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Evaluation of Predictors Associated with COVID-19 Pneumonia in Rheumatic Patients Using Biological or Targeted Therapies: Results from a Tertiary Center in Turkey

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Abstract

Aim: Disease-related immune dysfunction and/or treatment with immunosuppressive drugs may affect the course of coronavirus disease-2019 (COVID-19) infection in rheumatic patients. The aim of this study was to evaluate the course of COVID-19 infection and predictors of COVID-19 pneumonia in patients with rheumatological disease using biological or targeted therapies.

Methods: This cross-sectional study was conducted between April 2022 and July 12, 2022. Demographic and clinical parameters and COVID-19-related data in patients with and without COVID-19 pneumonia were recorded and compared. Logistic regression analyses were performed to identify the predictors of COVID-19-related pneumonia.

Results: A total of 110 patients (67 with spondyloarthritis, 25 with rheumatoid arthritis, 8 with familial Mediterranean fever, 5 with Takayasu arteritis, 3 with granulomatosis with polyangiitis, and 2 with Behçet's disease) were included in the study. The mean age of 110 rheumatic patients was 47.27±12.77 years. Their mean body mass index (BMI) was 29.59±5.59 kg/m^2, and 67.3% of them were female. Twenty-one (19.1%) patients had a history of COVID-19 pneumonia. The rates of hypertension (HT), diabetes mellitus, comorbidity status, comorbidity groups, cough, dyspnea, non-healing complaints, and COVID-19 treatment in addition to BMI, the total number of comorbidities, and the number of vaccines after COVID-19 infection were statistically different in the groups with and without pneumonia (for all, p<0.05). In logistic regression analyses, we found that BMI (OR: 1,113, p=0.040), HT (OR: 2,658, p=0.041), cough (OR: 4,982, p=0.029), and dyspnea (OR: 3,979, p=0.046) were the most important predictors associated with COVID-19 pneumonia.

Conclusion: Comorbidities such as HT and obesity pose an independent risk of COVID-19-related pneumonia in rheumatic patients using biological or targeted therapies. Furthermore, coughing and dyspnea in these patients may indicate COVID-19 pneumonia.

Keywords: Biologics, COVID-19, pneumonia, rheumatic diseases

Introduction

Coronavirus disease-2019 (COVID-19), the pathogen of which is severe acute respiratory syndrome-Coronavirus-2, emerged in Wuhan, China, in December 2019 (1). After the exponential increase in the number of cases and the porting of cases from other countries, the World Health Organization declared COVID-19 a pandemic on March 11, 2020 (2). Symptoms of COVID-19 usually appear within two weeks and have a spectrum that can range from asymptomatic to severe pneumonia. Fever, sore throat, cough, vomiting, diarrhea, and loss of taste and smell are frequently reported symptoms. Some infected individuals develop COVID-19 pneumonia and acute respiratory distress syndrome (ARDS), which is an undesirable and alarming situation (3,4). Individuals hospitalized with COVID-19-related pneumonia often require mechanical

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ventilation, and the elderly face an increased risk of mortality (5). In a nationwide study in Turkey, the mortality rate was reported as 4.5%, and older age, male gender, the presence of malignancy, interstitial lung disease, severe disease, or sepsis at first admission were defined as predictors of increased mortality (6).

Coronavirus disease-2019 infections can trigger an autoimmune rheumatic disease or unmask an existing but undiagnosed rheumatic disease (7). However, it has been reported that both the immune dysfunction inherent in the disease and the disease-modifying antirheumatic drugs (DMARDs) used in the treatment may affect the course of COVID-19 infection in rheumatic patients (8). In a study examining individuals with autoimmune rheumatic disease, it was determined that older age, comorbidities such as hypertension (HT) and malignancy, and delayed diagnosis of COVID-19 were the most important risk factors for hospitalization (9). In another study, the relationships between hospitalization, chest computed tomography (CT) pneumonia severity score, medications (non-steroidal anti-inflammatory drugs and prednisolone), and some comorbid conditions [diabetes mellitus (DM) and pulmonary disease] were noted in rheumatological diseases (10). Furthermore, high levels of cytokines, such as interleukin (IL)-6 and tumor necrosis factor (TNF), were found in severe COVID-19 patients. Anticytokine therapies [e.g., IL-6 inhibitors, IL-1 inhibitors, and Janus kinase (JAK) inhibitors] were effectively used in these patients based on this mechanism. Contrary to concerns in the first months of the pandemic, the use of biological DMARDs (bDMARDs) was not associated with serious disease in rheumatic patients and had a disease course similar to that of the general population. Indeed, it has been suggested that IL-6 inhibitors may have a protective effect (11-13).

