



Characteristics and evolution of 38 patients with rheumatic diseases and COVID-19 under DMARD therapy

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To date, we still have questions about the outcomes of patients with rheumatic inflammatory diseases who develop COVID-19 on disease-modifying antirheumatic drugs (DMARDs) therapy; consequently, efforts to reach conclusions continue. According to the review by Ladani et al. [1], autoimmune rheumatic diseases have not been identified as a risk factor for COVID-19. In like manner, it is expected that some patients with poorly controlled disease may be at increased risk of contracting SARS-CoV-2 infection; hence, they must be encouraged to continue their usual medication. On the other hand, although some therapies used by rheumatologists could potentially confer protection or even limit the serious manifestations of SARS-CoV-2, there is insufficient evidence to establish their safety while the patient is infected [1].

In this study, we report the characteristics and evolution of 38 patients with autoimmune rheumatic diseases from an outpatient rheumatology clinic in Monterrey, Mexico, who developed SARS-CoV-2 infection while on immunosuppressive therapy during July and August 2020.

Most of the patients were female ($n = 33$, 86.84%) and the mean age was 43.47 years (SD 14.58). The most frequent diagnosis was rheumatoid arthritis (RA) with 15 patients (39.47%), followed by systemic lupus erythematosus (SLE) with 13 (34.21%), spondylarthritis with 4 (8.5%), psoriatic arthritis with 3 (6.9%), and systemic sclerosis, Sjogren's syndrome, and systemic vasculitis with one patient each. Diagnosis of COVID-19 was confirmed by reverse

transcription polymerase chain reaction (RT-PCR) in all patients. Regarding immunosuppressive therapy, 29 patients were treated with csDMARDs (76.31%), eleven with bDMARDs (28.94%), and 3 (7.89%) with tsDMARDs (Table 1).

Most of the patients developed mild COVID-19, defined as no requirement of hospitalization or oxygen ($n = 31$, 81.57%); five (13.15%) developed moderate disease (need of hospitalization) of which 3 (7.89%) of them required supplemental oxygen; and two patients (5.26%) had severe COVID-19 (mechanical ventilation or death). None of the patients was treated with antiviral therapy. Among the treatments widely used in Mexico, seventeen patients (44.73%) were treated with azithromycin, and 6 (15.78%) with ivermectin. Sixteen patients (42.60%) continued their usual treatment after acquiring the infection.

One patient underwent orotracheal intubation (a 30-year-old woman with SLE and obesity under treatment with anti-malarials, methotrexate, and corticosteroids), and 1 patient died (65-year-old woman with RA and obesity under treatment with rituximab and leflunomide). The patient who died was the only one in the biologic therapy group that evolved to severe COVID-19. It is important to remark that she had other risk factors for severe COVID-19 including obesity and age. Nonetheless, B-cell depleting therapies like rituximab may be associated to worst outcomes although data is still limited to firmly conclude this [2].

Messina et al. [3, 4] reported the potential benefit of inhibition of the IL-23/IL-17 axis in COVID-19, perhaps preventing the “cytokine storm” which may lead to multiorgan failure and death. In our report, the two patients treated with IL-17 inhibitors (a 35-year-old woman with spondylarthritis treated with secukinumab and a 43-year-old man with psoriatic arthritis with ixekizumab) had a benign evolution of COVID-19. Notably, none of them had comorbidities. The number of patients reported so far receiving

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Table 1 Baseline characteristics of COVID-19 patients

