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Frequency, characteristics and outcome of coronavirus disease 2019 (COVID-19) infection in Iranian patients with rheumatic diseases

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A B S T R A C T

Aim of the work: To investigate the frequency, clinical characteristics and outcome of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in rheumatic diseases patients.

Patients and methods: One thousand patients with rheumatic diseases including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthritis (SpA), systemic sclerosis (SSc), Sjögren’s syndrome (SS), Behçets disease (BD), vasculitis, idiopathic inflammatory myositis (IM), relapsing polychondritis, sarcoidosis and antiphospholipid syndrome (APS) were studied. The following data were collected: age, sex, disease diagnosis, rheumatic disease medication.

Results: The 1000 patients mean age was 43.4 ± 13 years and 84.1% were females. The main diagnosis was RA (37.1%), followed by SLE (23.8%), SpA (13.4%), SSc (12.4%), vasculitis, BD and ruphus in 2.4%, 2.3% and 2.2% respectively, SS and SSc in 0.7% each. Most patients were taking glucocorticoids (78.4%). A large majority of patients were taking at least one of the cDMARDs. 16.1% were taking biologic therapy. 221 rheumatic diseases patients with COVID-19 were identified. Of these, 38 patients (17.2%) were hospitalized and 9 patients (4.1%) died. No significant difference was observed for compared variables in patients with and without COVID-19 except for prednisolone > 20 mg/d (0.64% vs 2.26%; p = 0.048).

Conclusion: Most rheumatic diseases do not seem to be a risk factor for developing COVID-19 infection and despite immunosuppressive therapies, there is no poorer outcome. Only, patients using prednisolone > 20 mg/d are at higher risk of developing COVID-19 infection.

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1. Introduction

Intrinsic immunological changes can produce chronic inflammation in multiple organs in autoimmune inflammatory disorders. The disorders themselves, as well as many of their treatments, are related to a higher risk of developing serious infections [1–4]. There is growing evidence of an association between COVID-19 infection and the development of autoimmune diseases [5] with a remarkable impact on the quality of life of those patients [6].

Whether patients with rheumatic diseases are more vulnerable to coronavirus disease 2019 (COVID-19) infection is still unknown and the possible susceptibility of rheumatic patients for more severe COVID-19 infection or a poorer outcome has raised serious concerns [7]. Several disease modifying anti-rheumatic drugs (DMARDS) with immune-modulating actions such as hydroxychloroquine and tocilizumab may have a therapeutic or preventive effect on the viral infection or the consequent cytokine storm syndrome seen in COVID-19 [8,9]. Patients with rheumatoid arthritis (RA) faced remarkable difficulty to obtain their medications during the pandemic with subsequent change in their disease status [10]. During the pandemic, low dose rituximab is an effective treatment option in the treatment of RA [11].

Patients with systemic rheumatic disease and low rate of acceptability to receive the COVID-19 vaccine, should be encouraged [12] as patient-reported adverse events were typical of those reported in the general population with a relatively low frequency of flare requiring medications [13].

Therefore patients with rheumatic disease represent an interesting study group because, on the one hand, this population is potentially more susceptible to severe COVID-19 infection due to the rheumatic disease and its treatment, on the other hand, many of these patients are receiving immune modulating medications, which have the potential to treat COVID-19 infection and improve prognosis.
The aims of this study were to describe the characteristics, clinical manifestations and outcomes of rheumatic patients diagnosed with COVID-19 infection and to determine the prevalence of COVID-19 infection in the study population and answer to the question whether this specific population have more susceptibility for COVID-19 and poorer outcome.

2. Patients and methods

This study was conducted at the outpatient clinics and inpatient Rheumatology ward of Emam Reza and Golestan Hospitals in Kermanshah, Iran. Between Feb 18 and Aug 22, 2020, data was collected from 1000 patients with rheumatic diseases including systemic lupus erythematosus (SLE) [14], rheumatoid arthritis (RA) [15], psoriatic arthritis (PsA) [16], axial spondyloarthritis (SpA) [17], systemic sclerosis (SSc) [18], Sjögren’s syndrome [19], Behçets disease (BD) [20], vasculitis, idiopathic inflammatory myositis (IM) [21], relapsing polychondritis, sarcoidosis and antiphospholipid syndrome (APS) and all fulfilling their corresponding classification criteria. The local ethics committee approved the study (IR.KUMS.REC.1399.912) conducted in accordance to the Declaration of Helsinki's. Patients provided their informed consent.

