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Research Article

Covid-19 And Inflammatory Rheumatic Diseases, Local Clinic Experience in Saudi Arabia

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Abstract

Objective: To assess how Coronavirus disease 19 (COVID-19) affects the progression of inflammatory rheumatic disorders (IRDs), as well as how various IRDs, and their treatment, may alter immunological function in COVID-19 patients.

Methods: This study, conducted from 1st January 2021 to 31st December 2021, screened 896 IRD patients from the rheumatology clinic of King Fahad Hospital, Medina, Saudi Arabia, and selected 93, who were divided into two groups. Group I (56 patients) consisted of IRD patients who tested positive for COVID-19 and group II (37 patients) were IRD patients who were in direct contact with COVID-19 positive patients. Data collected included: demographic data, smoking history, COVID-19 history, symptoms, medications used, type of IRD, medications used before and after COVID-19 infection, rheumatological disease activity during COVID-19 infection, and comorbidities.

Results: Within group I, 100% patients completely recovered, with 87.5% staying in home isolations, and 12.5% admitted to the hospital. Intensive care unit (ICU) admission and intubation were required for 3 patients, 2 required oxygen supply, and 2 were admitted due to inadequate oral intake. Group II patients also showed 100% recovery, with disease activity remaining stable. Only 10.8% of group II participants received treatment during home isolation, and 0% were admitted to the hospital.

Conclusion: IRD patients with COVID-19 have an increased disease activity than those who did not contract the disease but were in close contact with COVID-19 patients. Furthermore, IRD patients who were in close contact with COVID-19 patients recovered completely with few comorbidities, compared to those who tested positive for COVID-19.

Keywords: Inflammatory Rheumatoid Diseases, COVID-19, SARS-CoV-2, Rheumatological disease activity, Disease-Modifying Anti-Rheumatic Drugs, Connective tissue disorders, Autoimmune diseases

Introduction

In the industrialized world, inflammatory rheumatic diseases (IRD) are the leading cause of disability [1,2]. Systemic inflammatory disorders, such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS), can be the most damaging if not treated properly, despite being less common than degenerative diseases [3,4]. The health-related quality of life of patients with rheumatic disorders is considerably reduced. Increased disease activity, comorbidities, and treatment-related adverse effects are a few of the key factors that result in decreased physical, emotional, and social functioning [5,6].

Coronavirus disease 19 (COVID-19) is a highly transmissible virus produced by the severe acute respiratory syndrome

coronavirus 2 (SARS-CoV-2) that resulted in a global pandemic and a significant loss of human life [7]. The virus spreads from person to person through close contact with an infected person via coughing, sneezing, respiratory droplets, or aerosols. These aerosols trigger the infection after entering the human body through the nose or mouth after inhalation and penetrate the human lungs [7].

Immunosuppressive therapy, immune system imbalance, and the presence of comorbidities all raise the risk of infection in people with IRD. The COVID-19 epidemic has become a major public health concern, influencing the care of several chronic illnesses, including IRD. A study by Esatoglu et al. in 2021 found that one-third of subjects with IRD required oxygen support, 13% were treated in the intensive care unit (ICU), and the overall death rate owing to COVID-19 was 10%. They also discovered that glucocorticoid use, chronic kidney disease, lung disease, and obesity were all linked to a poorer outcome. Nevertheless, the probability of a poorer outcome was reduced in patients without comorbidities and those on conventional synthetic Disease-Modifying Anti-Rheumatic Drugs (DMARDs). Additionally, they stated that none of the IRD diagnoses were solely linked to a poor clinical outcome [8].

Similarly, Shin et al. [9] found that patients with autoimmune IRDs, such as inflammatory arthritis or connective tissue disease, had a higher likelihood of testing positive for SARS-CoV-2, contracting severe COVID-19, and having a COVID-19-related death. Therefore, the present study aims to evaluate how COVID-19 infection affects patients with IRD either directly (patients with COVID-19 infection) or indirectly (IRD patients exposed to a confirmed case of COVID-19) and to track how each group fared during the pandemic.

