

Prevalence of Coronavirus Disease 2019 in Rheumatic Patients and Evaluation of The Effect of Disease-Modifying Anti-Rheumatic Drugs

Soroush Moradi

TUMS

Somayeh Mohammadi

University of Medical Sciences and Health Services

Jamshid Vafaeimanesh

Qom University of Medical Sciences

Mohaddeseh Mohseni

Qom University of Medical Sciences and Health Services, Qom, Iran

Hossein Mahdavi

Shahid Beheshti University of Medical Sciences

Armin Aryannejad

Tehran University of Medical Sciences

Maryam Masoumi (✉ m.masoumi@gmail.com)

Clinical Research and Development Center, Qom University of Medical Sciences and Health Services,
Qom, Iran <https://orcid.org/0000-0003-2635-2656>

Research Article

Keywords: COVID-19, SARS-CoV-2, Rheumatic Diseases, DMARDs

Posted Date: July 27th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-44445/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at Internal and Emergency Medicine on October 31st, 2020. See the published version at <https://doi.org/10.1007/s11739-020-02535-5>.

Abstract

Background: One of the most controversial issues among rheumatologists is the best approach to managing a rheumatic patient (RP) with coronavirus disease 2019 (COVID-19).

Objectives: This study aims to evaluate the prevalence of COVID-19 in RPs and compare it to the general population (healthy individuals). Besides, it assesses the incidence of COVID-19 based on rheumatologic diseases (RDs) categories and immunosuppressive (IS) drug history.

Methods: In a cross-sectional study, all RPs of the rheumatology clinic of Shahid Beheshti Hospital, Qom, Iran were included (the case group), and the prevalence of COVID-19 was compared to that in healthy individuals (the control group), between December 1, 2019, and February 29, 2020. Qom city was the first city in Iran in which COVID-19 was identified and spread rapidly. The participants were recruited from hospital records for the case group and Qom Health Network's database for the control group.

Results: The prevalence of COVID-19 is significantly less in RPs than in the healthy population.

Moreover, patients who were under treatment with biologic disease-modifying anti-rheumatic drugs (DMARDs) and IS drugs had milder symptoms in the case of COVID-19. Two RPs died from COVID-19, both of whom had granulomatosis and polyangiitis (GPA).

Conclusion: The prevalence of COVID-19 in the RPs was lower than the general population, which was determined to be associated with more adherence to the quarantine and social distancing rules by RPs. Besides, using leflunomide (a DMARD) and IS drugs might have a protective effect against severe COVID-19.

Introduction

The global risk for the coronavirus disease 2019 (COVID-19) was assessed by World Health Organization (WHO) as very high; it was then considered as a pandemic that affected more than two million people worldwide [1]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mainly involves the lungs and shows typical patterns in the chest high-resolution computed tomography (HRCT) images, such as ground-glass opacity and consolidation [2]. There is no specific treatment option available yet for COVID-19; however, some potential drugs were considered to have a beneficial effect in treating patients with COVID-19, including some antibiotics and antivirals [3] as well as angiotensin-converting enzyme (ACE) inhibitors, hydroxychloroquine, and a disease-modifying anti-rheumatic drug (DMARD) [4-6].

During the outbreak, one of the most controversial issues among rheumatologists is the best approach to managing a rheumatic patient (RP) with COVID-19. Many rheumatologists state that patient's drugs should not be discontinued or reduced because of increasing the risk of disease flare-up and leading to uncontrolled rheumatic disease (RD) [7]. Nevertheless, some may consider reducing the doses of some drugs, such as prednisolone, cautiously, or even discontinue the therapy in the case of SARS-CoV-2 infection [8]. As mentioned earlier, some drugs which are commonly used in the treatment of RD has also been considered as potential candidates for COVID-19 treatment, based on recent studies, including chloroquine, hydroxychloroquine, leflunomide, tumor necrosis factor (TNF) inhibitors, Janus kinase (JAK) inhibitors, interleukin antagonists, and even corticosteroids [6,7]. In addition, there are controversial views on the use of the immunosuppressive (IS) drugs as well as their potential risks in RPs during the COVID-19 outbreak, and they should be addressed.

