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Original article

Investigating the clinical manifestations, severity and outcomes of COVID-19 among inpatients with rheumatic diseases: A retrospective cross-sectional study in Iran

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Abstract: Introduction — Patients with rheumatic diseases (RD) may be at an increased risk of developing severe symptoms of COVID-19. They are likely to have a wide range of manifestations and outcomes that can make it difficult to control the disease. The goal of this study was to investigate the clinical manifestations, severity, and outcomes of adult patients with RD hospitalized for COVID-19.
Methods — We conducted a retrospective cross-sectional study. Eligible rheumatology patients were confirmed by a rheumatologist in compliance with American College of Rheumatology (ACR) criteria and had COVID-19 confirmed by computed tomography (CT) scan or polymerase chain reaction (PCR) test. Information about their gender, age, and clinical manifestations of COVID-19, along with the variables pertaining to the outcomes of the patients, was collected. Descriptive statistics and Fisher's exact test were performed using IBM SPSS Statistics software.
Results — A total of 105 patients with RD and COVID-19 were included. Rheumatoid arthritis (RA) was the most common disease (86 patients). Most patients were female (75.2%). The mean age of the participants was 58.97±12.25 years. Myalgia/arthralgia was the predominant symptom of COVID-19 (77.1%), followed by shortness of breath, cough, and fever. Only platelet count exhibited a significant association with the type of RD ($p = 0.004$).
Conclusion — Common adverse outcomes included moderate severity based on CT grading, anemia, oxygen saturation levels (SpO2) below 90%, and severe CT-based grade of severity. The mortality rate was relatively high.

Keywords: COVID-19, inpatients, rheumatic diseases, outcomes.

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Introduction

Beginning in December 2019, an unprecedented virus spread rapidly throughout Wuhan and eventually around the world. The coronavirus disease 2019 (COVID-19) pandemic has put enormous strain on healthcare systems and still continues to pose a significant risk to all people [1]. As of April 12, 2023, there have been over 762 million confirmed cases of COVID-19, with over 6 million deaths [2]. Iran has experienced eight waves of COVID-19 so far [2], although future waves and seasonal outbreaks are expected worldwide. The disease is predicted to soon become endemic [3].

The trajectory of COVID-19 can vary greatly, from no symptoms to multiple organ failure, making it a diverse and unpredictable disease [3]. Symptoms of COVID-19 include fever, dry cough, rhinitis, asthenia, headache, and shortness of breath, but it can also lead to acute respiratory distress syndrome (ARDS), which can result in death. The main reported factors that increase the risk of mortality are diabetes, hypertension, chronic obstructive pulmonary disease, coronary artery disease, and chronic kidney disease [4].

Patients with rheumatic diseases (RD), especially those taking various immunosuppressive agents, such as corticosteroids and synthetic or disease-modifying antirheumatic drugs (DMARD), have been severely affected by the COVID-19 pandemic [5, 6]. It was reported that patients with RD have stopped taking biologics and DMARD due to concerns that these treatments may suppress their immune system and make them more susceptible to COVID-19 infection [7]. Thus, concerns about all aspects of the relationship between COVID-19 and chronic inflammatory RD have raised complex issues that need to be addressed adequately. Whether RD and their treatment increase the risk of intensive care unit (ICU) admission or death in infected patients is still unclear [4]. In addition, ensuring an optimal treatment strategy for the management of RD in the case of COVID-19 appears to be of fundamental importance for rheumatologists [4].

Studies show that patients with immune or inflammatory RD have a slightly higher risk of infection and poor medical outcomes, compared with the general population. Although part of this risk is related to comorbidities, there are also risks associated with high disease activity, as well as the use of glucocorticoids and DMARD [8].

Another study highlighted that elderly patients with RD and comorbidities were at a higher risk of hospitalization for COVID-19. Moreover, the use of conventional synthetic DMARD (csDMARD),

older age, and lung diseases were associated with an increased risk of COVID-19 pneumonia in this group [9].

Although numerous studies have been published on COVID-19 in patients with RD, there is still a paucity of data on the association between COVID-19 and RD. Previous meta-analyses have examined the potential risk of COVID-19 in patients with RD, but their results were inconsistent, and there is a lack of studies on the prevalence and severity of COVID-19 in this patient population [7]. That is why, we designed a study to examine the clinical manifestations, severity, and outcomes of COVID-19 in patients with RD to identify prognostic factors for adverse outcomes of COVID-19.

Material and Methods

This was a retrospective cross-sectional study. The study population consisted of all adult patients with RD who were hospitalized for COVID-19 at Vali-e-Asr Hospital in Zanjan, Iran, between February 2020 and May 2021.

