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Original Article

Variability of clinical manifestations in rheumatoid arthritis patients with COVID-19 infection

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Abstract

Objective

The authors conducted the present retrospective study to assess the epidemiological, clinical, laboratory, and radiological characteristics in coronavirus disease-2019 (COVID-19) associated with rheumatoid arthritis (RA). As known, COVID-19 can cause fatal respiratory infection and may be accompanied with multiorgan affection, including the kidney and heart. The morbidity and mortality may be higher in patients with the immune-deficiency condition.

Patients and methods

The present study is a retrospective cohort study that retrieved the data of 307 patients with and/or without RA evaluated in Rheumatology Department in Mataria Teaching Hospital, who were previously infected with SARS-CoV-2. Patients' medical record IDs were reviewed between April and May, following the peak of SARS-CoV-2 infection. Selected patients were classified into two groups: the first group included 257 RA patients infected with COVID-19 versus 52 control groups infected with COVID-19. RA cases with confirmed COVID-19 through the period of April 2020 and May 2021. The diagnosis of COVID-19 was based on positive RT–PCR.

Results

The number of RA patients infected with COVID was 257 (83.7%). Fever (56.0%), fatigue (78.2%), myalgia (37.0%), and arthralgia (9.7%). Some patients developed shortness of breath (29.6%), chest pain that was found in 32.8% of patients. Ground-glass opacities were present in 31.3% and 18.7% presented with consolidation, 30% of rheumatoid patients developed respiratory failure. RA patients receiving conventional synthetic disease-modifying antirheumatic drugs were 96.8%.

Conclusion

Most rheumatic disorders, including RA, were likely to develop COVID-19 infection, but there was no evidence of a worse prognosis or poor outcome, despite immunosuppressive therapy.

Keywords: Coronavirus, COVID-19, rheumatoid arthritis, SARS-COV-2

Introduction

Coronavirus illness 2019 (COVID-19) is rapidly spreading over the world due to SARS-CoV-2 virus infection. It is unclear whether COVID-19 has unique manifestations in patients with rheumatic immunological disorders, or makes them more likely to develop severe COVID-19 [1].

COVID-19 has prompted widespread dread and concern among international populations in recent months; nevertheless, reports reveal that mortality rates are higher in cases with underlying comorbidities such as diabetes, heart, and lung diseases, as well as patients receiving immunosuppressive medication [2].

A local outbreak of a coronavirus (CoV) disease escalated quickly into a global healthcare emergency. Increased incidence of SARS-CoV-2 infection may be linked to an 'inflammatory

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storm.' Cytokines play a major role in multiple organ failure and death. Patients with rheumatic immune diseases and/or immune dysfunction receiving immunosuppressant therapy and/or glucocorticoids, are more prone to increased risk of TSARS-CoV-2 infection. The existence of COVID-19 in individuals with rheumatic illnesses has been documented in a few investigations [1].

Some published studies of COVID-19 in rheumatic diseases highlighted on the probability of severe outcomes in individuals with rheumatic illnesses and COVID-19 are linked to age and comorbidities [3,4].

Hydroxychloroquine (HCQ) and other disease-modifying antirheumatic drugs (DMARDs) with immune-modulating actions may have a therapeutic or prophylactic effect on the viral infection or the cytokine-storm syndrome seen in COVID-19 [5,6], on the other hand, during the pandemic, patients with rheumatoid arthritis (RA) stopped taking their immunosuppressive drugs for fear of deterioration of their general condition. As a result of stopping immunosuppressive drugs, there was improvement of their COVID infection [7].

Patients with rheumatic disease are an interesting study group because they are more susceptible to severe COVID-19 infection as a result of their disease and treatment, but many of these patients are also receiving immune-modulating medications, which have the potential to treat COVID-19 infection and improve prognosis.

Aim

The aim of our study was to describe the clinical characteristics and variability of RA patients infected with coronavirus disease (COVID-19) and detect their outcome, and find out their susceptibility to develop either a better or worse outcome with COVID-19 infection.

Patients and Methods

The study protocol was approved by the Ethnic Committee of GOTHI. Our retrospective cohort study included a number of 307 patients with and/or without RA evaluated in the outpatient clinic of the Rheumatology Department in Mataria Teaching Hospital who were previously infected with SARS-CoV-2, together with inpatient cases who were admitted in the hospital according to patients' medical record and IDs, all data were reviewed and recorded in the period of April–May 2020, following the peak of SARS-CoV-2 infection.