The current study aims to firstly evaluate the prevalence of COVID-19 in RPs and compare it to the prevalence of SARS-CoV-2 infection in healthy individuals without any history of immunodeficiencies or immunosuppressive therapies. Secondly, this study assesses the prevalence of COVID-19 in different subgroups of RD as well as RPs with a history of taking IS drugs. The results of this study could provide evidence to help to resolve the controversy regarding the use of IS drugs in RPs during the COVID-19 outbreak.

Materials And Methods

Study design

In a cross-sectional study, RPs who were coming routinely for follow ups to the rheumatology clinic of Shahid Beheshti Hospital (Qom University of Medical Sciences, Qom, Iran)—the case group. and the healthy healthy individuals residing in Qom, Iran (the control group) were enrolled. The prevalence of COVID-19 was assessed in these two major groups. The subgroups of RDs and IS drug history was also assessed and compared to each other. The study protocol was implemented based on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [9] and was approved by the Qom University of Medical Sciences and Health Services' Research and Ethics Committee.

Setting and Data Source

The data of the patients of rheumatology clinic between December 1, 2019 and February 29, 2020, was obtained from the Shahid Beheshti Hospital records. For the control group, the data was collected from the records of the Qom Health Network, in the same manner as the case group. For the control group, residents of Qom were telephoned, and a survey of the signs, symptoms, exposure, and any history of COVID-19 was conducted. Besides, records of Qom Health Network for each person regarding the most recent hospital admission, clinical data, imaging and laboratory results, and history of COVID-19 and treatment were collected. The patient selection from the records was blinded utilizing the record number distribution in the period of the study.

Participants

To increase the power of analysis, the recruitment process resulted in 249 patients from the rheumatology clinic as the case group, and 207 residents of Qom city, categorized as the control group. The eligibility criteria comprised all patients of the rheumatology clinic, having an updated hospital record from December 1, 2019, to February 29, 2020, and residents of Qom city, who have been called by and had a record in Qom Health Network in the same date range. The recruitment of the control group was a blinded process in which participants were selected randomly from the records only using the record number—the other data were not visible to the selectors. For the case group, all eligible patients were included.

Variables

The demographic variables as well as the participants' history of RD, hypertension, diabetes, hyperlipidemia, thyroid disorders, pulmonary disease, and cardiovascular disorders were included. Also, the symptoms of patients in the study time comprising cough, hemoptysis, shortness of breath, fever, chills, headache, myalgia, malaise, diarrhea, nausea, vomiting, constipation, abdominal pain, anosmia, sore throat, and sneezing were evaluated. Moreover, the participants' history of admission, imaging, COVID-19, and any treatments for that were included. The subgroups for the case group were categorized based on the type of their RDs and the pharmacological/complementary treatments which they received. The diagnostic criteria for COVID-19 stood on the national guidelines of the Ministry of Health of the Islamic Republic of Iran, mainly by the signs and symptoms and chest computed tomography (CT) scan; in the non-conclusive results of the latter, the reverse transcription polymerase chain reaction (RT-PCR) test was considered.

Bias

The selection bias has been minimized by blinded recruitment for the control group. To reduce potential sources of bias the data were extracted after the selection of participants. The skilled staff of Qom Health Network performed the data gathering through telephone calls while they were completely unaware of this study.

Study Size

Because of the pandemic situation but uncommonness of COVID-19 (with an estimated prevalence of 0.025% by the Ministry of Health), the sample size calculated by the conventional protocols was unachievably large. Thus, to increase the test power, all 249 patients of the rheumatology clinic were included in the case group and 207 residents of Qom city in the control group.

Statistical Methods

The software used for statistical analysis was IBM SPSS Statistics for Windows, version 26.0 (IBM Corporation, Armonk, NY, USA). Descriptive analyses for all variables in all participants were performed

and presented. To compare categorical data, Fisher's exact test was executed, and a t-test was used to compare the means. All confidence intervals were set to 95%. Statistical significance was considered as $p < 0.05$.

Results

Participants

All records of the referred patients, as well as followed-up cases of the rheumatology clinic from December 1, 2019, to February 29, 2020, consisting of 249 RPs, were included in the case group. The records of Randomly-selected 207 residents of Qom city, who were followed up by phone calls from the Qom Health Network within the same days, were included in the control group.

