ORIGINAL ARTICLE

RQ Rheumatology Quarterly

DOI: 10.4274/qrheumatol.galenos.2022.43534
Rheumatology Quarterly

THE COURSE AND OUTCOMES OF COVID-19 IN PATIENTS WITH TAKAYASU ARTERITIS: CASE SERIES OF 15 PATIENTS FROM A TERTIARY SINGLE CENTER

Gizem Sevik, Seda Kutluğ Ağaçkıran, Kerem Yiğit Abacar, Alida Aliyeva, Haner Direskeneli, Fatma Alibaz Öner

Marmara University Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, İstanbul, Turkey

Abstract

Aim: Coronavirus disease-2019 (COVID-19) has affected more than three hundred million individuals, and many risk factors for increased mortality and morbidity in COVID-19 have been defined. There are many studies evaluating the course of COVID-19 in inflammatory rheumatic diseases, however, fewer data are available for patients with Takayasu arteritis (TAK). This study assessed the characteristics and outcomes of TAK patients with COVID-19.

Material and Methods: A phone survey was conducted among TAK patients that are followed up in our clinic between February 2021 and March 2021. All patients were asked whether they were diagnosed with COVID-19 during the pandemic. The patients who had a history of COVID-19 were asked about the symptoms, hospitalization status, and treatment received for COVID-19. Information about their chronic diseases was obtained from the patient files.

Results: Among 118 TAK patients, 15 had COVID-19 during the first year of the pandemic; 13 were female, and the mean age was 42.5±12.04 years. Nine of the patients were taking prednisone therapy, 12 were taking conventionally synthetic disease-modifying antirheumatic drugs (csDMARDs), 7 patients were taking biological disease-modifying antirheumatic drugs (bDMARDs), and 5 patients were taking a combination of csDMARD and bDMARD therapy when they were diagnosed with COVID-19. Two patients were hospitalized, and one of them was admitted to the intensive care unit for 5 days. All the patients fully recovered, and there was no mortality related to COVID-19.

Conclusion: Our data suggest that there is no increased risk for morbidity or mortality related to COVID-19 in TAK patients.

Keywords: Takayasu arteritis, COVID-19, SARS-CoV-2

INTRODUCTION

Patients with inflammatory rheumatic diseases (iRMD) receiving immunosuppressive therapy have an increased risk of severe infections (1,2). Since the start of the coronavirus disease-2019 (COVID-19) pandemic, a significant concern among rheumatologists has been raised.

Recent studies have evaluated the severity of COVID-19 in patients with iRMD, and it has been reported that glucocorticoid use is associated with severe disease (3-5). Also, the risk factors for severe COVID-19 in patients with iRMD were identified as risk factors in the general population, such as male gender, older age, hypertension, and obesity (6). Strangfeld et al. (7) reported

Address for Correspondence: Gizem Sevik, Marmara University Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, İstanbul, Turkey **Phone:** +90 533 515 33 63 **E-mail:** gizemseven@gmail.com **ORCID ID:** orcid.org/0000-0003-2941-4381
Received: 30.08.2022 **Accepted:** 29.11.2022

that higher disease activity, higher dosages of glucocorticoids, and immunosuppressant use were associated with COVID-19 related death. Currently, there is no large study that is specifically evaluating the impact of COVID-19 among Takayasu arteritis (TAK) patients. In a case report, two TAK patients had a full recovery from COVID-19 and did not require hospitalization (8). In another published report, four TAK patients had confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, and 1 of them who had multiple comorbidities died (9). This study assesses the outcome of COVID-19 in patients with TAK.

MATERIAL AND METHODS

This case series includes patients with TAK and confirmed SARS-CoV-2 infection by a positive real-time polymerized chain reaction (RT-PCR) test from the nasopharyngeal swab between March 2020 and March 2021. A phone survey was conducted between February 2021 and March 2021 among TAK patients that are followed up at our clinic to ask whether they had confirmed SARS-CoV-2 infection during the pandemic.