	All patients	Mild COVID-19	Moderate COVID-19	Severe COVID-19
Number of patients	38	31	5	2
Sex, female, <i>n</i> (%)	33 (86.84)	26 (83.87)	5 (100)	2 (100)
Age at COVID-19 onset, median (range)	43.47 (20–82)	42.74 (20–82)	46.40 (30–64)	47.5 (30–65)
Rheumatic disease				
Rheumatoid arthritis, <i>n</i> (%)	15 (39.47)	12 (38.70)	2 (40)	1 (50)
Systemic lupus erythematosus, <i>n</i> (%)	13 (34.21)	9 (29.03)	3 (60)	1 (50)
Psoriatic arthritis, <i>n</i> (%)	3 (7.89)	3 (9.67)	0	0
Systemic sclerosis, <i>n</i> (%)	1 (2.63)	1 (3.22)	0	0
Ankylosing spondylitis, <i>n</i> (%)	4 (10.52)	4 (12.90)	0	0
Systemic vasculitis, <i>n</i> (%)	1 (2.63)	1 (3.22)	0	0
Sjögren's syndrome, <i>n</i> (%)	1 (2.63)	1 (3.22)	0	0
Comorbidities and risk factors				
Diabetes, <i>n</i> (%)	2 (5.26)	2 (6.45)	0	0
Hypertension, <i>n</i> (%)	8 (21.05)	8 (25.80)	0	0
Overweight/obesity, <i>n</i> (%)	17 (44.73)	12 (38.70)	3 (60)	2 (100)
Heart failure, <i>n</i> (%)	1 (2.63)	1 (3.22)	0	0
Smoking, <i>n</i> (%)	1 (2.63)	1 (3.22)	0	0
Corticosteroids, <i>n</i> (%)	17 (44.73)	11 (35.48)	4 (80)	2 (100)
csDMARDs				
Hydroxychloroquine, <i>n</i> (%)	16 (42.60)	13 (41.93)	2 (40)	1 (50)
Methotrexate, <i>n</i> (%)	15 (39.47)	10 (32.25)	4 (80)	1 (50)
Sulfasalazine, <i>n</i> (%)	4 (10.52)	4 (12.90)	0	0
Leflunomide, <i>n</i> (%)	6 (15.78)	5 (16.12)	0	1 (50)
Azathioprine, <i>n</i> (%)	0	0	0	0
Mycophenolate, <i>n</i> (%)	3 (7.89)	3 (9.67)	0	0
Cyclophosphamide, <i>n</i> (%)	0	0	0	0
tsDMARDs				
Baricitinib, <i>n</i> (%)	2 (5.26)	2 (6.45)	0	0
Tofacitinib, <i>n</i> (%)	1 (2.63)	0	1 (20)	0
bDMARDs				
Anti-TNF, <i>n</i> (%)	6 (15.78)	6 (19.35)	0	0
Tocilizumab, <i>n</i> (%)	1 (2.63)	1 (3.22)	0	0
Ixekizumab, <i>n</i> (%)	1 (2.63)	1 (3.22)	0	0
Secukinumab, <i>n</i> (%)	1 (2.63)	1 (3.22)	0	0
Abatacept, <i>n</i> (%)	1 (2.63)	0	1 (20)	0
Rituximab, <i>n</i> (%)	1 (2.63)	0	0	1 (50)
Monotherapy of csDMARDs	5 (13.15)	5 (16.12)	0	0
Monotherapy of tsDMARDs	2 (5.26)	2 (6.45)	0	0
Combination of csDMARDs and bDMARDs/tsDMARDs, <i>n</i> (%)	3 (7.89)	1 (3.22)	1 (20)	1 (50)
Other medications				
ACEi, <i>n</i> (%)	4 (10.52)	4 (12.90)	0	0
ARB, <i>n</i> (%)	4 (10.52)	4 (12.90)	0	0
NSAIDs, <i>n</i> (%)	18 (47.36)	13 (41.93)	4 (80)	1 (50)
Celecoxib, <i>n</i> (%)	6 (15.78)	5 (16.12)	1 (20)	0
Treatment for COVID-19				
Azithromycin, <i>n</i> (%)	17 (44.73)	12 (38.70)	4 (80)	1 (50)
Ivermectin, <i>n</i> (%)	6 (15.78)	6 (19.35)	0	0
Dexamethasone, <i>n</i> (%)	7 (18.42)	2 (6.45)	4 (80)	1 (50)
Convalescent plasma, <i>n</i> (%)	1 (2.63)	0	1 (20)	0

ACEi angiotensin-converting-enzyme inhibitors, ARBs angiotensin II receptor blockers, bDMARDs biologic disease-modifying antirheumatic drugs, csDMARDs conventional synthetic disease-modifying antirheumatic drugs, NSAIDs nonsteroidal anti-inflammatory drugs, RT-PCR reverse transcription polymerase chain reaction, tsDMARDs targeted synthetic disease-modifying antirheumatic drugs

inhibitors of the IL-23/IL-17 signaling axis is too few to draw solid conclusions as many factors including comorbidities, age, and other treatments influence the evolution of COVID-19.