Descriptive Data

Of 249 RPs, 194 persons were female (77.9%), and 55 persons were male (22.1%); among 207 participants of the control group, 157 were female (75.8%), and 50 were men (24.2%). No significant difference between the sex composition between the groups was found ($p = 0.655$). The mean age for the case group was 50.2 ± 13.1 years and 47.7 ± 14.4 years for the control group; the unpaired t-test did not show a statistically significant difference regarding age ($p = 0.058$). All demographic characteristics, comorbidities, symptoms, as well as any history of hospital admissions and COVID-19 for the participants are summarized in Table 1. Also, the detailed number of patients by their RD could be found in Table 2. The prevalence of hypertension in the case group (26.9%) was significantly higher ($p = 0.018$) than the control group (17.4%). The same was applied to hypothyroidism ($p < 0.001$); in contrast, the prevalence of hypothyroidism was significantly higher in the control group ($p = 0.034$). Regarding the symptoms, malaise, constipation, and sneezing were significantly more frequent in the control group ($p = 0.001$, 0.026, and 0.042, respectively). Vomiting, however, markedly occurred more in the case group ($p = 0.008$). In the case of RDs, rheumatoid arthritis was the most prevalent disorder (80.3%) followed by systemic lupus erythematosus (7.2%), granulomatosis with polyangiitis (GPA; formerly known as Wegener's disease) (3.6%), anti-phospholipid syndrome (2.8%), and ankylosing spondylitis (2.4%). The history of taking IS drugs and the three most frequently used supplements (folic acid, vitamin D₃, and calcium) in the case group are summarized in Table 3.

Main Results

The data showed that 9 out of 249 RPs (3.6%) and 18 out of 207 residents of Qom (8.7%) were diagnosed with COVID-19 (Table 1). The prevalence in the control group was significantly higher than that in RPs ($p = 0.028$). A chest HRCT with the patterns suggestive of COVID-19 was also significantly more common in the control group (2.8% in comparison to 8.7%; $p = 0.007$). While eight patients (3.9%) in the control group had a positive RT-PCR for SARS-CoV-2, no positive results were obtained in the case group ($p = 0.002$). Besides, two out of the RPs (0.8%) died because of COVID-19; however, no deaths were

recorded in the control group ($p = 0.503$). It is noteworthy that both patients who died from COVID-19 were among the patients with GPA (Table 2).

In the case of IS therapy, 202 of 249 patients (81.1%) were receiving prednisolone, and 132 patients (53.0%) were using methotrexate. Eight of the patients who received prednisolone (3.2%) and two of the patients who received methotrexate (0.8%) were diagnosed with COVID-19. Moreover, both the above-mentioned death cases, who had a GPA, had received prednisolone and cyclophosphamide; one of them also had received rituximab. Of 108 patients (43.4%) receiving hydroxychloroquine as an immunomodulator for their RDs, one patient (0.4%) was using 50 mg/day, eighty-one patients (32.5%) were using 200 mg/day; two (8.3%), twenty-three (46.9%), and one patient (0.4%) were using 300 mg/day, 400 mg/day, and 600 mg/day, respectively. Three of the mentioned patients (1.2%) had COVID-19 and manifested lung involvement. Notably, none of the 25 patients who were receiving adalimumab or infliximab (10.0% of total patients), and none of the 24 patients (9.6%) who received leflunomide were diagnosed with COVID-19. Among the patients receiving alendronic acid, sulfasalazine, cyclophosphamide, and rituximab, the prevalence of COVID-19 was 0.4%, 0.8%, 0.8%, and 0.4%, respectively.

Discussion

The prevalence of COVID-19 was assessed among the RPs and compared to the randomly-selected healthy group of the general population. The prevalence of COVID-19 was significantly higher in the control group than RPs. Based on the subgroups of RDs, 80.3% of patients in the case group had rheumatoid arthritis, among which 2.8% were diagnosed with COVID-19. Moreover, two patients in the case group died because of COVID-19, both of whom suffered from GPA. Still, no one died from COVID-19 in the control group. Regarding IS therapy, 81.1% of RPs were receiving prednisolone, and only 3.2% were diagnosed with COVID-19.