Demographic characteristics, comorbidities, disease duration, disease status at the last visit, and patient medications were recorded from the patient files. The patients were asked about the time of the COVID-19 diagnosis, contact with a COVID-19 patient, symptoms, hospital admission status, immunosuppressive medication use during infection, and the treatment received for COVID-19.

The study protocol was approved by the Institutional Review Board (no: 09.2021.850) and carried out following the Declaration of Helsinki. All patients provided consent for the use of their clinical and demographic data.

Statistical Analysis

Statistical analysis was performed using SPSS version 22.0 (IBM Corp, Armonk, NY). Results were expressed as mean and standard deviation for parametric data, and frequency (%) for categorical data.

RESULTS

A total of 118 patients with TAK could be contacted by phone and included in the study. Among them, 15 patients with TAK had a SARS-CoV-2 infection confirmed by an RT-PCR test from the nasopharyngeal swab, and 2 of them also had suggestive thoracic computed tomography (CT) scans. All the patients had the infection before the COVID-19 vaccination. The mean age of the patients was 42.50±12.04 years, and 13 (86.6%) of them were female. The mean body mass index of the patients was 25.70±4.96 kg/m^2, and 3 of them were obese. Nine of the patients were taking prednisone therapy during infection, and 3 of them were using a dosage of ≥10 mg/day. Twelve patients were taking conventionally synthetic disease-modifying antirheumatic drugs (csDMARDs), seven were taking biological disease-modifying antirheumatic drugs (bDMARDs), and five were taking a combination of csDMARD and bDMARD therapy. Three of the patients taking bDMARDs were using tocilizumab, two were using adalimumab, and two were using infliximab therapy. One patient was in remission and was not using any immunosuppressive treatment for five years. During the last rheumatology visit 6 months before the diagnosis of COVID-19, 4 of the patients were accepted to have active disease, and 3 of them were taking moderate to high dose glucocorticoids during the infection period. The demographic and clinical characteristics of the patients are shown in Table 1.

All the patients stopped taking their immunosuppressive medications, except glucocorticoids, during COVID-19.

Close contact history with a COVID-19 patient was present in 7 patients. The most common symptom was fatigue, followed by cough and fever. Pneumonia was detected on thoracic CT scans in 2 patients, and both of them were hospitalized. The other patients had a non-severe disease, and a chest X-ray or thoracic CT scan was not performed.

COVID-19 treatment guidelines defined by the Ministry of Health of Turkey have recommend favipiravir as a first-line treatment agent to all patients with a confirmed COVID-19 diagnosis (10). Therefore, all 15 patients had used favipiravir treatment at a dosage of 1,600 mg twice daily on day 1, 600 mg twice daily on days 2-5.

Two of the 15 patients required hospital admission. One of them was taking infliximab 300 mg/6 weeks (the last infusion was 4 weeks ago), methotrexate 15 mg/week, and prednisone 5 mg/day for TAK when COVID-19 diagnosis was confirmed and hospitalized for 5 days and followed up with nasal oxygen and did not require admission to intensive care unit (ICU) or mechanical ventilation. The patient was given favipiravir, dexamethasone 6 mg/day, enoxaparin 4,000 IU/day, and one plasma exchange therapy during hospitalization.

The other patient who was taking leflunomide 20 mg/day and prednisone 7.5 mg/day for TAK was admitted to the hospital for a severe asthma attack and had a fever after the first week of hospitalization, and COVID-19 diagnosis was confirmed. She was hospitalized for 30 days and required ICU admission and non-invasive mechanical ventilation for 4 days because to comorbidities, including severe asthma and chronic thromboembolic pulmonary hypertension.