These patients were furtherly classified into two groups: the first group included 257 RA patients infected with COVID-19 and the second group included a number of 52 control groups infected with COVID-19, according to the association of COVID-19 infection with or without the presence of other comorbidities. Updated databases of the rheumatoid patients with severe acute respiratory syndrome coronavirus-2-positive PCR tests versus the nonrheumatic patients were matched.

Data extraction included demographics, epidemiology, and clinical characteristics of the infection together with their radiographic features, laboratory tests, immunosuppressive treatment, comorbidities and the outcome were collected from the electronic health records.

Inclusion criteria

Our RA patients received DMARDs, specifically HCQ, leflunomide, methotrexate, or biological disease-modifying antirheumatic drug (bDMARD), and nonrheumatic patients were observed and followed up in the outpatient clinic of our Rheumatology Department, after being infected with COVID-19.

Exclusion criteria

We excluded all cases that did not need hospitalization or referral to emergency departments in hospitals.

Statistical analysis

The Statistical Package for Social Science (SPSS) was used to generate the results (version 28, IBM Corp, Armonk, NY). Medians and ranges were used to describe quantitative numerical data. Frequencies and percentages were used to describe qualitative data. The Mann–Whitney *U*-test and the χ^2-test, were used to do comparisons.

Results

The present study recruited a number of 307 patients that included 56 males (12.2%) and 251 females (81.8%), in Mataria Teaching Hospital with a median age of 47 years, divided into two groups: rheumatic group (N = 257) and nonrheumatic control group (N = 52). In our study, 39.7% had comorbidities of diabetes, hypertension, or ischemic heart disease. The number of RA patients infected with COVID was 257 (83.7%).

The clinical features of rheumatoid/nonrheumatoid patients with COVID-19 are described in Table 1. The characteristic features of RA patients with COVID-19 patients were fever (56.0%), fatigue (78.2%), myalgia (37.0%), and arthralgia (9.7%). Some patients developed shortness of breath (29.6%), chest pain that was found in 32.8% of patients.

In HRCT assessment, a number of 186 (60.0%) cases had an abnormal parenchymal pattern, and 60% of cases presented the usual pattern of COVID-19 (bilateral multifocal ground glass opacity (GGO)/consolidation). These findings are useful for comparing clinical and paraclinical instances in RA cases with normal cases, despite the fact that it is a restricted report. Ground-glass opacities were present in 31.3 and 18.7% presented with consolidation, 30% of rheumatoid patients developed respiratory failure.

Of 257 recruited RA patients, 70 patients (27.2%) were admitted to the ICU with respiratory failure defined as peripheral oxygen saturation of less than 90%, which showed a high significant difference between RA and non-RA cases ($P < 0.001$).

The RA group showed higher inflammatory markers than those of non-RA group with a high significant value of less

than 0.001 as regards erythrocyte sedimentation rate, lactate dehydrogenase, and D-dimer that showed a significant value of less than 0.001 between the two groups as shown in Table 2.

There is also a high significant difference between RA and non-RA cases as regards arthralgia, myalgia (Figs. 1 and 2), ground-glass appearance, respiratory failure, and ICU admission ($P < 0.001$) as shown in Table 1.

There was a high significant difference between RA and non-RA cases as regards headache, loss of taste, and smell ($P < 0.001$) as shown in Table 1.

There was no significant difference between RA and non-RA cases as regards fever, fatigue, chest pain, and shortness of breath. There were no significant values between the two groups as regards C-reactive protein, leukopenia, and lymphopenia.

Patients were taking at least one of the conventional synthetic DMARDs: HCQ was 96.8% as for Methotrexate and leflunoamide was stopped during infection with COVID-19.

There was a high significant difference between RA group and non-RA control as regards the medication, especially DMARD *P* value less than 0.001, but no significant difference between the two groups as regards the biological treatment (Table 3).

Discussion

COVID-19 is a unique viral disease with a wide variety of clinical symptoms and severity levels. COVID-19 infection is yet to be fully understood in people with underlying rheumatic illnesses. COVID-19 can cause fatal respiratory infection and may be accompanied with multiorgan affection, including the kidney and heart. The morbidity and mortality may be higher in patients with the immune-deficiency condition.