Materials and Methods

Of a total number of 896 patients with IRD who were screened, 93 patients were included in the present study after obtaining approval from the Institutional Review Board (IRB) of King Fahad Hospital, Ministry of Health, Madina, Saudi Arabia. Patients with various types of IRD such as systemic lupus erythematosus (SLE), Anti-phospholipid syndrome (APS), RA, systemic sclerosis, Sjogren's disease, AS, PsA, enteropathic arthritis, reactive arthritis, rheumatic fever, inflammatory myopathy, overlap syndrome, mixed connective tissue diseases, familial Mediterranean fever (FMF), vasculitis, juvenile idiopathic arthritis (JIA), crystal-induced arthritis, and polymyalgia rheumatic (PMR) were included in the study.

The study was conducted from 1st January 2021 to 31st December 2021. All data were collected directly from patients at the rheumatology clinic of King Fahad Hospital by a rheumatologist. The 93 participants were divided into two groups; 56 patients in group I which included patients infected directly with COVID-19 and 37 patients in group II where the IRD patients were in direct contact with individuals with COVID-19 infection but did not acquire the infection at the commencement of the study. A survey form was used to collect the following information: personal information (age, sex, nationality), smoking status, COVID-19 infection (symptoms, source of infection, symptom of disease, course of disease, medications used, whether the patient changed medications on his or her own during COVID-19 infection or exposures, and outcome), type of IRD, medications used before and after COVID-19 infection, rheumatological disease activity during COVID-19 infection, and the type of comorbidity experienced by the patient.

Also examined throughout the study's data collection was whether the doctor adjusted the patient's medicine, or the patient changed it on their own, whether the patient continued their therapy, and if there was a pharmaceutical shortage. COVID-19 infection was verified in all patients using a polymerase chain reaction (PCR) assay of the nasopharyngeal swab. The survey also asked if the patients were hospitalized or needed oxygen supplementation, as well as the medications they were taking for COVID-19 infection.

Statistical analysis

The data collected from patients directly, by a rheumatologist in a rheumatology clinic, were analysed through statistical methods and techniques. The statistical analysis was performed using IBM SPSS 22. Data were presented as mean with standard deviation (SD) for normal distribute continuous data and as the frequency with proportion n (%) for categorical data. The patients were divided into two groups, group I and group II. The differences in characteristics of patients in each group were assessed using the t-test for continuous variables and the Chi-square test was employed for frequency data to test the inter-group differences of the categorical variables. All statistical analysis was done at a 5% significance level or 95% confidence interval.

Results

Our research included 93 participants who had been diagnosed with inflammatory arthritis. With each visit to our clinic, we questioned if they had been infected or had direct exposure to a COVID-19 patient. The total number of outpatient clinic visits for all study participants totalled 2,185. Of the 93 participants, 56 tested positive for COVID-19 infection, and 37 had had direct contact with COVID-19 positive patients. During that period, 81 patients did not attend our clinic at all. The patients were assessed via phone calls, and 6 of them acquired infection and were included in our study. For 44 patients, the hospital's electronic mailing system did not have the correct contact information for them; thus, they were excluded from the study.

The results of the study revealed that the average age of group I participants diagnosed with Covid-19 was 46.21±14.36 years. Of those 56 people, 74.5% were women, and 92.7% were Saudi Arabians. The average age of group II subjects who were exposed to COVID-19-infected patients was 45.59±17.57 years. All participants in this group were Saudi Arabian citizens (Table 1), and 81.1% were male. The mean ages of the participants of groups I and II were 46.21±14.36 and 45.59±17.57 years, respectively, and this difference was not significant (t-test, p=0.186).

The percentage of females (75%) was higher compared to males (25%) in group I, whereas there were more males (81.1%) than females (18.9%) in group II (Table 1). On applying the Chi-square test, there was a significant difference in male and female patients in the studied groups (P<0.05).

Table 1: Comparison between the groups on the basis of demographic factor.