Table 1. Distribution of patients by age and gender

Variable	*Female*	*Male*	*All*
	Number (%)/ Mean±SD		
Age, years	59.46±11.50	57.50±14.45	58.97±12.25
Gender	79 (75.24)	26 (24.76)	105 (100)
Myalgia/Arthralgia			
Yes	62 (78.5)	19 (73.1)	81 (77.1)
No	17 (21.5)	7 (26.9)	24 (22.9)
Shortness of breath			
Yes	56 (70.9)	19 (73.1)	75 (71.4)
No	23 (29.1)	7 (26.9)	30 (28.6)
Cough			
Yes	52 (65.8)	16 (61.5)	68 (64.8)
No	27 (34.2)	10 (38.5)	37 (35.2)
Fever			
Yes	36 (45.6)	14 (53.8)	50 (47.6)
No	43 (54.4)	12 (46.2)	55 (52.4)
Nausea			
Yes	30 (38.0)	6 (23.1)	36 (34.3)
No	49 (62.0)	20 (76.9)	69 (65.7)
Vomiting			
Yes	23 (29.1)	7 (26.9)	30 (28.6)
No	56 (70.9)	19 (73.1)	75 (71.4)
Loss of appetite			
Yes	22 (27.8)	8 (30.8)	30 (28.6)
No	57 (72.2)	18 (69.2)	75 (71.4)
Headache			
Yes	19 (24.1)	5 (19.2)	24 (22.9)
No	60 (75.9)	21 (80.8)	81 (77.1)
Dizziness			
Yes	14 (17.7)	4 (15.4)	18 (17.1)
No	65 (82.3)	22 (84.6)	87 (82.9)
Diarrhea			
Yes	11 (13.9)	5 (19.2)	16 (15.2)
No	68 (86.1)	21 (80.8)	89 (84.8)
Abdominal pain			
Yes	10 (12.7)	2 (7.7)	12 (11.4)
No	69 (87.3)	24 (92.3)	93 (88.6)
Chest pain			
Yes	8 (10.1)	2 (7.7)	10 (9.5)
No	71 (89.9)	24 (92.3)	95 (90.5)
Olfactory disorder			
Yes	2 (2.5)	2 (7.7)	4 (3.8)
No	77 (97.5)	24 (92.3)	101 (96.2)
Loss of/decreased consciousness			
Yes	3 (3.8)	1 (3.8)	4 (3.8)
No	76 (96.2)	25 (96.2)	101 (96.2)

The study protocol was reviewed and approved by the Ethics Committee of Zanjan University of Medical Sciences [IR.ZUMS.REC.1400.329]. Since we directly assessed patients' medical records that were not anonymized, written informed consent was obtained from all participants or their legal guardians, as appropriate. We adhered to the requirements of the Declaration of Helsinki.

Eligibility criteria

We included all adult (age ≥18 years) patients with RD confirmed by a rheumatologist based on the American College of Rheumatology (ACR) criteria who were hospitalized due to COVID-19 disease confirmed by chest computed tomography (CT) or a positive polymerase chain reaction (PCR) test.

The diagnosis of other chronic diseases unrelated to the RD (e.g., heart disease, lung disease, kidney disease), as well as diabetes mellitus or malignancies currently being treated, led to exclusion from the study. Patients discharged against physician recommendations or referred to other medical centers, along with patients with incomplete medical records, were also excluded from the study.

Examined variables

A checklist was used to collect data from the patients' medical records. Gender, age, and clinical manifestations of COVID-19 (e.g., fever, cough, shortness of breath, myalgia/arthralgia) were the independent variables. Pneumonia, oxygen saturation (SpO2) level on admission, acute cardiac injury (ACI), acute kidney injury (AKI), sepsis, venous thromboembolism (VTE), brain involvement, liver injury, secondary nonpulmonary infection, admission to the ICU, need for mechanical ventilation, length of hospitalization, RD flare, hematologic complications, Glasgow Coma Scale (GCS) score, mean arterial pressure (MAP), serum creatinine level, bilirubin level, platelet count, computed tomography severity score (CTSS), and mortality were the dependent variables. Sequential organ failure assessment (SOFA) criteria were used to define the severity of COVID-19, with a score of ≥2 considered severe.

ACI was defined as acute injury or stress to the heart muscle attributable to COVID-19. AKI was considered a sudden and rapid deterioration in kidney function that occurred as a complication of COVID-19. Brain involvement was specified as neurological effects and complications that may occur due to COVID-19 (e.g., encephalopathy, meningitis, encephalitis, and stroke). Liver injury was defined as liver damage or dysfunction that occurred as a result of COVID-19 (e.g., hepatitis, cholestasis, elevated liver enzymes). Secondary nonpulmonary infection was designated as infection in body parts other than the lungs as a consequence of the primary SARS-CoV-2 viral infection (e.g., sepsis, secondary bacterial infections, and secondary fungal infections).

To determine the CTSS, the extent of lung involvement was initially assessed using the CT severity grading system. The involvement of each lobe was assessed visually and classified as follows: a score of 1 pt for involvement of less than 5% of the area, 2 pts for involvement of 5% to 25%, 3 pts for involvement of more than 25% to 50%, 4 pts for involvement of more than 50% to 75%, and 5 pts for involvement of more than 75% of the lobe area. The CTSS was calculated by adding the individual scores for each of the five lobes based on the percentage of involvement of each lobe, yielding a total maximum possible score of 25 pts. As a result,

three severity grades were obtained: mild (<8 pts), moderate (9-15 pts), and severe (>15 pts) [10].

Statistical data processing

Data was analyzed using IBM SPSS Statistics software for Windows, version 26.0. (Armonk, NY, IBM Corp.). We reported descriptive statistics using mean ± standard deviation (SD) for normally distributed data and median (interquartile range) for non-normally distributed data. For categorical data, number (%) were used to report the results. To explore the normality of data distribution, Shapiro-Wilk's test was employed. Fisher's exact test was conducted to assess the relationship between the type of RD and outcome variables for categorical data. All graphs were generated using the R ggplot2 package. The statistical significance was assumed at $p<0.05$ (two-tailed tests) for all data.