Table 1: Clinical symptoms and outcome among the participants

Characteristics	Total (*n*=307) [*n* (%)]	RA cases (*n*=257) [*n* (%)]	Control (*n*=50) [*n* (%)]	*P*
Fever	168 (54.7)	144 (56.0)	24 (48.0)	0.297
Headache	73 (23.8)	39 (15.2)	34 (68.0)	<0.001
Loss of taste	73 (23.8)	45 (17.5)	28 (56.0)	<0.001
Anosmia	110 (35.8)	78 (30.4)	32 (64.0)	<0.001
Chest pain	98 (31.9)	83 (32.3)	15 (30.0)	0.750
Shortness of breath	87 (28.3)	76 (29.6)	11 (22.0)	0.277
Cough	134 (43.6)	108 (42.0)	26 (52.0)	0.193
Fatigue	239 (77.9)	201 (78.2)	38 (76.0)	0.731
Arthralgia	49 (16.0)	25 (9.7)	24 (48.0)	<0.001
Myalgia	129 (42.0)	95 (37.0)	34 (68.0)	<0.001
Consolidation	64 (20.8)	48 (18.7)	16 (32)	0.034
GGO	122 (39.7)	80 (31.3)	42 (84.0)	<0.001
Respiratory failure	77 (25.1)	77 (30.0)	0 (0)	<0.001
ICU admission	72 (23.5)	70 (27.2)	2 (4.0)	<0.001

ICU, intensive care unit.

Table 2: Laboratory finding among participants

Characteristics	Total (*n*=307)	RA cases (*n*=257)	Control (*n*=50)	*P*
ESR	35 (15-95)	35 (15-75)	51 (15-96)	<0.001
CRP	24 (0.1-380.2)	24 (2.2-167)	20.1 (0.1-380.2)	0.064
Serum ferritin	271.5 (22-4005)	267 (22-788)	298.3 (28-4005)	0.070
LDH	200 (97-955)	189 (97-400)	300 (111-955)	<0.001
D-dimer	0.5 (0.1-55)	0.5 (0.1-2.5)	5.5 (0.4-55.1)	<0.001

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; RA, rheumatoid arthritis.

Table 3: Comparison of treatment

Drugs	Total (*n*=307) [*n* (%)]	RA cases (*n*=257) [*n* (%)]	Control (*n*=50) [*n* (%)]	*P*
Biologic				
No	254 (82.7)	205 (79.8)	49 (98)	
Yes	53 (17.3)	52 (20.2)	1 (2)	0.002
Hydroxychloroquine				
No	16 (5.2)	8 (3.1)	8 (16)	
Yes	291 (94.8)	249 (96.8)	42 (84)	<0.001

RA, rheumatoid arthritis.

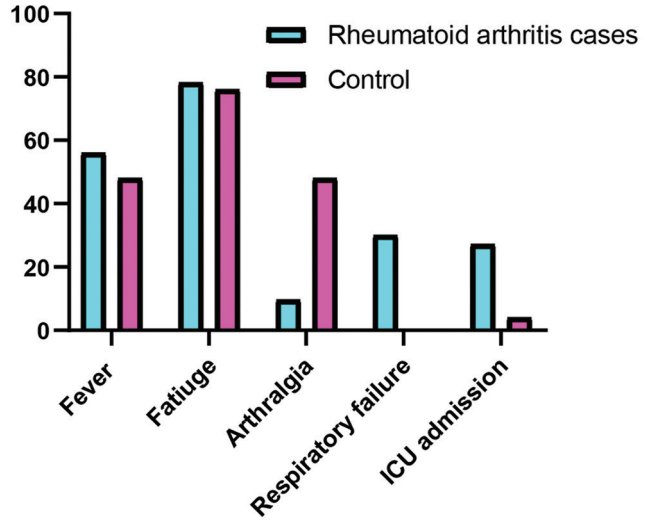

Figure 1: Clinical symptoms and outcome among the participants.