Demographic factors		Group infected directly with COVID-19 (N=56)	Group in contact with COVID-19 patients (N=37)	Test Statistics Chi square test / T test	P value
		(Group I)	(Group II)		
Gender	Male	14 (25%)	30(81.1%)	28.1097	0
	Female	42 (75%)	7(18.9%)		
Age, Month	Mean±SD	46.21±14.36	45.59±17.57	0.1861	0.8527
	Range	(19-85)	(19-80)		
Respondent	Patients	54(96.4%)	37 (100%)	1.35	0.2452
	Relative	2(3.6%)	0 (0%)		
Patients Nationality	Saudi	52(92.8%)	37 (100%)	2.762	0.0965
	Non-Saudi	4(7.2%)	0 (0%)		
Smoking	Yes	0(0%)	1(2.7%)	1.53	0.2161

Patients Diagnosed with COVID-19 (Group I)

The diagnosis of COVID-19 was confirmed by RT-PCR in 56 participants, and all of them completely recovered from the illness. Within the group, 87.5% had home isolations, 12.5% (7 participants) were admitted to the hospital, 3 required ICU admissions and intubation, 2 participants required oxygen in general wards, and 2 patients were admitted due to inadequate oral intake. Two ICU patients required home oxygen bilevel positive airway pressure (BIPAP) after discharge from the hospital (Table 2).

Table 2: Clinical Parameters assessed for the participants of both the groups.

Clinicopathologic factors		Group infected directly with COVID-19 (N=56)	Group in contact with COVID-19 patients (N=37)
		(Group I)	(Group I I)
Flu Vaccine	No	56(100%)	37(100%)
Pneumococcal Vaccine	No	56(100%)	37(100%)
Herpes Zoster Vaccine	No	56(100%)	37(100%)
COVID19 swab test	Yes	56(100%)	37(100%)
Symptoms	Fever	42(75%)	0 (0%)
	Runny nose	13(23.2%)	0 (0%)
	Sore throat	13(23.2%)	0 (0%)
	Shortness of Breath	18(32.1%)	0 (0%)
	Loss of smell/taste	36(64.3%)	0 (0%)
	Chest pain	10(17.9%)	0 (0%)
	Cough	23(41.1%)	0 (0%)
	Sputum	13(23.2%)	0 (0%)
	Headache	7(12.5%)	0 (0%)
	Myalgia	28(50%)	0 (0%)
	Bone-ache	28(50%)	0 (0%)
	Vomiting	55(98.2%)	0 (0%)
	Diarrhea	55(98.2%)	0 (0%)
Treatment place	Home isolation	49(87.5%)	4(10.8%)
	Admission in hospital	7(12.5%)	0 (0%)
Oxygen Requirement	Yes	5(8.93%)	0 (0%)
	No	51(91.07%)	37 (100%)
ICU Admission	Yes	3(5.36%)	0 (0%)
	No	53(94.64%)	37 (100%)

Medication during RA attack	Glucocorticoid	7(12.5%)	0 (0%)
	Antibiotic	12(21.43%)	0 (0%)
	Antiviral	6(10.71%)	0 (0%)
	Anticoagulant	3(5.36%)	0 (0%)
	Analgesic	53(94.64%)	0 (0%)
Shortage of Medications	Yes	3(5.36%)	0 (0%)
	No	53(94.64%)	37 (100%)
Treatment stopped	Stop by Doctor	4(7.2%)	0 (0%)
	Stop by Himself	13(23.2%)	0 (0%)
Co-morbidity	Diabetes Mellitus	9(16.07%)	3(8.1%)
	Hypertension	14(25.0%)	6(16.2%)
	Ischemic Heart Disease	1(1.79%)	0 (0%)
	Hypothyroidism	4(7.14%)	3(8.1%)
	Osteoporosis	6(10.71%)	1(2.7%)
	Interstitial lung disease	1(1.79%)	0 (0%)
	Bronchial Asthma	0(0%)	2(5.4%)
Type of Rheumatological disease	Systemic lupus erythematosus	15(26.7%)	14(37.8%)
	Anti-phospholipid syndrome	1(1.79%)	0 (0%)
	Rheumatoid arthritis	31(55.36%)	15(40.5%)
	Systemic sclerosis	1(1.79%)	0 (0%)
	Sjogren	1(1.79%)	0 (0%)
	Psoriatic arthritis	1(1.79%)	0 (0%)
	Rheumatic Fever	2(3.6%)	0 (0%)
	Vasculitis	2(3.6%)	4(10.8%)
	Gout	2(3.6%)	1(2.7%)
	familial Mediterranean fever	1(1.79%)	0 (0%)
	Inflammatory arthritis	1(1.79%)	0 (0%)
Medication for Rheumatological disease	Methotrexate	19 (33.93%)	9(24.3%)
	Leflunomide	2(3.6%)	0 (0%)
	Sulfasalazin	6(10.71%)	5(13.5%)
	Hydroxychloroquine	35(62.5%)	18(48.6%)
	Azathioprine	6(10.71%)	11(29.7%)
	Mycophenolate Mofetil	4(7.14%)	2(5.4%)
	Colchicine	4(7.14%)	3(8.1%)
	Allopurinol	0(0%)	1(2.7%)
	Adalimumab	2(3.6%)	1(2.7%)
	Penicillin	1(1.79%)	0(0%)