The lower prevalence of COVID-19 in the RPs than the healthy population could be associated with two factors. Firstly, it should be mentioned that the nature of the RDs and their treatment—consisting of IS drugs—forced the patients to adhere more strictly to the quarantine and social distancing rules; most of the patients included in our study were suggested by their rheumatologist to take precautions more seriously. Secondly, using hydroxychloroquine and leflunomide as DMARDs in the treatment of RDs might also have a protective effect against COVID-19, as mentioned in recent studies [10,11].

Hydroxychloroquine had had promising in vitro assessments of its effectiveness [12], and leflunomide was determined to inhibit the T cell proliferation [7]; both drugs were considered candidates for the treatment of COVID-19 based on previous studies. It is worth noting that 43.4% of the patients were receiving hydroxychloroquine daily, and 9.6% were receiving leflunomide in our study, and the lower prevalence of COVID-19 in these patients might be associated with it. No doubt that more studies are needed to evaluate this probable protective effect.

Of nine patients with GPA, a rare RD, eight were immunosuppressed extensively by prednisolone and cyclophosphamide, and even in two of the patients, the immunosuppression was also accompanied by azathioprine. One of the two death cases also received rituximab. Although this treatment regimen is a typical drug regimen in GPA patients, it might make the patient more susceptible to viral infections due to extensive bone marrow and immunosuppression [13]. The death of two GPA patients from COVID-19 might be associated with this extreme immune system suppression. Thus, the GPA patients should be advised to adhere to the quarantine and social distancing rules more intensively than other RPs during the COVID-19 outbreak.

COVID-19 is associated with a cytokine storm that involves T-helper-1. A higher concentration of TNF- α as well as other cytokines in critically ill patients, demonstrated a positive correlation between the severity of the infection and the cytokine storm [14]. In our study, RPs— especially patients who were under treatment with leflunomide and other biologic agents—experienced milder COVID-19 symptoms. Although treatment with these agents could put the patients at a higher risk for COVID-19, symptoms manifested milder than the others. So, these drugs might be useful in reducing the severity of COVID-19 [15].

Our study showed that leflunomide and other DMARDs and biologic agents might prevent RPs from severe infections with SARS-CoV-2; however, they could make RPs more susceptible to mild COVID-19 symptoms. More studies are needed to be conducted on the effect of different IS drugs in preventing patients from severe infections with SARS-CoV-2 in order to address the controversial views on the use of IS drugs for RPs as well as non-rheumatic patients. The experience gained from previously emerged epidemics, such as severe acute respiratory syndrome, would also be helpful [16].

This study indeed had some limitations; the main limitation was that the assumed prevalence for COVID-19 at the time of the study was very little. The approach to this issue would be similar to rare conditions. So, the conventional methods of sample size calculation would result in huge numbers, while this study could not be performed on a larger scale. In order to address this issue, all the patients of the rheumatology clinic were included as much as it was possible. Besides, assessment of the effects of IS drugs in healthy individuals was not in the scope of our study; however, it would make any probable protective effects clearer.

In summary, the results of our study showed that COVID-19 was not more prevalent among patients with RDs than the general population. Nevertheless, the number of deaths was significantly higher among RPs with COVID-19 than the general population. Deaths occurred in RPs who were suffering from GDA, a rare RD. IS drugs could not cause severe infections in RPs; on the contrary, some RPs receiving IS agents even experienced milder symptoms in the case of SARS-CoV-2 infection. So, these agents might have a protective effect on RPs against COVID-19. Further studies need to be conducted to assess the effect of IS agents on COVID-19 in RPs as well as healthy individuals.

Declarations

Conflict of Interests

The authors of this study declare that there is no conflict of interests.

Author Contributions

All authors contributed equally to this study. The authors agreed on the protocol to be implemented and the final manuscript to be published.

Acknowledgments

None

Funding

This study was funded by Qom University of Medical Sciences and Health Services, Qom, Iran. The university had no role in any of the study steps.

Ethical Approval Information

The study protocol was approved and implemented under the supervision of Qom University of Medical Sciences' Research and Ethics Committee.

Data Availability

All data would be available on request.