Data from patients scheduled for a visit were recorded and a survey conducted by interview and the development of COVID-19 infection since the beginning of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic investigated. The following variables were considered: demographics, type of rheumatic disease and medications used.

A confirmed or highly suspected COVID-19 infection was considered in cases with positive reverse transcription polymerase chain reaction (RT-PCR), chest computerized tomography (CT) findings consistent with COVID-19 pneumonia, elevated levels of serum coronavirus IgM/IgG or those with symptoms and contact history to a patient diagnosed as COVID-19 infection. Patients were divided into those infected or non-infected during six months of the survey.

In cases with COVID-19 the following clinical symptoms were recorded: persistent fever >37.5 °C, malaise, non-productive cough, anosmia, ageusia, headache, loss of appetite, sore throat, diarrhea, abdominal pain, sweating, rhinorrhea, nausea and vomiting, arthritis and arthralgia, deterioration of the rheumatic disease, confusion, hemiplegia, eye redness and skin rash. COVID-19 clinical outcomes were determined by assessing the recovery with and without hospitalization, intensive care admission and death.

Statistical analysis: Statistical Package for the Social Sciences (SPSS) version 25 was used. Variables were reported as frequency, percentage, mean and standard deviation (SD). Mann-Whitney, Chi-square and Fisher’s exact tests were used to compare variables. Odds ratio (OR) with 95% confidence intervals (CI) were determined. Significance was defined at a p < 0.05.

3. Results

One thousand rheumatic diseases patients were studied with a mean age of 43.4 ± 13 years and were 841 (84.1%) females. RA was the most common diagnosis (37.1%), followed by SLE (23.8%), axial SpA (13.4%) and SSc (12.4%). The majority of the patients were on steroids (78.4%) and NSAIDs were used by 50.5%. Patients were taking at least one conventional synthetic disease modifying anti-rheumatic drugs (DMARDs): methotrexate (34.1%), sulfasalazine (21.5%), azathioprine (19.3%), mycophenolate mofetil (13.9%), leflunomide (11.2%), hydroxychloroquine (35.5%) and 16.1% were taking targeted synthetic biologic DMARDs: adalimumab (11%), etanercept (2.4%) and infliximab (2%).

221 (22.1%) were infected with COVID-19. The age of the patients with and without COVID-19 was comparable (43.4 ± 13.3 vs 43.3 ± 11.9 years; p = 0.99). Clinical symptoms, way of diagnosis and clinical outcomes are reported in Tables 1–3. Distribution of rheumatic diseases and medications used between patients with and without COVID-19 infection are presented in Tables 4 and 5.

4. Discussion

Corona virus disease 2019 (COVID-19) is a novel infectious disease with diverse clinical manifestations and a wide range of disease severity. The influence of COVID-19 infection on patients with underlying rheumatic diseases is still not fully revealed. In this work the data of a large observational survey on rheumatic diseases patients with confirmed or highly suspected COVID-19 infection was presented, all of whom were followed up in rheumatology outpatient or inpatient.

A thousand rheumatic diseases patients were investigated and 221 (22.1%) were diagnosed with COVID-19 infection. Of these, 17.2% were hospitalized, 3.6% were admitted to ICU, and 4.1% died. In line, the frequency of COVID-19 infection was not different from that estimated in the reference general population [22]. However, in this survey, only symptomatic rheumatic patients who had at least one positive PCR test for Covid-19, or symptomatic individuals who had close contact with an infected person were considered as COVID-19 infected. Yet, asymptomatic individuals may also be infected and the sensitivity of PCR tests to diagnose the COVID-19 infection is not definitive implying that the presented frequency could be underestimated. The mortality rate was also consistent with the general population [23,24].

Consistent with the current results, up to now, neither rheumatic diseases nor their treatments were associated with higher infection rates or worsening of COVID-19 outcomes [9,25].