Results

Of the 9,649 hospitalized patients with COVID-19, 138 were patients with RD. However, due to incomplete medical records, only records of 105 patients were evaluated and included in the study, of which 86 were diagnosed with rheumatoid arthritis (RA), 11 with systemic lupus erythematosus (SLE), 2 with spondyloarthritis (SA), 2 with systemic sclerosis (SS), 2 with Behçet's disease (BD), and 2 with sarcoidosis.

Overall, 79 (75.2%) patients were female and 26 (24.7%) were male. The mean age of the participants was 58.97±12.25 years (min=27 years, max = 84 years). The most common symptom of COVID-19 among patients was myalgia/arthralgia: N=81 (77.1%). Shortness of breath, cough, and fever were the most common symptoms after myalgia/arthralgia: they were detected in 75 (71.4%), 68 (64.8%), and 50 (47.6%) patients, respectively (*Table 1*, *Figure 1*).

The most common COVID-19 outcomes were moderate CT severity, anemia, SpO2 <90%, and severe CT severity grade observed in 50 (47.6%), 39 (37.1%), 39 (37.1%) and 37 (35.2%) patients, respectively (*Table 2*, *Figure 2*).

We performed Fisher's exact test to examine the association of outcome variables with the specific type of RD, as well as with their gender and age (68 patients were <65 years of age, while 37 study subjects were ≥65 years old).

The results of Fisher's exact test revealed a significant association between the gender of patients and liver injury ($p=0.046$), hematologic complications ($p=0.039$), and plasma bilirubin level ($p=0.009$). No statistically significant association was observed between the remaining variables and the gender of patients ($p\geq0.05$) (*Table 1*).

As for liver injury, it seems that men showed a higher tendency to experience liver injury vs. women. On the other hand, females were more likely to avoid liver injury.

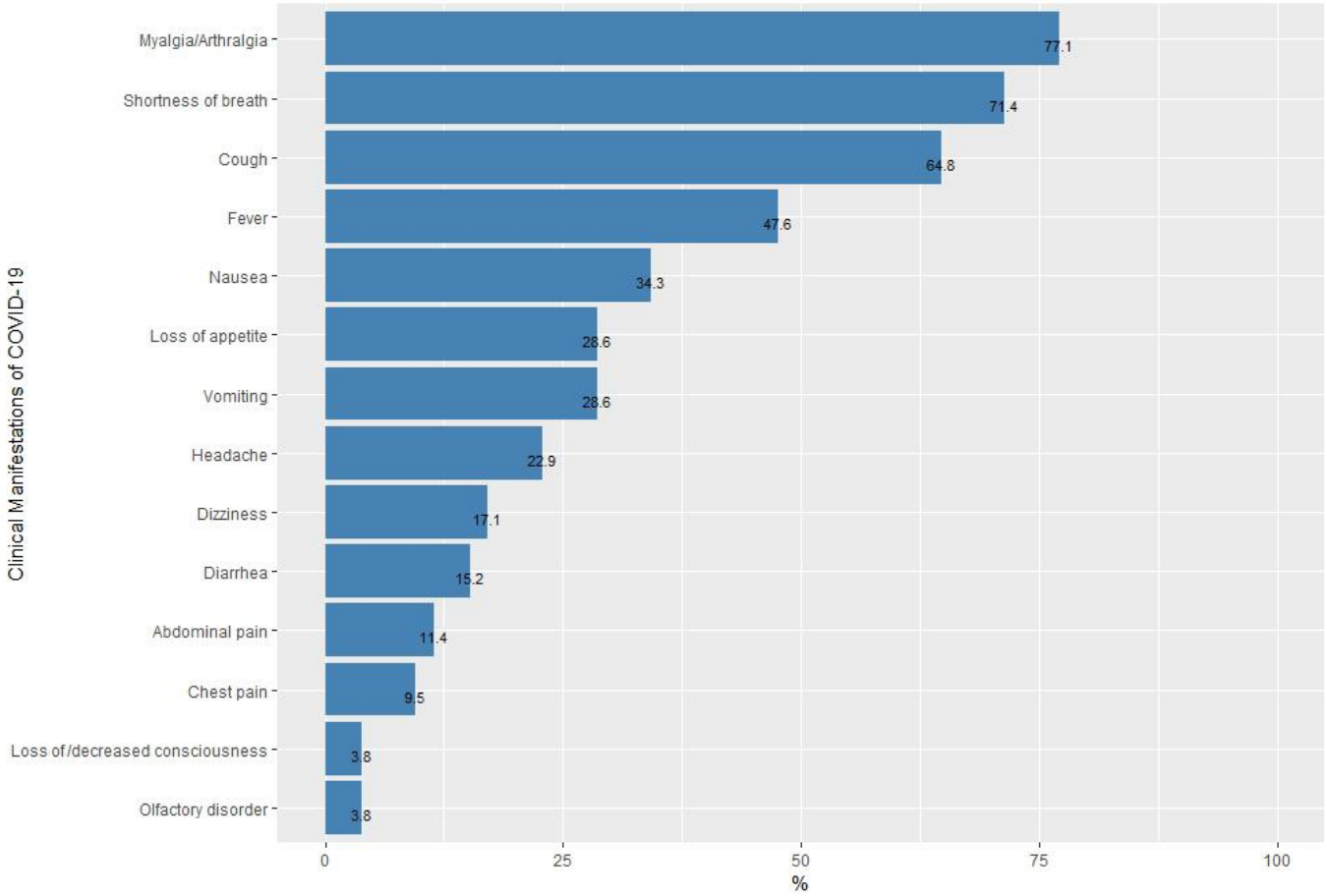

Figure 1. Clinical manifestations of COVID-19 in hospitalized patients with rheumatic diseases.