Abbreviations

COVID-19, coronavirus disease 2019; **CT**, computed tomography; **DMARD**, disease-modifying anti-rheumatic drug; **GPA**, granulomatosis with polyangiitis; **HRCT**, high-resolution computed tomography; **IS**, immunosuppressive; **RD**, rheumatic disease; **RP**, rheumatic patient; **RT-PCR**, reverse-transcription polymerase chain reaction; **SARS-CoV-2**, severe acute respiratory syndrome coronavirus 2; **TNF**, tumor necrosis factor.

References

1. Organization WH (2020) Coronavirus Disease 2019 Situation Reports.
2. Diao K, Han P, Pang T, Li Y, Yang Z (2020) HRCT imaging features in representative imported cases of 2019 novel coronavirus pneumonia. *Precision Clinical Medicine* 3 (1):9-13
3. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, Wang W, Song H, Huang B, Zhu N (2020) Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *The Lancet* 395 (10224):565-574

4. Liu J, Cao R, Xu M, Wang X, Zhang H, Hu H, Li Y, Hu Z, Zhong W, Wang M (2020) Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro. *Cell discovery* 6 (1):1-4
5. Pires da Rosa G, Ferreira E (2020) Therapies used in rheumatology with relevance to coronavirus disease 2019. *Clinical and experimental rheumatology* 38 (2):370
6. Sarzi-Puttini P, Giorgi V, Sirotti S, Marotto D, Ardizzone S, Rizzardini G, Antinori S, Galli M (2020) COVID-19, cytokines and immunosuppression: what can we learn from severe acute respiratory syndrome? *Clinical and experimental rheumatology* 38 (2):337-342
7. Ferro F, Elefante E, Puxeddu I, Baldini C, Bartoloni E, Baratè C, Galimberti S, Talarico R, Mosca M, Bombardieri S (2020) COVID-19: the new challenge for rheumatologists. First update. *Clinical and experimental rheumatology* 38 (3)
8. Misra DP, Agarwal V, Gasparyan AY, Zimba O (2020) Rheumatologists' perspective on coronavirus disease 19 (COVID-19) and potential therapeutic targets. *Clinical Rheumatology*:1-8
9. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP (2007) The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Annals of internal medicine* 147 (8):573-577
10. Kearney J (2020) Chloroquine as a potential treatment and prevention measure for the 2019 novel coronavirus: a review.
11. Zhou D, Dai S-M, Tong Q (2020) COVID-19: a recommendation to examine the effect of hydroxychloroquine in preventing infection and progression. *Journal of Antimicrobial Chemotherapy*
12. Kapoor KM, Kapoor A (2020) Role of Chloroquine and Hydroxychloroquine in the Treatment of COVID-19 Infection-A Systematic Literature Review. *Medrxiv*
13. Khan A, Elahi F, Hashmi S, Mahida K, Ingrams D (2006) Wegener's granulomatosis: a rare, chronic and multisystem disease. *The Surgeon* 4 (1):45-52
14. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet* 395 (10223):497-506
15. Bashyam AM, Feldman SR (2020) Should patients stop their biologic treatment during the COVID-19 pandemic. *J Dermatolog Treat* 19:1-2
16. Vincent MJ, Bergeron E, Benjannet S, Erickson BR, Rollin PE, Ksiazek TG, Seidah NG, Nichol ST (2005) Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. *Virology journal* 2 (1):1-10

Tables

Table 1. Demographic characteristics, comorbidities, symptoms, history of hospital admission, and COVID-19 involvement for all participants

Variables		Rheumatic patients		Residents of Qom		P value
		Number	%	Number	%	
Participants		249	100%	207	100%	-
Sex	Female	194	77.9%	157	75.8%	0.655
	Male	55	22.1%	50	24.2%	
Comorbidity	Hypertension	67	26.9%	36	17.4%	0.018
	Diabetes	43	17.3%	36	17.4%	1.000
	Hyperlipidemia	37	14.9%	24	11.6%	0.336
	Hypothyroidism	43	17.3%	13	6.3%	<0.001
	Hyperthyroidism	6	2.4%	0	0.0%	0.034
	Cardiovascular disease	29	11.6%	20	9.7%	0.545
Symptoms	Dry cough	21	8.4%	23	11.1%	0.344
	Productive cough	5	2.0%	2	1.0%	0.464
	Hemoptysis	0	0.0%	0	0.0%	1.000
	Shortness of breath	19	7.6%	11	5.3%	0.349
	Fever	21	8.4%	13	6.3%	0.475
	Chills	25	10.0%	11	5.3%	0.080
	Headache	22	8.8%	15	7.2%	0.607
	Myalgia	23	9.2%	19	9.2%	1.000