Three hundred and seven COVID-19 patients with or without RA were investigated, 27.2% of RA COVID patients were admitted in the ICU versus 4% of non-RA COVID were admitted in the ICU, which was against a recent study from the United States [8], which found that hospitalized patients with rheumatic disease had greater rates of ICU admission and in need to mechanical ventilation that may be the large number of RA cases in relation to the controls, which made a percentage difference, or may be that our RA-collected cases were not severely critical. Unlike Iranian researchers, Assar *et al.* [9], who found that neither rheumatic diseases nor their treatments were linked to higher infection rates or worsening COVID-19 outcomes [6,10], their explanation could be a lack of ICU beds in Iran during the pandemic, which resulted in a low rate of ICU admission.

The characteristic features of RA patients with COVID-19 patients were fever (56.0%), fatigue (78.2%), myalgia (37.0%), and arthralgia (9.7%), which goes with the results of Sun *et al*. [11] and D'Silva *et al*. [8], the most frequently reported symptoms of COVID-19 infection were fever, myalgia, dyspnea, and cough.

In our study, the number of RA patients infected with COVID was 257 (83.7%), which goes with a large Italian study that reported a higher prevalence of COVID-19 infection in patients with systemic autoimmune diseases [12]. Unlike the study of Assar *et al.* [9], which stated that 'Neither SLE patients nor RA, SpA, PsA, SSc, vasculitis, BD, IIM was more susceptible to COVID-19,' this difference may be because in our study, we were more focused on RA cases rather than rheumatic diseases that made our study specific.

Although the preventative or therapeutic impact of HCQ in COVID-19 infections has been postulated [13], a large survey of RA patients revealed its nonprotective effect [14,15], which goes with our study that 96.8% of our RA patients developed COVID inspite of administration of DIMARDs during their course of treatment of RA.

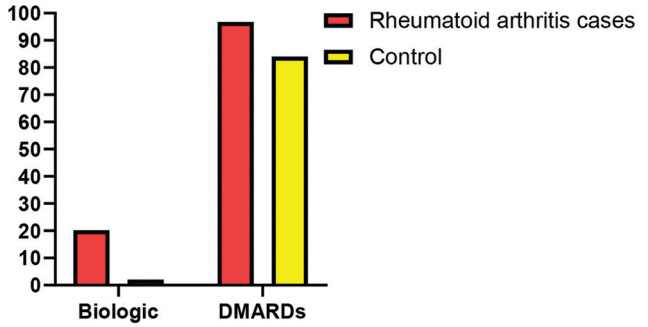

Figure 2: Comparison of treatment.

Similar to our study, 84% of non-RA COVID-19 patients were treated with HCQ. The majority of earlier investigations observed the same conclusion in the past that COVID-19 susceptibility was not linked to the usage of NSAIDs or DMARDs [16–18].

Our data back up the idea that additional risk factors, rather than pre-existing rheumatic illnesses or continuous immunosuppressive therapy, influence COVID-19 infection outcome. The high number of patients with RA in this investigation allowed us to estimate the prevalence of COVID-19 in the study population and compare the clinical characteristics and outcomes of SARS-CoV-2 infections in infected and noninfected groups.

There were some limitations to this investigation. First, we lacked a healthy control group with which to examine the occurrence and result of COVID-19 in our cases. As a result, the results and mortality rate were compared with those of prior international studies.

In our study, there was a high significant association between rheumatoid disease and controls as regards medications, especially hydroxychloroquine and susceptibility to COVID-19 infection, but no significant association as regards biological treatment. The mortality rate in rheumatoid patients was similar to the general population, which was against a previous study from Spain, which reported a greater prevalence of COVID-19 in patients on ts/bDMARDs therapy [17], which may be due to that the percentage of people who received biological treatment was lower in our study because of the high expenses of the biological therapy/also may be due to that hydroxychloroquine was given as the first line of treatment protocol for COVID-19. Most rheumatic disorders do not appear to be a risk factor for COVID-19 infection, and these individuals do not have a worse result, despite immunosuppressive and immunomodulatory therapy. During the COVID-19 pandemic, these findings could be crucial for controlling rheumatologic illnesses.

Conclusion

Most rheumatic disorders, including RA, were likely to develop COVID-19 infection, but there was no evidence of a worse prognosis or poor outcome, despite immunosuppressive therapy.

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Nil.

Conflicts of interest

None declared.

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