Various clinical parameters, including underlying rheumatological disease, co-morbidities of COVID-19 symptoms, and treatments received for COVID-19, are presented in Table 2. The most common symptom was fever (76.4% of cases) followed by loss of smell or taste (65.5%), myalgia or body ache (50.9%), cough (41.8%), and shortness of breath (32.7%). Analgesics were taken by the majority of subjects (96.4%), while antibiotics were utilized by only 21.8% of patients. Approximately 74.5% of IRD participants had stable disease activity despite COVID-19 infection, whereas 25.5% of patients showed increased disease activity (Table 2).

Regarding anti-rheumatic medications, 30.9% of the participants mentioned limited availability of drugs, and 23.6% stopped taking the medications themselves when they tested positive for COVID-19. Regarding anti-rheumatic medicine, 23.2% utilized Glucocorticoids (dosage: 5 - 7.5 mg), 62.5% used Hydroxychloroquine, 33.9% Methotrexate (MTX), 10.7% Sulfasalazine, 10.7% Azathioprine, 7.1% Mycophenolate Mofetil (MMF), 7.1% Colchicine, 3.6% Leflunomide, 3.6% Adalimumab, and 1.8% Penicillin (Table 2). The common co-morbidities were hypertension (HTN, 25% cases) followed by diabetes mellitus (DM, 16%), osteoporosis (10.7%), and hypothyroidism (7.1%) (Table 2).

Patients Exposed to a COVID-19 positive patient (group II)

This group consisted of 37 individuals. In terms of IRD, 40.5% of the cases had RA, 37.8% had SLE, and 10.8% had vasculitis. Systemic sclerosis, overlap syndrome, mixed connective tissue disease, psoriatic arthritis, and gout were seen in 2.7% (1 case each). In all of the patients, IRD remained stable (100%). Regarding medication, 29.7% used Glucocorticoid (2.5mg - 7.5 mg), 48.6% used Hydroxychloroquine, 29.7% used an unknown medication, 5.4% used MMF, 2.7% used Allopurinol, and 2.7% used Adalimumab as an anti-rheumatic disease drug (Table 2). In group II, 16.2% of the participants had HTN, 8.1% had DM, 8.1% had hypothyroidism, 5.4% had bronchial asthma, and 8.1% had depression (Table 2).

Among group I patients, 87.5% received treatment while in home isolation, and 12.5% were admitted to the hospital, whereas only 10.8% of the group II participants received treatment during home isolation and 0% were admitted to hospital (Table 3). There was a significant difference in the location of treatment between the studied groups (Chi-square test, $p<0.05$). As shown in tables 3 and 4, there was no significant difference between the groups based on the comorbidities ($p=0.3107$), underlying IRD ($p=0.502$), and the medicine used for IRDs ($p=0.375$).

Table 3: Comparison between groups on the basis of Clinical parameters.