Table 2. COVID-19 outcome variables among patients with rheumatic diseases by gender

Variable	*Female*	*Male*	*All*	*Rate % (Total patients = 9,649)*	*P-value**
	Number (%)				
Pneumonia					
Yes	9 (69.2)	4 (30.8)	13 (100)	0.13	0.732
No	70 (76.1)	22 (23.9)	92 (100)		
SpO2					
≥90%	49 (74.2)	17 (25.8)	66 (100)	0.40	0.819
<90%	30 (76.9)	9 (23.1)	39 (100)		
Cardiac injury					
Yes	8 (88.9)	1 (11.1)	9 (100)	0.09	0.446
No	71 (74.0)	25 (26.0)	96 (100)		
Brain involvement					
Yes	5 (100)	0	5 (100)	0.05	0.329
No	74 (74.0)	26 (26.0)	100 (100)		
Liver injury					
Yes	1 (25.0)	3 (75.0)	4 (100)	0.04	0.046
No	78 (77.2)	23 (22.8)	101 (100)		
AKI					
Yes	1 (33.3)	2 (66.7)	3 (100)	0.03	0.151
No	78 (76.5)	24 (23.5)	102 (100)		
Sepsis					
Yes	5 (83.3)	1 (16.7)	6 (100)	0.06	1.000
No	74 (74.7)	25 (25.3)	99 (100)		
Secondary nonpulmonary infection					
Yes	1 (50.0)	1 (50.0)	2 (100)	0.02	0.436
No	78 (75.7)	25 (24.3)	103 (100)		
VTE					
Yes	1 (100)	0	1 (100)	0.01	1.000
No	78 (75.0)	26 (25.0)	104 (100)		
ICU admission					
Yes	16 (76.2)	5 (23.8)	21 (100)	0.21	1.000
No	63 (75.0)	21 (25.0)	84 (100)		
Mechanical ventilation					
Yes	16 (76.2)	5 (23.8)	21 (100)	0.21	1.000
No	63 (75.0)	21 (25.0)	84 (100)		
Length of hospitalization, days					
≥14	11 (91.7)	1 (8.3)	12 (100)	0.12	0.286
<14	68 (73.1)	25 (26.9)	93 (100)		
Rheumatic disease flare					
Yes	1 (100)	0	1 (100)	0.01	1.000
No	78 (75.0)	26 (25.0)	104 (100)		
Hematologic complications					
Leukopenia	15 (88.2)	2 (11.8)	17 (100)	0.17	0.039
Thrombocytopenia	15 (78.9)	4 (21.1)	19 (100)	0.19	
Leukopenia and thrombocytopenia	15 (62.5)	9 (37.5)	24 (100)	0.24	
Leukocytosis	1 (100)	0	1 (100)	0.01	
Thrombocytosis	0	2 (100)	2 (100)	0.02	
Leukocytosis and Thrombocytosis	2 (2.3)	0	2 (100)	0.02	
Normal	30 (83.3)	6 (16.7)	36 (100)	-	
Anemia					
Yes	30 (76.9)	9 (23.1)	39 (100)	0.40	0.819
No	49 (74.2)	17 (25.8)	66 (100)		
CT severity grading					
Normal	4 (100)	0	4 (100)	-	0.424
Mild	10 (71.4)	4 (28.6)	14 (100)	0.14	
Moderate	40 (80.0)	10 (20.0)	50 (100)	0.51	
Severe	25 (67.6)	12 (32.4)	37 (100)	0.38	
Mortality					
Yes	14 (77.8)	4 (22.2)	18 (100)	0.18	1.000
No	65 (74.7)	22 (25.3)	87 (100.0)		
GCS					
15	59 (74.7)	20 (25.3)	79 (100)	-	0.150
13-14	2 (66.7)	1 (33.3)	3 (100)	0.03	
10-12	8 (72.7)	3 (27.3)	11 (100)	0.11	
6-9	9 (100)	0	9 (100)	0.09	
<6	1 (33.3)	2 (66.7)	3 (100)	0.03	
Creatinine					
<1.2	64 (78.0)	18 (22.0)	82 (100)	-	0.498
1.2-1.9	11 (61.1)	7 (38.9)	18 (100)	0.18	
2-3.4	2 (66.7)	1 (33.3)	3 (100)	0.03	
3.5-4.9	1 (100)	0	1 (100)	0.01	
≥5	1 (100)	0	1 (100)	0.01	
Bilirubin					
<1.2	66 (78.6)	18 (21.4)	84 (100)	-	0.009
1.2-1.9	13 (76.5)	4 (23.5)	17 (100)	0.17	
2-5.9	0	3 (100)	3 (100)	0.03	
6-11.9	0	1 (100)	1 (100)	0.01	
Platelet count					
>150,000	48 (78.7)	13 (21.3)	61 (100)	-	0.632
100,000-150,000	21 (67.7)	10 (32.3)	31 (100)	0.32	
50,000-<100,000	9 (75.0)	3 (25.0)	12 (100)	0.12	
<50,000	1 (100)	0	1 (100)	0.01	
MAP					
>70	76 (76.0)	24 (24.0)	100 (100)	-	0.595
≤70	3 (60.0)	2 (40.0)	5 (100)	0.05	

*All P-values were obtained using Fisher's exact test. SpO2, peripheral oxygen saturation; AKI, acute kidney injury; VTE, venous thromboembolism; ICU, intensive care unit; CT, computed tomography; GCS, Glasgow Coma Scale; MAP, mean arterial pressure.