We hypothesized that COVID-19 may increase both the risk of infection and the severity of the COVID-19 course in rheumatic patients under biological or targeted DMARD therapies. Although the effect of various treatments used in rheumatic diseases during the course of COVID-19 infection has been examined (14), we planned this study considering that race and ethnicity may have different effects.

Methods

Compliance with Ethical Standards

This cross-sectional study was conducted in the rheumatology department of the Erciyes University Faculty of Medicine Hospital, between April 2022 and July 2022, after the approval of the Erciyes University Faculty of Medicine Clinical Research Ethics Committee (date: 09.03.2022, approval no: 2022/205).

Study Design

Rheumatic patients [spondyloarthritis (SpA), rheumatoidarthritis (RA), familial Mediterranean fever (FMF), Takayasu arteritis, granulomatosis with polyangiitis, Behçet's disease] were included in the study. The flow chart according to the inclusion and exclusion criteria is shown in Figure 1. The patients met the diagnosis or classification criteria (15-20) of the disease that they had. The inclusion criteria were as follows: age ≥18 years, rheumatic patients with a history of COVID-19, those with COVID-19 real-time polymerase chain reaction (RT-PCR) test positivity, and those on bDMARD or targeted pentetic DMARD (tsDMARD) therapies for a rheumatologic diagnosis. Those younger than 18 years of age, uninfected with COVID-19, and not using bDMARD or tsDMARD therapies were excluded from the study.

Variables

Demographic characteristics (age, gender, height, and weight), clinical parameters (diagnosis, diagnosis duration, medications, smoking status, and comorbidities), and COVID-19-related data (dates of a positive COVID-19 PCR test, COVID-19 disease course, information about COVID-19 vaccination, and treatment details of COVID infection) of the patients were recorded. Then, the patients were divided into groups according to their status of having or not having COVID-19 pneumonia. The recorded data were compared between the two groups. Our study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from all patients.

Statistical Analysis

The normality of the distribution of the data was tested using the Shapiro-Wilk test. Descriptive statistics for numerical variables are expressed as mean ± standard deviation or median (minimum-maximum), whereas those for categorical variables are expressed as numbers and percentages. Between the two independent groups, the independent samples t-test was used to compare normally distributed data, and the Mann-Whitney U test was used for non-normally distributed data. Categorical variables were compared using the chi-square test. Logistic regression analysis (univariate and enter models) was also used to identify the predictors of COVID-19-related pneumonia. IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. All p-values <0.05 were considered statistically significant.

Results

The study was conducted with 110 patients (67 with SpA, 25 with RA, 8 with FMF, 5 with Takayasu arteritis, 3 with granulomatosis with polyangiitis, and 2 with Behçet's

disease) who met the inclusion criteria. The diagram is shown in Figure 2. The mean age of the patients was 47.27±12.77 years, and 67.3% of them were female, and their mean body mass index (BMI) was 29.59±5.59 kg/m^2. A total of 21 (19.1%) patients had a history of COVID-19 pneumonia. Other demographic and clinical data and the COVID-19 disease course of the patients are shown in Table 1. The first and subsequent symptoms of the COVID-19 infection are shown in Table 2.

Table 1. Demographic characteristics, clinical data, and the COVID-19 disease course of patients

Total number of patients, n	110
Age (years), mean ± SD	47.27±12.77
BMI (kg/m^2), mean ± SD	29.59±5.59
Gender, n (%)	
Female	74 (67.3)
Male	36 (32.7)
Disease duration, years, median (min.-max.)	10 (2-40)
Diseases, n (%)	
SpA	67 (60.9)
RA	25 (22.7)
Behçet and other vasculitis	10 (9.1)
FMF	8 (7.3)
DMARDs, n (%)	
TNF inhibitors	83 (75.5)
IL-1 inhibitors	10 (9.1)
IL-6 inhibitor	6 (5.5)
JAK inhibitors	5 (4.5)
Anti-CD20	3 (2.7)
Anti-CTLA4	2 (1.8)
IL-17 inhibitors	1 (0.9)
Smoking, n (%)	
No	93 (84.5)
Yes	17 (15.5)
HT, n (%)	
No	72 (65.5)
Yes	38 (34.5)
DM, n (%)	
No	82 (74.5)
Yes	28 (25.5)
Comorbidity status, n (%)	
No	48 (43.6)
Yes	62 (56.4)
Number of comorbidities, median (min.-max.)	1 (0-4)
Comorbidity diseases, n (%)	
<2	80 (72.7)
≥2	30 (27.3)
COVID-19 medication, n (%)	
No	25 (22.7)
Yes	85 (77.3)
Hospitalization, n (%)	
No	89 (80.9)
Yes	21 (19.1)
Pneumonia, n (%)	
No	89 (80.9)
Yes	21 (19.1)
Oxygen treatment, n (%)	
No	88 (80)
Yes	22 (20)
History of intensive care unit, n (%)	
No	107 (97.3)
Yes	3 (2.7)