Clinical Parameters		Group infected directly with COVID-19 (N=56)	Group in contact with COVID-19 patients (N=37)	Test Statistics Chi square test	P value
		(Group I)	(Group II)		
Treatment place for COVID	Home isolation	49(87.5%)	4(10.8%)	77.563	0
	Admission in hospital	7(12.5%)	0 (0%)		
	Others	0(%)	33(89.2%)		
Oxygen Requirement	Yes	5(8.93%)	0 (0%)	3.491	0.0617
	No	51(91.07%)	37 (100%)		
ICU Admission	Yes	3(5.36%)	0 (0%)	2.048	0.1524
	No	53(94.64%)	37 (100%)		
Shortage of medications	Yes	3(5.36%)	0 (0%)	2.048	0.1524
	No	53(94.64%)	37 (100%)		
Treatment stopped	Stop by Doctor	4(7.2%)	0 (0%)	13.745	0.001
	Stop by Himself	13(23.2%)	0 (0%)		
	Nil	39(59.6%)	37(100%)		
Comorbidity	Diabetes Mellitus	9(16.07%)	3(8.1%)	7.041	0.31707
	Hypertension	14(25.0%)	6(16.2%)		
	Ischemic Heart Disease	1(1.79%)	0 (0%)		
	Hypothyroidism	4(7.14%)	3(8.1%)		
	Osteoporosis	6(10.71%)	1(2.7%)		
	Interstitial lung disease	1(1.79%)	0 (0%)		
	Bronchial Asthma	0(0%)	2(5.4%)		

Table 4: Comparison between groups on the basis of Rheumatological disease.

Demographic Factors		Group infected directly with COVID-19 (N=56) (Group I)	Group in contact with COVID-19 patients (N=37) (Group II)	Test Statistics Chi square test / T test	P value
Type of Rheumatological disease	Systemic lupus erythematosus	15(26.7%)	14(37.8%)	8.318	0.502
	Anti-phospholipid syndrome	1(1.79%)	0 (0%)		
	Rheumatoid arthritis	31(55.36%)	15(40.5%)		
	Systemic Sclerosis	1(1.79%)	0 (0%)		
	Sjogren	1(1.79%)	0 (0%)		
	Psoriatic arthritis	1(1.79%)	0 (0%)		
	Rheumatic Fever	2(3.6%)	0 (0%)		
	Vasculitis	2(3.6%)	4(10.8%)		
	Gout	2(3.6%)	1(2.7%)		
	Familial Mediterranean fever	1(1.79%)	0 (0%)		
	Inflammatory arthritis	1(1.79%)	0 (0%)		
Medication for Rheumatological disease	Methotrexate	19 (33.93%)	9(24.3%)	9.699	0.375
	Leflunomide	2(3.6%)	0 (0%)		
	Sulfasalazine	6(10.71%)	5(13.5%)		
	Hydroxychloroquine	35(62.5%)	18(48.6%)		
	Azathioprine	6(10.71%)	11(29.7%)		
	Mycophenolate Mofetil	4(7.14%)	2(5.4%)		
	Colchicine	4(7.14%)	3(8.1%)		
	Allopurinol	0(0%)	1(2.7%)		
	Adalimumab	2(3.6%)	1(2.7%)		
	Penicillin	1(1.79%)	0(0%)		

Discussion

COVID-19 can affect people of all ages and patient demographics, but those who are older and have co-morbidities are at a higher risk of developing more severe disease. For a variety of reasons, IRDs have been a source of concern [10], particularly in regard to COVID-19 infection. Immune dysregulation caused by IRDs, or the drugs used to treat them, may have an impact on innate immune responses, which are important in limiting viral replication and developing an adaptive immune response. Immunological changes caused by rheumatoid arthritis or as a side effect of its treatment have the potential to lead to poor COVID-19 outcomes [11].

Studies have shown that COVID-19 patients with IRDs have a greater infection rate than their systemically healthy family members and had a higher rate of respiratory failure than those without IRDs [12,13]. COVID-19 results may be influenced by medications used to treat IRDs. Antiviral effects were suggested for hydroxychloroquine, chloroquine, and Baricitinib, and patients taking these medications were thought to be less likely to have severe COVID-19 outcomes due to lower viral replication during the early phase [14]. Grainger et al. stated that people with IRD may have a higher risk of SARS-CoV-2 infection after exposure than the general population; however, the risk is likely to be minor [15]. This is in accordance with the results of the present study, where 100% of the participants of group I completely recovered. Amongst the participants of this group, nearly 87.3% were in home isolation, and only 12.7% (7 participants) were admitted to the hospital. Only 2 participants required admission to the ICU.