As for hematologic complications, when examining the residuals in the contingency table, we noted that none of the residuals were significantly high (>2), implying that the evidence for a difference was insufficient.

Regarding plasma bilirubin level, the significance seems to be due to the range of serum bilirubin from 2 to 5.9, so that males are more likely to develop bilirubin level in this range compared with females.

Speaking of RD, none of the variables demonstrated significant association except platelet count. The results of Fisher's exact test (p=0.004) indicated a significant association between platelet count and disease type (*Table 3*, *Figure 3*).

It was proven that none of the residuals were extreme, hence the evidence of difference was not robust. However, SLE had fewer zero scores and more positive scores, compared with other groups.

None of the outcome variables exhibited significant association with patient age categories (p≥0.05).

Discussion

Individuals with RD may face unique challenges during the COVID-19 pandemic, such as increased susceptibility to SARS-CoV-2 infection and potentially aggravated outcomes caused by COVID-19. We conducted a study to evaluate the clinical symptoms and outcomes of hospitalized patients with COVID-19 who had RD.

The results of the present study showed that the type of disease was significantly associated with platelet count. Moreover, the gender of the patients demonstrated a significant association with liver injury, hematologic complications, and plasma bilirubin level. The mortality rate was 0.18, with moderate CT severity being the predominant adverse outcome, occurring at a rate of 0.51.

Previous studies have shown that individuals diagnosed with rheumatic and musculoskeletal diseases (RMD) faced an increased likelihood of adverse outcomes after COVID-19 infection, with a 74% elevated mortality risk. However, several severity markers, including hospitalization rate, oxygen administration, ICU admission, and mechanical ventilation, showed no statistically significant differences in patients with RMD vs. patients without such diseases [11].

RD may aggravate the effects of COVID-19 and lead to poorer outcomes for patients, compared with the general population. The exact cause of this finding remains somewhat uncertain. On the one hand, there is evidence suggesting a potential link between certain cytokines (e.g., IL-6), previously associated with various rheumatic conditions, and the occurrence of multiple organ damage in patients with COVID-19. On the other hand, some studies suggested that people with RD (viz., SLE and RA) may face increased susceptibility to infections due to the use of immunosuppressive drugs such as glucocorticoids, tocilizumab, and hydroxychloroquine [12]. However, a recent study in the United States involving a group of 30,775 people diagnosed with autoimmune RD confirmed that after adjusting for confounding factors, there was no statistically significant association with increased risk of mortality or worse outcomes for patients with autoimmune RD who required hospitalization due to COVID-19 [13].

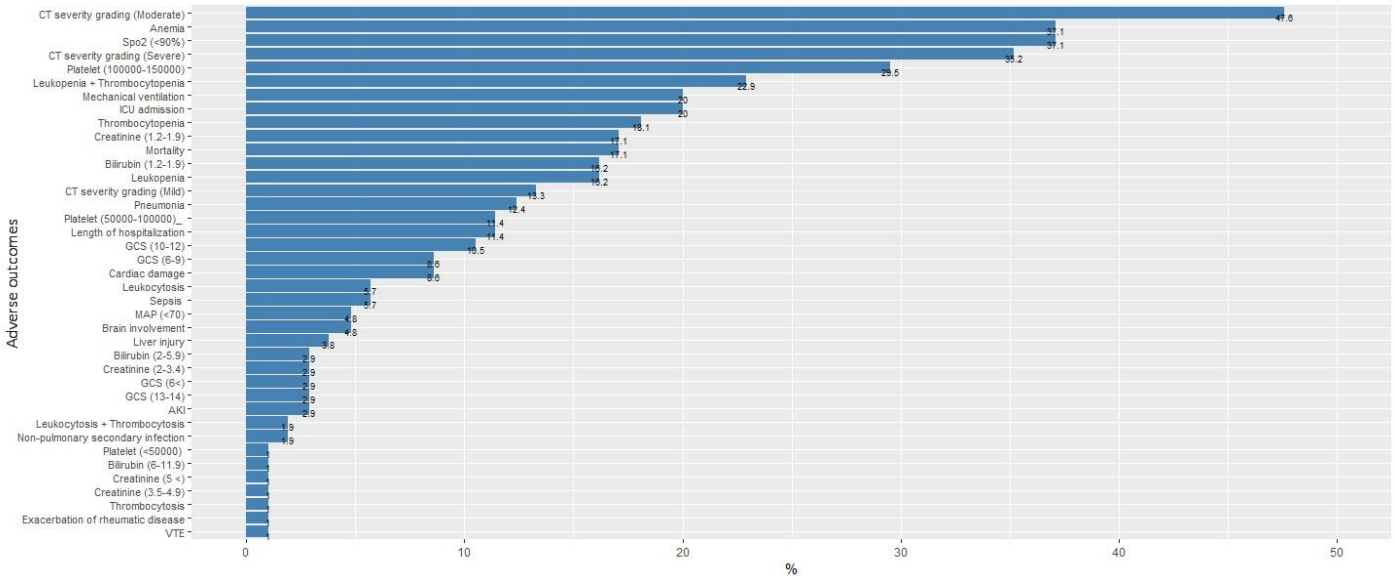

Figure 2. Adverse COVID-19 outcomes among hospitalized patients with rheumatic diseases. SpO2, peripheral oxygen saturation; AKI, acute kidney injury; VTE, venous thromboembolism; ICU, intensive care unit; CT, computed tomography; GCS, Glasgow Coma Scale; MAP, mean arterial pressure.