SD: Standard deviation, BMI: Body mass index, min.: Minimum, max.: Maximum, SpA: Spondyloarthritis, RA: Rheumatoid arthritis, FMF: Familial Mediterranean fever, DMARDs: Disease-modifying antirheumatic drugs, TNF: Tumor necrosis factor, IL: Interleukin, JAK: Janus kinases, CTLA4: Cytotoxic T lymphocyte-associated antigen 4, HT: Hypertension, DM: Diabetes mellitus

Table 2. First and subsequent symptoms of COVID-19 infection

First symptoms n (%)		Subsequent symptoms n (%)
29 (26.3)	Arthralgia	80 (72.7)
27 (24.5)	Myalgia	80 (72.7)
16 (14.5)	Headache	72 (65.5)
7 (6.4)	Loss of taste and/or smell	69 (62.7)
23 (20.9)	Fever	62 (56.4)
18 (16.4)	Cough	61 (55.5)
9 (8.2)	Throat ache	53 (48.2)
4 (3.6)	Dyspnea	51 (46.4)
3 (2.7)	Anorexia	41 (37.3)
2 (1.8)	Sweating	40 (36.4)
–	Chest pain	38 (34.5)
2 (1.8)	Nausea	32 (29.1)
–	Eye redness	26 (23.6)
–	Diarrhea	22 (20)
1 (0.9)	Stuffy nose	20 (18.2)
2 (1.8)	Stomachache	16 (14.5)
2 (1.8)	Vomiting	15 (13.6)
–	Restlessness	5 (4.5)

COVID-19: Coronavirus disease-2019

When we recorded the data, 91.8% of the patients had been vaccinated at least once with the COVID-19 vaccine. The vaccine-related adverse effects and data related to COVID-19 vaccinations are presented in Table 3. We also compared the demographic and clinical parameters and COVID-19-related data according to the presence or absence of COVID-19-related pneumonia. The rates of HT, DM, comorbidity status, comorbidity groups, cough, dyspnea, non-healing complaints, and COVID-19 treatment in addition to BMI, the total number of comorbidities, and the number of vaccines after COVID-19 infection were statistically different between the two groups (for all, $p<0.05$) (Table 4). Using logistic regression analyses, we initially evaluated the potential factors affecting COVID-19-related pneumonia separately using a univariate model. In these analyses, BMI, HT, DM, the total number of comorbidities, comorbidity groups, cough, and dyspnea were determined to have significant effects (for all, $p<0.05$). The candidate predictors were then entered into the multiple models. After adjusting for the effects of age in the enter model, we found that BMI [Odds ratio (OR): 1,113 [confidence interval (CI): 1,005-1,233], p=0.040], HT [OR: 2,658 (CI: 1,053-12,355), p=0.041], cough [OR: 4,982 (CI: 1,177-21,090), p=0.029], and dyspnea [OR: 3,979 (CI: 1,022-12,301), p=0.046] were the most significant independent risk factors associated with pneumonia due to COVID-19 infection (Table 5).

Table 3. Data related to COVID-19 vaccination(s)

Variables	n (%)
COVID-19 vaccination	
No	9 (8.2)
Yes	101 (91.8)
Amount of COVID-19 vaccinations	
0	9 (8.2)
1	5 (4.5)
2	40 (36.4)
3	38 (34.5)
4	18 (16.4)
Vaccination before COVID-19 infection	
No	78 (70.9)
Yes	32 (29.1)
Amount of vaccinations before COVID-19 infection	
0	78 (70.9)
1	2 (1.8)
2	19 (17.3)
3	11 (10)
Type of COVID-19 vaccination	
None	9 (8.2)
Sinovac	29 (26.4)
BioNTech	37 (33.6)
Sinovac + BioNTech	35 (31.8)
Adverse effect status	
No	40 (36.4)
Yes	61 (55.5)
Adverse effects after vaccination	
Pain in the upper extremity	32 (31.7)
Malaise	13 (12.9)
Fever	12 (11.9)
Headache	10 (9.9)
Arthralgia	7 (6.9)
Myalgia	6 (5.9)
Flu-like symptoms	4 (4.0)
Chest pain	3 (3.0)
Increase in blood pressure	1 (1.0)
Vomiting	1 (1.0)
Diarrhea	1 (1.0)
Dyspnea	1 (1.0)