According to Gianfrancesco et al. [5], it was suggested that the use of anti-TNF therapy could influence a lower incidence of hospitalization. In our population, all patients with anti-TNF therapy had mild disease.

Compared to a general population study from southeastern Europe [6], we had more hospitalized patients receiving steroids; however, similar recovery rates were obtained (85.71 vs. 87.7%). This highlights the role of steroids as a treatment for SARS-CoV-2 infection in patients with exaggerated immune responses [7].

Our results are similar to those reported by Duret et al. [8] and the use of DMARDs does not seem to contribute to an unfavorable evolution of COVID-19. Rheumatologists however should pay special attention to the use of rituximab as, due to its distinct mechanism of action, may be associated to complications and a worse outcome in SARS-CoV-2 infection. Limitations of our present report include the single-center design and the limited number of patients. As evidence continues to accumulate, the impact of different DMARDs in the evolution of COVID-19 starts to become clearer.

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Data sharing statement Additional data will be shared if needed by the corresponding author by e-mail.

Compliance with ethical standards

Disclosures None.

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References

- Ladani AP, Loganathan M, Danve A (2020) Managing rheumatic diseases during COVID-19. *Clin Rheumatol*. 39(11):3245–3254. <https://doi.org/10.1007/s10067-020-05387-8>
- Schulze-Koops H, Krueger K, Vallbracht I et al (2020) Increased risk for severe COVID-19 in patients with inflammatory rheumatic diseases treated with rituximab. *Ann Rheum Dis*. <https://doi.org/10.1136/annrheumdis-2020-218075>
- Messina F, Pampaloni F, Piaserico S (2020, 2020) Comment on: recovery from COVID-19 in a patient with spondyloarthritis treated with TNF-alpha inhibitor etanercept. A report on a patient with COVID-19 with psoriatic arthritis receiving ustekinumab. *Ann Rheum Dis*. <https://doi.org/10.1136/annrheumdis-2020-218029>
- Messina F, Piaserico S (2020) SARS-CoV-2 infection in a psoriatic patient treated with IL-23 inhibitor. *J Eur Acad Dermatol Venereol* 34(6):e254–e255. 1-2. <https://doi.org/10.1111/jdv.16468>
- Gianfrancesco M, Hyrich KL, Al-Adely S et al (2020) Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 79(7):859–866. <https://doi.org/10.1136/annrheumdis-2020-217871>
- Popov GT, Baymakova M, Vaseva V et al (2020, 2020) Clinical characteristics of hospitalized patients with COVID-19 in Sofia, Bulgaria. *Vector Borne Zoonotic Dis*. <https://doi.org/10.1089/vbz.2020.2679>
- Galluccio F, Ergonenc T, Garcia-Martos A et al (2020) Treatment algorithm for COVID-19: a multidisciplinary point of view. *Clin Rheumatol* 39(7):2077–2084. <https://doi.org/10.1007/s10067-020-05179-0>
- Duret PM, Spielmann L, Messer L (2020, 2020) Rheumatic diseases and COVID-19: a cohort of 17 patients under DMARDs. Response to: Comment on: Recovery from COVID-19 in a patient with spondyloarthritis treated with TNF-alpha inhibitor etanercept. A report on a COVID-19 patient with psoriatic arthritis receiving ustekinumab by Messina et al. *Ann Rheum Dis*. <https://doi.org/10.1136/annrheumdis-2020-218147>

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