]. The treatment groups were also similar with respect to comorbidities, the most common of which were DM, HT, and CVD. These results are compatible with previous findings[8,19].

High levels of fatigue, pain, and headache during COVID-19 were more frequent in the csDMARDs group than in the other groups. In past research, headache at the onset of the disease was linked with elevated level of fatigue and headache frequency in the post-COVID-19 period[20]. In a study of COVID-19 patients with and without headaches, interleukin-10 levels were higher in those with a headache, which could be a counter-response to stronger cytokine secretion[21], and research evaluating the relationship between hand grip strength and fatigue and muscle-joint pain in patients with COVID-19 has suggested muscle involvement as the cause of these symptoms[22]. In addition, in a study assessing pain in hospitalized patients due to COVID-19, pain distribution ranged from muscle-joint pain, low back pain, and throat and chest pain to headache and abdominal pain, and pain was the most common complaint[23]. The relationship between pain and fatigue in our study was similar to the results of the study conducted by Murat et al. in patients with COVID-19[23].

The main persistent symptoms that did not improve were fatigue, arthralgia and myalgia, back pain, dyspnea, insomnia, headache, cough, anosmia, poor mental health, and dysrhythmia. Most of those symptoms are recognized as part of post-COVID-19 syndrome[24] or post-acute sequelae of SARS-CoV-2 infection[25]. These globally reported unresolved symptoms are considered part of long-term COVID.

There were some limitations to this study. Because of its retrospective nature, the available data were limited. The lack of a control group and the inclusion of only patients who recovered from COVID-19 were also limitations. Since the study included only patients who visited the rheumatology outpatient clinic for a normal follow-up visit and recovered from COVID-19, the mortality rates are not known.

In conclusion the study results showed that, based on the received treatment, the clinical course and symptoms of COVID-19 were similar between the csDMARD, biologic agent, and NSAID groups. In addition, individuals who received csDMARD therapy reported more pain, fatigue, and headache symptoms compared to the other two groups. Prospective and more comprehensive studies consisting of multicenter, homogeneous disease groups are needed to better understand the COVID-19 outcomes in patients with rheumatic disease.

Yazar Katkıları: Çalışma konsepti/Tasarımı: GC, SŞ; Veri toplama: GC, SŞ; Veri analizi ve yorumlama: GC; Yazı taslağı: GC; İçeriğin eleştirel incelenmesi: GC, SŞ; Son onay ve sorumluluk: GC, SŞ; Teknik ve malzeme desteği: SŞ; Süpervizyon: GC, SŞ; Fon sağlama (mevcut ise): yok.
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