COVID-19: Coronavirus disease-2019

Discussion

This study showed that BMI, HT, cough, and dyspnea were the most important predictors associated with COVID-19 pneumonia in rheumatic patients receiving bDMARD or tsDMARD therapies. Moreover, the presence and number of comorbidities were higher in the group that developed pneumonia. Although the number of vaccines administered before COVID-19 infection was similar in the groups with and without pneumonia, the number of vaccines administered after COVID-19 pneumonia was significantly higher in the pneumonia group. These findings can be attributed to different COVID-19 variants. Coronavirus disease-2019 can affect various organs or systems, but respiratory system involvement is prominent. Symptoms due to a respiratory tract infection can range in severity from cough and sputum to ARDS and respiratory failure. It has been demonstrated that some abnormalities in pulmonary function tests persist in patients discharged after recovering from COVID-19 pneumonia (21).

Non-contrast CT has become an important imaging tool for diagnostic purposes in individuals with false-negative COVID-19 RT-PCR tests and for the prediction of disease prognosis and choice of treatment in patients diagnosed with COVID-19. Significant relationships have been determined between CT severity scores and the severity and course of COVID-19 (22). In the present study, pneumonia was determined at a 19.1% rate. In a systematic review, Shi et al. (23) drew attention to risk factors that increase mortality rates due to COVID-19 infection, such as advanced age, male gender, smoking, comorbidities, and dyspnea symptoms. Peters et al. (24)

Table 4. Comparison of demographic characteristics, clinical data, and COVID-19 data according to the presence or absence of COVID-19-related pneumonia

Pneumonia status variables	Without pneumonia (n=89)	Pneumonia (n=21)	p-value
Age (years), mean ± SD	46.44±12.85	51.50±10.50	0.114
BMI (kg/m^2), mean ± SD	28.93±4.90	33.02±6.28	0.002*
Gender, n (%)			0.478
Female	58 (65.2)	16 (76.2)	
Male	31 (34.8)	5 (23.8)	
Disease duration, years, median (min.-max.)	10 (2-30)	8 (2-40)	0.279
Diseases, n (%)			0.063
SpA	55 (61.8)	12 (57.1)	
RA	22 (24.7)	3 (14.3)	
Behcet and other vasculitis	5 (5.6)	5 (23.8)	
FMF	7 (7.9)	1 (4.8)	
Biologics			0.846
Anti-TNF	68 (76.4)	15 (71.4)	
Non-TNF	21 (23.6)	6 (28.6)	
Smoking, n (%)			0.116
No	73 (82.0)	20 (95.2)	
Yes	16 (18.0)	1 (4.8)	
HT, n (%)			0.030*
No	63 (70.8)	9 (42.9)	
Yes	26 (29.2)	12 (57.1)	
DM, n (%)			0.043*
No	70 (78.7)	12 (57.1)	
Yes	19 (21.3)	9 (42.9)	
Comorbidity status, n (%)			0.043*
No	43 (48.3)	5 (23.8)	
Yes	46 (51.7)	16 (76.2)	
Total number of comorbidities, median (min.-max.)	1 (0-4)	1 (0-3)	0.018*
Comorbid diseases, n (%)			0.021*
<2	69(77.5)	11(52.4)	
≥2	20(22.5)	10(47.6)	
Cough, n (%)			0.003*
No	46 (51.7)	3 (14.3)	
Yes	43 (48.3)	18 (85.7)	
Dyspnea, n (%)			0.014*
No	53 (59.6)	6 (28.6)	
Yes	36 (40.4)	15 (71.4)	
Vaccination before COVID-19 infection, n (%)			
No	62 (69.7)	16 (76.2)	
Yes	27 (30.3)	5 (23.8)	0.745
Total amount of COVID-19 vaccinations, median (min.-max.)	2 (0-4)	3 (2–4)	0.100
Amount of vaccinations before COVID-19 infection, median (min.-max.)	0 (0-3)	0 (0–3)	0.514
Amount of vaccinations after COVID-19 infection, median (min.-max.)	2 (0-4)	3 (0–4)	0.043*
Non-healing complaints, n (%)			0.028*
No	61 (68.5)	9 (42.9)	
Yes	28 (31.5)	12 (57.1)	
COVID-19 treatment, n (%)			0.003*
No	25 (28.1)	0 (0)	
Yes	64 (71.9)	21 (100)	