	Malaise	7	2.8%	23	11.1%	0.001
	Diarrhea	2	0.8%	5	2.4%	0.253
	Nausea	13	5.2%	11	5.3%	1.000
	Vomiting	11	4.4%	1	0.5%	0.008
	Constipation	1	0.4%	7	3.4%	0.026
	Abdominal pain	11	4.4%	9	4.3%	1.000
	Anosmia	16	6.4%	19	9.2%	0.293
	Sore throat	4	1.6%	5	2.4%	0.738
	Sneezing	0	0.0%	4	1.9%	0.042
	History of hospital admission	10	4.0%	5	2.4%	0.433
COVID-19	COVID-19 patients	9	3.6%	18	8.7%	0.028
	HRCT involvement	7	2.8%	18	8.7%	0.007
	Any chest imaging involvement	3	1.2%	3	1.4%	1.000
	Positive RT-PCR	0	0.0%	8	3.9%	0.002
	Negative RT-PCR	2	0.8%	2	1.0%	1.000
	Intubation	1	0.4%	0	0.0%	1.000
	O ₂ therapy	5	2.0%	6	2.9%	0.557
	Treatment for COVID-19	4	1.6%	17	8.2%	0.001

Death by COVID-19	2	0.8%	0	0.0%	0.503
-------------------	---	------	---	------	-------

COVID-19, coronavirus disease 2019; HRCT, high-resolution computed tomography; RT-PCR, reverse transcription polymerase chain reaction

Table 2. Rheumatic diseases of the case group

Disease	Number	%	Positive COVID-19	
			Number	%
Adult-onset Still's disease	2	0.8%	0	0.0%
Anti-phospholipid syndrome	7	2.8%	0	0.0%
Anti-phospholipid syndrome + systemic lupus erythematosus	1	0.4%	0	0.0%
Ankylosing spondylitis	6	2.4%	0	0.0%
Ankylosing spondylitis in inflammatory bowel disease	1	0.4%	0	0.0%
Dermatomyositis	1	0.4%	0	0.0%
Osteoporosis + osteoarthritis	1	0.4%	0	0.0%
Psoriatic arthritis	3	1.2%	0	0.0%
Psoriasis	1	0.4%	0	0.0%
Rheumatoid arthritis	200	80.3%	7	2.8%
Rheumatoid arthritis + Osteoporosis	1	0.4%	0	0.0%
Sarcoidosis	2	0.8%	0	0.0%
Sjögren syndrome	2	0.8%	0	0.0%
Systemic lupus erythematosus	18	7.2%	0	0.0%
Systemic sclerosis	3	1.2%	0	0.0%
Granulomatosis with polyangiitis (Wegener's disease)	9	3.6%	2	0.8%

Total	249	100.0%	9	3.6%
-------	-----	--------	---	------

COVID-19, coronavirus disease 2019

Table 3. Immunosuppressive drugs and supplements in rheumatic patients

Drug	Number	%	Positive COVID-19	
			Number	%
Adalimumab	24	9.6%	0	0.0%
Alendronic acid	39	15.7%	1	0.4%
Azathioprine	14	5.6%	0	0.0%
Calcium supplement	36	14.5%	0	0.0%
Cyclophosphamide	9	3.6%	2	0.8%
Cyclosporine	1	0.4%	0	0.0%
Etanercept	1	0.4%	0	0.0%
Folic acid	15	6.0%	0	0.0%
Hydroxychloroquine	108	43.4%	3	1.2%
Infliximab	2	0.8%	0	0.0%
Leflunomide	24	9.6%	0	0.0%
Methotrexate	132	53.0%	2	0.8%
Mycophenolate	9	3.6%	0	0.0%
Prednisolone	202	81.1%	8	3.2%
Rituximab	2	0.8%	1	0.4%
Sulfasalazine	38	15.3%	2	0.8%

Vitamin D3	25	10.0%	1	0.4%
Zolendronic acid	1	0.4%	0	0.0%

COVID-19, coronavirus disease 2019