Shahram et al. confirmed that the prevalence of COVID-19 was not increased in patients with BD. These individuals tend to have a less severe form of the infection, resulting in lower morbidity and mortality rate. Furthermore, no significant effect on the progression of BD was observed when it was accompanied by COVID-19 [14].

The reported incidence of COVID-19 among individuals with RD may be inaccurately overestimated, possibly due to bias arising from increased initial interactions with healthcare settings or a lower threshold for seeking medical help when symptoms occur [11]. Another factor contributing to the susceptibility of patients with RD may be their tendency to have a greater burden of comorbid health problems, often associated with adverse outcomes. Furthermore, it is possible that immune dysregulation, either due to RD treatment or inherent to the diseases per se, could potentially lead to an increased incidence of symptomatic COVID-19 and more severe outcomes [11].

A total of 10 studies, including 138 hospitalized individuals with RD and COVID-19, were examined in a systematic review and meta-analysis. Among all patients admitted to the hospital, the rates of oxygen support, ICU admission, and mortality were 0.61, 0.13, and 0.13, respectively. In Asia, the rates of oxygen support and ICU admission were 0.66 and 0.11, respectively, and these rates were not significantly different from those observed in Europe and North America. However, the mortality rate was higher in Europe (0.19) vs. North America (0.12) or Asia (0.11) [15]. In the present study, the mortality rate was 0.18, surpassing the rates observed in Asia and North America. However, the ICU admission rate was 0.21, indicating a higher value both overall and compared with Asian countries. The oxygen support rate was 0.40, i.e., lower than the overall average and compared with Asian countries.

Regarding the clinical manifestations of COVID-19, in a study by Ye et al., fever (76%), shortness of breath (67%), and cough (57%) were the most frequently documented symptoms among hospitalized rheumatic patients with COVID-19 [16]. However, in the current study, myalgia/arthralgia (77.1%) was the most common clinical manifestation, the second and third most common symptoms were shortness of breath (71.4%) and cough (64.8%). Moreover, regarding laboratory markers, lymphopenia was reported to be present in 57% of patients, while leukopenia was uncommon (5%). Increased neutrophil counts were noted in approximately 20% of patients, while 76% of patients were shown to develop anemia [16]. We demonstrated that the primary hematologic complication was anemia, affecting 37.1% of individuals, with leukopenia combined with thrombocytopenia in 22.9% of study subjects. Furthermore, leukopenia was present in 16.2% of patients, indicating a higher incidence compared to the referenced study.

When considering the factors that contribute to the increased risk of severe outcomes in this population, there are studies that have shown a number of different influencing factors [11, 17].

Age, gender, comorbidities, and disease activity level are known to influence COVID-19 outcomes in patients with RMD [11].

Moreover, older age has been identified as a potential risk factor, with individuals over the age of 66 years showing a higher likelihood of mortality vs. individuals aged 65 years or younger. Male gender and the type of RD (e.g., RA) have also been associated with increased odds of mortality [17]. Furthermore, another study showed that older age, male gender, and the presenfce of connective tissue disease were independent significant factors associated with the development of severe COVID-19 cases [18].

Although we failed to demonstrate a significant association of any of the aforementioned variables with mortality, platelet count and disease type (e.g., SLE), in addition to gender, liver injury and plasma bilirubin level (in men), along with hematologic complications, showed a significant association.

Sattui et al. confirmed a significant association among a cohort of patients diagnosed with primary systemic vasculitis or polymyalgia rheumatica. They found that older age, higher prevalence of concurrent health conditions, higher disease activity, and prednisolone intake of 10 mg/day or more were significantly associated with poorer outcomes in COVID-19 cases [19].