*P<0.05
SD: Standard deviation, BMI: Body mass index, min.: Minimum, max.: Maximum, TNF: Tumor necrosis factor, HT: Hypertension, DM: Diabetes mellitus

Table 5. Identification of predictor(s) associated with COVID-19 pneumonia								
Univariate analyses					**Enter model**			
	B	**95% CI**	**OR**	**value**	**B**	**95% CI**	**OR**	**value**
Age	0.032	0.992-1.075	1.032	0.117				
Male gender	-0.532	0.196-1.747	0.585	0.337				
BMI	0.127	1.041-1.237	1.135	0.004*	0.107	1.005-1.233	1.113	0.040*
HT (Yes/Ref. No)	1.173	1.215-8.587	3.231	0.019*	1.233	1.053-12.355	2.658	0.041*
DM (Yes/Ref. No)	1.016	1.014-7.526	2.763	0.047*				
Total number of comorbidities	0.524	1.050-2.716	1.689	0.031*				
Disease duration	-0.014	0.905-1.075	0.986	0.755				
Comorbid diseases (≥2/Ref. <2)	1.143	1.165-8.445	3.136	0.024*				
Number of COVID-19 vaccinations before infection	-0.158	0.532-1.370	0.854	0.512				
Cough (Yes/Ref. No)	1.859	1.765-23.341	6.419	0.005*	1.606	1.177-21.090	4.982	0.029*
Dyspnea (Yes/Ref. No)	1.303	1.305-10.383	3.681	0.014*	1.266	1.022-12.301	3.979	0.046*

*P<0.05
CI: Confidence interval, BMI: Body mass index, HT: Hypertension, Ref.: Reference, DM: Diabetes mellitus

showed that obesity significantly impacts COVID-19 mortality and that higher BMI values are associated with higher mortality rates in women than in men. Similarly, Cottini et al. (25) reported that obesity increases hospitalization and worsens the outcome of COVID-19. In another study examining the predictors of mortality in COVID-19 pneumonia, comorbidities also had a significant effect (26).

In our study, the factors associated with pneumonia, an involvement that affected the mortality of COVID-19, were as follows: comorbidities (especially HT), BMI, cough, and symptoms of dyspnea, which Shi et al. (23) correlated with mortality. Smoking rates, which have been emphasized for their importance to the prognosis of COVID-19, were low in our patient group. Looking at it in reverse, not smoking may be a factor in their survival. In one study, which is the first report on factors associated with COVID-19 pneumonia in Turkey, researchers found that in multivariate analysis, obesity, not being actively smoking, cough at first admission, and shortness of breath were determined as independent risk factors for the development of pneumonia. CRP, D-dimer, and ferritin values among 108 (26.1%) patients with a BMI >30 were high, and 60.9% of the patients had pneumonia (27). In this study, coughing, shortness of breath, and obesity were related to COVID-19 pneumonia. Laboratory parameters such as neutrophil/lymphocyte ratio and d-dimer levels can predict mortality (28). In this study, labaratory parameters during infection were not reached. No correlation was detected between smoking and COVID-19. In the present study, 15.5% of the study group smoked. Frequent hospital visits can encourage patients with rheumatic diseases to stop smoking. Similar to the general population, the relationship between severe COVID-19 and comorbidities has also been demonstrated in individuals with rheumatic disease (29). Fredi et al. (30) found that poor outcomes in rheumatic diseases were related to advanced age and accompanying comorbidities rather than the type of disease. In their case-control study, it was also noted that obesity and HT were higher in severe COVID-19 cases. Bakasis et al. (31) reported that the presence of underlying lung involvement, along with advanced age and comorbidities, is a risk factor for hospitalization due to COVID-19. In addition, a French rheumatic disease cohort (28) indicated that advanced age, obesity, male gender, and HT were associated with severe COVID-19. Consistent with the literature in the current study, comorbidities and their subgroups were higher in rheumatic patients with pneumonia than in those without pneumonia and showed significant effects in univariate regression analyses. Moreover, obesity and HT were independent risk factors associated with COVID-19-related pneumonia in the multiple regression model. Similar to the results of Fredi et al. (30), there was no difference between the groups with and without pneumonia in terms of disease subtypes. Dyspnea, a risk factor associated with hospitalization in previous studies (31), was significantly higher in the pneumonia group and was an independent risk factor for predicting pneumonia in the regression analysis. Conversely, age had no significant effect on pneumonia in our cohort.