Cordtz et al. [16] conducted a study to determine the rate of COVID-19 hospitalization in patients with IRD, patients with RA treated with particular DMARDs, and the rate of severe COVID-19 infection among hospitalized RA patients. The findings revealed that patients with IRD were more likely than the general population to be treated with COVID-19 and that COVID-19 admitted patients with RA were at a higher risk of a severe outcome. The use of certain DMARDs did not affect the likelihood of hospitalization [16]. The results of the present study are similar to the above study, with nearly 5.4% of patients in group I and 4.1% of patients in group II becoming infected, according to the findings.

The clinical course of COVID-19 was evaluated by Monti et al in a group of patients with chronic arthritis who were being treated with immunosuppressive targeted treatments [17]. The authors gathered data on 320 patients (68% of whom were female, with a mean age of 55±14 years) who were treated with biological DMARDs or targeted synthetic DMARDs. Thirteen COVID-19 patients were confirmed or suspected to have the virus. Only one patient, who was 65 years old, required hospitalization. There

were no deaths reported. This is in accordance with the outcome of the current study, where approximately 74.5% of group I IRD participants had stable disease activity despite the COVID-19 infection, whereas 25.5% of IRD patients with COVID-19 infection showed disease activity. However, 100% of the group II individuals recovered without any signs of an increase in disease activity. There was no reported death in either group.

When patients with RA, SLE, or PsA were assessed as a group in a study by Williamson et al in 2020, it was found that they had a slightly higher risk of dying from COVID-19 than those without these diseases, even though the impact of disease activity and therapy in this risk calculation was not considered [18]. The findings of our study are in harmony with this statement as individuals of group I had a slightly increased incidence of disease activity during COVID-19 infection, whereas individuals of group II showed stable disease activity.

Although rheumatic disease therapies have been linked to an increased risk of other infections, it is unknown whether any specific rheumatologic treatments are linked to an increased risk of COVID-19 or its complications. Although glucocorticoids may be an effective treatment for severe COVID-19 in some patients, limited observational evidence has raised the question of whether glucocorticoid medication is linked to a higher risk of more severe disease in IRDs. To fill this void in the treatment of IRD patients with COVID-19 infection, more long-term clinical trials are needed.

Study Limitations

Readers should be aware of some significant limitations when evaluating the study's findings. These limitations mostly resulted from attempts to use several different methods of inquiring and collecting data from the participants. The retrospective study design and a smaller sample size significantly affected the outcome of the study. Some important statistics cannot be obtained in retrospective investigations, and major biases such as recall bias may influence the choice of controls and the study results. Also, the results may be inconclusive if the sample size is too small.

Conclusions

In conclusion, our study suggests that IRD patients with COVID-19 infection are at risk of increased disease activity than the IRD patients who did not acquire COVID-19 but were in close contact with COVID-19 patients. Additionally, the IRD patients who were in close contact with COVID-19 patients showed complete recovery with minimal comorbidities, which was in contrast with the patients who tested positive for COVID-19 infection. This suggests that COVID-19 infection increases the disease severity and alters the course of the disease in patients with IRDs.

Acknowledgment

None.

Conflicts of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

Data Availability

Technical appendix, statistical code, and dataset available from the corresponding author.

Funding disclosure

No funding was received for this manuscript.

Author's contributions

All authors whose names appear on the submission made substantial contributions to the conception or design of the study. A.H. and A.A. were the main contributor to the study design. A.H. and B.S. wrote the first draft of the manuscript. K.A., B.S., M.Z., M.B., and A.J. contributed to the acquisition and analysis. A.H., B.S., and A.A. contributed to the validation and review of the manuscript. All authors critically reviewed the results and approved the final version of the manuscript.

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