Table 3. Outcome variables by type of rheumatic disease

Variable	RA	SLE	SA	SS	BD	Sarcoidosis	P-value*
	Number (%)						
Pneumonia							
Yes	10 (11.6)	2 (18.2)	1 (50.0)	0	0	0	0.525
No	76 (88.4)	9 (81.8)	1 (50.0)	2 (100.0)	2 (100.0)	2 (100.0)	
SpO2							
90%≤	53 (61.6)	6 (54.5)	1 (50.0)	2 (100.0)	2 (100.0)	2 (100.0)	0.686
<90%	33 (38.4)	5 (45.5)	1 (50.0)	0	0	0	
Cardiac injury							
Yes	7 (8.1)	2 (18.2)	0	0	0	0	0.653
No	79 (91.9)	9 (81.8)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	
Brain involvement							
Yes	5 (5.8)	0	0	0	0	0	1.000
No	81 (94.2)	11 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	
Liver injury							
Yes	3 (3.5)	0	1 (50.0)	0	0	0	0.320
No	83 (96.5)	11 (100.0)	1 (50.0)	2 (100.0)	2 (100.0)	2 (100.0)	
AKI							
Yes	1 (1.2)	2 (18.2)	0	0	0	0	0.084
No	85 (98.8)	9 (81.8)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	
Sepsis							
Yes	4 (4.7)	2 (18.2)	0	0	0	0	0.470
No	82 (95.3)	9 (81.8)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	
Secondary nonpulmonary infection							
Yes	1 (1.2)	0	1 (50.0)	0	0	0	0.157
No	85 (98.8)	11 (100.0)	1 (50.0)	2 (100.0)	2 (100.0)	2 (100.0)	
VTE							
Yes	1 (1.2)	0	0	0	0	0	1.000
No	85 (98.8)	11 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	
ICU admission							
Yes	16 (18.6)	4 (36.4)	1 (50.0)	0	0	0	0.453
No	70 (81.4)	7 (63.6)	1 (50.0)	2 (100.0)	2 (100.0)	2 (100.0)	
Mechanical ventilation							
Yes	17 (19.8)	4 (36.4)	0	0	0	0	0.777
No	69 (80.2)	7 (63.6)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	
Length of hospitalization, days							
≥14	9 (10.5)	1 (9.1)	1 (50.0)	1 (50.0)	0	0	0.281
<14	77 (89.5)	10 (90.9)	1 (50.0)	1 (50.0)	2 (100.0)	2 (100.0)	
Rheumatic disease flare							
Yes	0	1 (9.1)	0	0	0	0	0.181
No	86 (100.0)	10 (90.9)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	
Hematologic complications							
Leukopenia	14 (16.3)	3 (27.3)	0	0	0	0	
Thrombocytopenia	17 (19.8)	2 (18.2)	0	0	0	0	
Leukopenia and thrombocytopenia	17 (19.8)	3 (27.3)	2 (100.0)	0	2 (100.0)	0	
Leukocytosis	5 (5.8)	0	0	0	0	1 (50.0)	0.606
Thrombocytosis	1 (1.2)	0	0	0	0	0	
Leukocytosis and thrombocytosis	2 (2.3)	0	0	0	0	0	
Normal	30 (34.9)	3 (27.3)	0	2 (100.0)	0	1 (50.0)	
Anemia							
Yes	33 (38.4)	4 (36.4)	0	1 (50.0)	1 (50.0)	0	0.924
No	53 (61.6)	7 (63.6)	2 (100.0)	1 (50.0)	1 (50.0)	2 (100.0)	
CT severity grading							
Normal	3 (3.5)	0	0	1 (50.0)	0	0	
Mild	11 (12.8)	1 (9.1)	0	0	1 (50.0)	1 (50.0)	0.370
Moderate	42 (48.8)	5 (45.5)	1 (50.0)	1 (50.0)	1 (50.0)	0	
Severe	30 (34.9)	5 (45.5)	1 (50.0)	0	0	1 (50.0)	
Mortality							
Yes	14 (16.3)	4 (36.4)	0	0	0	0	0.589
No	72 (83.7)	7 (63.6)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	
GCS							
15	65 (75.6)	7 (63.6)	1 (50.0)	2 (100.0)	2 (100.0)	2 (100.0)	
13-14	2 (2.3)	0	1 (50.0)	0	0	0	
10-12	10 (11.6)	1 (9.1)	0	0	0	0	0.524
6-9	6 (7.0)	3 (27.3)	0	0	0	0	
<6	3 (3.5)	0	0	0	0	0	
Creatinine							
<1.2	69 (80.2)	7 (63.6)	2 (100.0)	1 (50.0)	1 (50.0)	2 (100.0)	
1.2-1.9	15 (17.4)	2 (18.2)	0	0	1 (50.0)	0	
2-3.4	2 (2.3)	1 (9.1)	0	0	0	0	0.075
3.5-4.9	0	1 (9.1)	0	0	0	0	
≤5	0	0	0	1 (50.0)	0	0	
Bilirubin							
<1.2	72 (83.7)	6 (54.5)	1 (50.0)	2 (100.0)	1 (50.0)	2 (100.0)	
1.2-1.9	12 (14.0)	4 (36.4)	0	0	1 (50.0)	0	0.076
2-5.9	1 (1.2)	1 (9.1)	1 (50.0)	0	0	0	
6-11.9	1 (1.2)	0	0	0	0	0	
Platelet count							
>150,000	51 (59.3)	6 (54.5)	0	2 (100.0)	0	2 (100.0)	
100,000-150,000	27 (31.4)	0	2 (100.0)	0	2 (100.0)	0	0.004
50,000-<100,000	8 (9.3)	4 (36.4)	0	0	0	0	
<50,000	0	1 (9.1)	0	0	0	0	
MAP							
>70	81 (94.2)	11 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	1.000
≤70	5 (5.8)	0	0	0	0	0	

*All P-values were obtained using Fisher's exact test; SpO2, peripheral oxygen saturation; AKI, acute kidney injury; VTE, venous thromboembolism; ICU, intensive care unit; CT, computed tomography; GCS, Glasgow Coma Scale; MAP, mean arterial pressure; SLE, Systemic lupus erythematosus; SA, Spondyloarthritis; SS, Systemic sclerosis; BD, Behçet's disease.