This finding can be explained by the fact that the average age of the patients in our study was 47 years; that is, the majority were not elderly. In the present study, not age but obesity is a risk factor, similar to the literature. With the onset of the COVID-19 pandemic, it was thought that the biological treatments used in rheumatic diseases would lead to a serious COVID-19 infection due

to decreased immunity (30,31). However, in the cytokine storm associated with the pathological immune response in some individuals infected with COVID-19, biological therapies have become significant treatment options in subsequent periods (11). IL-6, IL-1, JAK, and TNF inhibitors, which are frequently prescribed for rheumatic diseases, have been used for this purpose (11,13). Santos et al. (11) reported that the use of biologics in rheumatologic diseases was typically not associated with poor outcomes in COVID-19 and that IL-6 inhibitors might even have a protective effect. Baslılar and Pehlivan (32) determined that COVID-19 patients treated with anti-TNF agents had mild clinical signs and a good disease prognosis. Contrary to these good results, several studies have emphasized the importance of the direct relationship between rituximab and severe COVID-19 (33,34). In our study, 94.6% of the patients used IL-6, IL-1, TNF, or JAK inhibitors. Only three patients underwent rituximab therapy. Although some of them had pneumonia, the high rate of treatment use associated with a good prognosis in our patients who recovered after the COVID-19 infection may be one of the factors that ensured their survival. Moreover, when we classified the patients' medications as anti-TNF and non-TNF treatments, we could not detect a significant difference between the groups with and without pneumonia. In a study from Turkey, it was reported that high-dose anakinra can be effective in COVID-19 (35). Biological and synthetic DMARDs can prevent a cyotokine storm and lead to a better prognosis. In addition, these results may be due to the young age of our cohort. 25 patients with systemic rheumatic diseases who received the COVID-19 vaccine have been shown to have better COVID-19 infection outcomes than those who did not (36). In our cohort, 91.8% of patients had at least one vaccination at the time of data collection, whereas this rate was only 29.1% during COVID-19 RT-PCR positivity. The number of vaccines administered after the COVID-19 infection was significantly higher in the group with pneumonia than in the group without pneumonia. This difference can be explained by the fact that, as Karlsson et al. (37) noted, people who believe that COVID-19 is a serious disease are more likely to get vaccinated. A study showed that the unvaccinated patients developed more severe forms compared with the vaccinated ones, and a higher proportion of them needed hospitalization (38).

As the vaccination rates increased, we detected a decrease in pneomonia. A recent meta-analysis suggests After COVID-19 mRNA vaccination, patients with autoimmune diseases had lower total antibody titers, IgG seroconversion, and local and systemic adverse events compared with healthy controls (39). In the present study, the most frequent side effect was pain in the upper extremity. Furthermore, healthy controls were not included in this study. In addition, total antibody titers and IgG seroconversion were not studied. The strength of this study is that, to the best of our knowledge, it is the first to consider only patients using biological therapy and to evaluate rheumatic patients who survived after a COVID-19 infection. Nevertheless, this study has some limitations. First, we excluded healthy controls or patients who died of COVID-19 while using biological therapy to compare our results. Second, the negative impact of rituximab could not be compared with treatments thought to positively impact COVID-19 prognosis in terms of pneumonia development. The main factor was that only three patients were using rituximab. In addition, the study was conducted in a heterogeneous group.

Conclusion

Our study demonstrated that comorbidities, especially BMI and HT, were the most important predictors associated with COVID-19 pneumonia in rheumatic patients receiving bDMARD or tsDMARD therapies. It was also found that new-onset cough and dyspnea in rheumatic patients using these therapies may serve as warning symptoms of COVID-19-related pneumonia for rheumatologists. However, we failed to find a relationship between the number of pre-infectional COVID-19 vaccines and pneumonia. A healthy diet, regular exercise program, cessation of smoking, and vaccination can be beneficial in preventing COVID-19.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Erciyes University Faculty of Medicine Clinical Research Ethics Committee (date: March 9, 2022, approval no: 2022/205).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Y.O.E., A.S.S., Concept: S.S., Design: S.S., Data Collection or Processing: Y.O.E., S.S., Analysis or Interpretation: H.K., A.S.S., Literature Search: Y.O.E., H.K., Writing: H.K.

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