A previous study from the United States [26] showed higher rates of ICU admission and the need for mechanical ventilation among hospitalized patients suffering from rheumatic disease.

| Table 1 | Clinical symptoms of rheumatic diseases patients with coronavirus disease 2019 (COVID-19) infection. |
|---------|-----------------------------------------------------------------------------------------------|
| **Clinical symptoms of COVID-19 n (%)** | **RD patients with COVID-19 (n = 221)** |
| Fever | 132 (59.7) |
| Myalgia | 100 (45.2) |
| Chills | 94 (42.5) |
| Dyspnea | 71 (32.1) |
| Malaise | 68 (30.8) |
| Cough | 64 (28.6) |
| Anosmia | 63 (28.5) |
| Ageusia | 55 (24.9) |
| Headache | 41 (18.6) |
| Loss of appetite | 38 (17.2) |
| Sore throat | 25 (11.3) |
| Diarrhea | 25 (11.3) |
| Abdominal pain | 16 (7.2) |
| Sweating | 16 (7.2) |
| Rhinorrhea | 15 (6.8) |
| Vomiting | 13 (5.9) |
| Arthritis/Arthralgia | 8 (3.6) |
| Deterioration of RD | 7 (3.2) |
| Confusion | 1 (0.45) |
| Hemiplegia | 1 (0.45) |
| Eye redness | 1 (0.45) |
| Skin rash | 1 (0.45) |

COVID-19: coronavirus disease 2019; RD: rheumatic disease.
Different types of rheumatic disease compared between patients with and without coronavirus disease 2019 (COVID-19) infection.

| RD n (%) | non COVID-19 (n = 779) | COVID-19 (n = 221) | p   | OR  | 95%CI |
|----------|------------------------|--------------------|-----|-----|-------|
| SLE      | 184 (23.6)             | 54 (24.4)          | 0.8 | 1.1 | 0.7–1.5|
| RA       | 293 (37.6)             | 78 (35.3)          | 0.53| 0.9 | 0.7–1.2|
| SLE/RA (rheumatoid arthritis) | 18 (2.3)            | 4 (1.8)            | 0.65| 0.78| 0.3–2.3|
| SSc      | 100 (12.8)             | 24 (10.9)          | 0.43| 0.83| 0.5–1.3|
| SLE + SSc| 4 (0.5)                | 1 (0.5)            | >0.99| 0.88| 0.1–7.9|
| Axial SpA| 101 (12.9)             | 33 (14.9)          | 0.45| 1.18| 0.8–1.8|
| PsA      | 12 (1.5)               | 8 (3.6)            | 0.06| 2.4 | 0.97–5.9|
| SS       | 6 (0.8)                | 1 (0.5)            | 0.96| 0.59| 0.4–4.9|
| BD       | 19 (2.4)               | 4 (1.8)            | 0.79| 0.74| 0.3–2.2|
| IIM      | 5 (0.6)                | 2 (0.9)            | 0.96| 1.41| 0.3–7.3|
| Vasculitis| 17 (2.2)              | 7 (3.2)            | 0.45| 1.47| 0.6–3.6|
| APS      | 1 (0.1)                | 1 (0.5)            | 0.39| 3.54| 0.2–56.7|
| SLE/APS  | 9 (1.2)                | 1 (0.5)            | 0.59| 0.39| 0.1–3.1|
| SLE/RA/APS | 3 (0.4)              | 0 (0)              | –   | –   | –     |
| RP       | 0 (0)                  | 1 (0.5)            | –   | –   | –     |
| Sarcoidosis| 3 (0.4)              | 0 (0)              | –   | –   | –     |
| SSC + PM | 3 (0.4)                | 0 (0)              | –   | –   | –     |
| SLE + AS | 0 (0)                  | 1 (0.5)            | –   | –   | –     |
| RA + vasculitis| 1 (0.1)          | 1 (0.5)            | –   | –   | –     |

RA: rheumatoid arthritis, SLE: systemic lupus erythematosus, SSc: systemic sclerosis, APS: anti phospholipid syndrome, SpA: axial spondyloarthritis, PsA: psoriatic arthritis, SS: Sjögren’s syndrome, BD: Behcet’s disease, IIM: idiopathic inflammatory myositis, APS: anti-phospholipid syndrome, RP: relapsing polychondritis, PM: polymyositis.
PCR testing. Finally, as mentioned above, we did not consider the asymptomatic patients in this survey.

In conclusion, there is no significant association between type of rheumatic disease or medications and susceptibility to COVID-19 infection except for prednisolone > 20 mg/daily. The mortality rate in rheumatic patients was similar to the general population. Most rheumatic diseases do not seem to be a risk factor for developing COVID-19 infection, and despite immunosuppressive, and immunomodulatory therapies, there is no poorer outcome in these patients. These findings may be important for managing rheumatologic diseases during COVID-19 pandemic.

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The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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