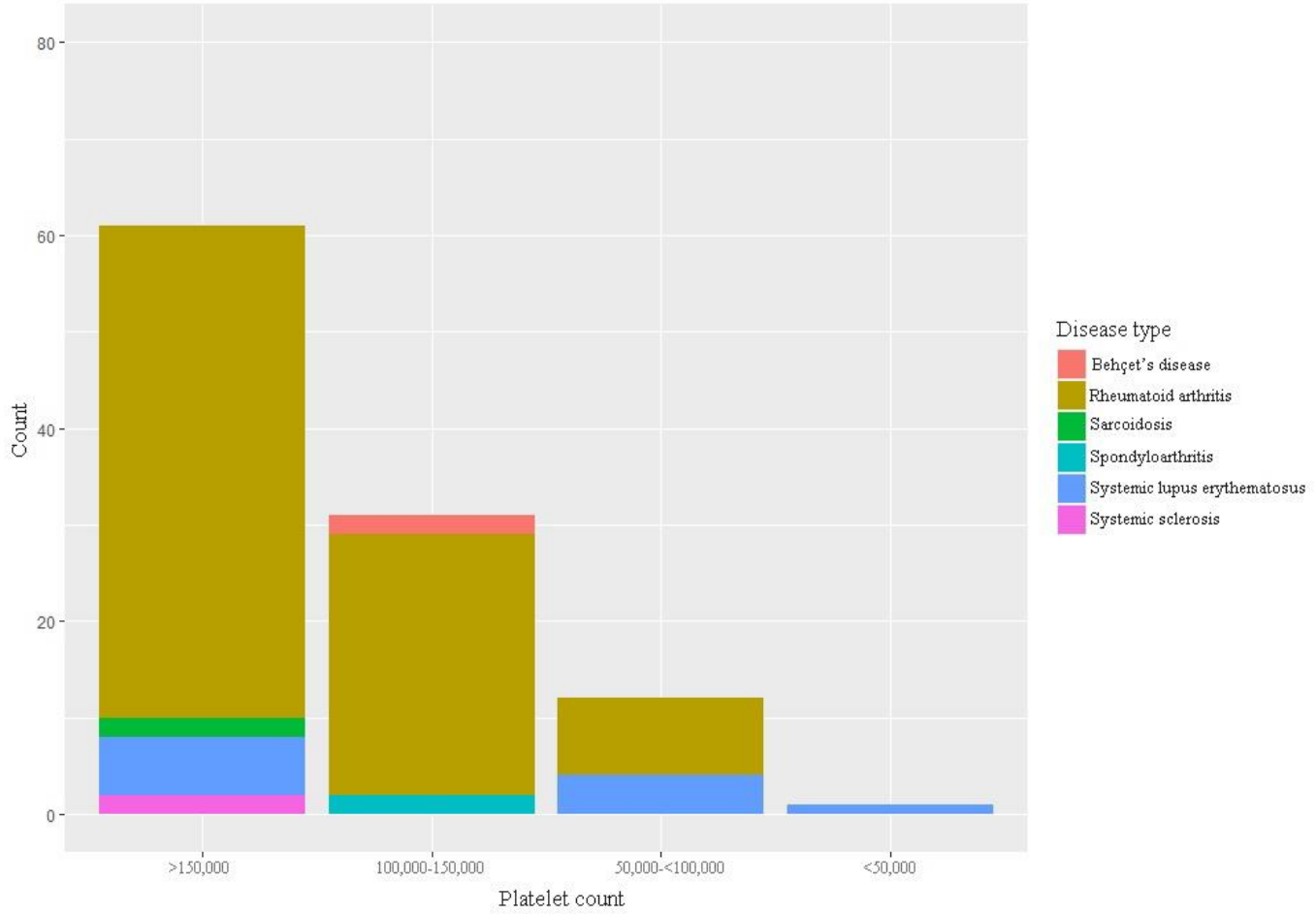

Figure 3. Stacked histogram of platelet count by type of rheumatic disease.

The primary objective of our study was to investigate the various clinical manifestations and consequences of COVID-19 in individuals diagnosed with RD. Notably, the study did not aim to examine potential risk factors associated with adverse COVID-19 outcomes in this population. However, during the review of the existing literature, it became apparent that there was a paucity of studies examining the various adverse outcomes of COVID-19 among individuals with RD. Most existing studies have focused on three specific outcomes: mortality, admission to the ICU, and the need for oxygen support. Hence, we acknowledge that our study has the advantage of examining a broader range of outcomes among inpatients with both COVID-19 and RD.

Limitations of the study

There are some limitations to this study that should be acknowledged. First, due to its retrospective design, which relies on data extraction from patient records, there is potential for selection bias. Second, the lack of comparison group based on an entire population hampers our ability to draw parallels between individuals with and without rheumatic diseases. Moreover, given the largely observational nature of the study, we are unable to infer causal relationships from our results. Finally, the considered cases were collected from a single center over a relatively short period of time, thereby including a limited number of patients with rheumatic diseases. This has led to the inclusion of only a minimal number of individuals with rarer diseases. Therefore, we recommend exploring more longitudinal multicenter studies that include a comparison group, cover a longer period, and delve into a wider range of potential COVID-19 clinical outcomes.

Conclusion

In summary, the most common symptom reported in COVID-19 cases was myalgia/arthralgia. Frequently observed outcomes included moderate severity based on CT grading, anemia, SpO2 <90%, and severe CT-based grade. A significant association was found between disease type and platelet count. In addition, patient gender demonstrated a significant association with liver injury, hematologic complications, and plasma bilirubin levels. The observed mortality rate was relatively high. These findings have important implications for clinicians, highlighting the need to recognize a range of distinct adverse outcomes among hospitalized individuals with RD.

Ethical approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines and approved by the Ethics Committee of Zanjan University of Medical Sciences [IR.ZUMS.REC.1400.329]. Written informed consent was obtained from all participants or their legal guardians, as appropriate. We adhered to the requirements of the Declaration of Helsinki.

Data availability statement

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

Conflict of interest

The authors declare that they have no conflicts of interests.

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Author contributions

A.S., S.G., F.A., and S.A.S. contributed to conceptualization, methodology, and data analysis. S.G. collected data. M.R. conducted the literature review and prepared the text of the manuscript. M.R. performed the statistical analysis, interpreted the results, and prepared the figures. A.S., M.R., S.G., F.A., and S.A.S. critically reviewed the manuscript. A.S. supervised the entire project.

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