Table 1. Clinical features of Takayasu arteritis patients with confirmed COVID-19

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Demographics								
Age (years)	65	46	21	31	49	38	50	46
Gender	Female	Female	Female	Female	Female	Female	Male	Female
Comorbidities	DM	HT	None	None	None	HT	None	CVD
Body mass index (kg/m^2)	23.62	34.85	21.37	29.76	31.23	28.13	23.63	26.67
Disease characteristics								
Disease duration (months)	96	8	48	72	60	36	14	130
Disease activity at last visit	Active	Inactive	Inactive	Active	Inactive	Inactive	Inactive	Inactive
Prednisone, mg/day	None	2.5	None	15	5	5	5	None
csDMARD	MTX 15mg/week	MTX 15 mg/week	None	AZA 2x50 mg	MTX 15mg/week	AZA 2x50 mg	AZA 3x50 mg	None
bDMARD	None	None	TOC 162 mg/week	ADA 40 mg/2 weeks	INF 300 mg/6 weeks	INF 400 mg/8 weeks	ADA 40 mg/2 weeks	None
COVID-19 infection								
Symptoms	Fatigue, headache	Fatigue	Fatigue, fever, cough	Fatigue, cough	Fatigue, fever, cough	Fatigue, cough	None	Fever, diarrhea
Contact with COVID-19 patient	None	Yes	Yes	None	None	Yes	Cough	Yes
Treatment for COVID-19	HCQ Favipiravir	Favipiravir	Favipiravir	Favipiravir	Favipiravir Dexamethasone Enoxaparin Plasma exchange	Favipiravir	Favipiravir	Favipiravir
Hospital admission	None	None	None	None	Yes	None	No	None
Length of hospitalization (days)	-	-	-	-	5	-	-	-
Oxygen supplementation	-	-	-	-	Yes	-	-	-
ICU admission	-	-	-	-	None	-	-	-
Outcome	Recovery	Recovery	Recovery	Recovery	Recovery	Recovery	Recovery	Recovery

Table 1. Continue

	Patient 9	Patient 10	Patient 11	Patient 12	Patient 13	Patient 14	Patient 15
Demographics							
Age (years)	50	48	40	34	29	31	60
Gender	Female	Female	Female	Male	Female	Female	Female
Comorbidities	CVD	HT	None	None	None	None	CTEPH, CVD, HT
Body mass index (kg/m^2)	22.94	16.20	29.55	23.12	19.53	24.84	30.20
Disease characteristics							
Disease duration (months)	26	60	108	72	80	28	120
Disease activity at last visit	Inactive	Inactive	Inactive	Active	Inactive	Inactive	Active
Prednisone, mg	None	2.5	5	15	None	None	7.5
csDMARD	MMF 2x500 mg	LEF 1x20 mg	LEF 1x 20 mg	AZA 2x50 mg	None	MTX 10 mg/week	LEF 1x20 mg
bDMARD	None	None	None	TOC 162 mg/ week	TOC 162 mg/week	None	None
COVID-19 infection							
Symptoms	Fatigue, cough	Back pain, myalgia	None	Fatigue, fever, cough	Fatigue, cough	Fatigue, cough	Fever, cough
Contact with COVID-19 patient	None	Yes	Yes	Yes	None	None	None
Treatment for COVID-19	Favipiravir	Favipiravir	Favipiravir	Favipiravir	Favipiravir	Favipiravir	Favipiravir Dexamethasone Enoxaparin
Hospital admission	None	None	None	None	None	None	Yes
Length of hospitalization (days)	-	-	-	-		-	30
Oxygen supplementation	-	-	-	-	-	-	Yes
ICU admission	-	-	-	-	-	-	Yes
Outcome	Recovery	Recovery	Recovery	Recovery	Recovery	Recovery	Recovery

ADA: Adalimumab, AZA: Azathioprine, bDMARD: biological disease-modifying antirheumatic drugs, csDMARD: conventional synthetic disease-modifying antirheumatic drugs, CTEPH: Chronic thromboembolic pulmonary hypertension, CVD: Cardiovascular disease, DM: Diabetes mellitus, HCQ: Hydroxychloroquine, HT: Hypertension, ICU: Intensive care unit, INF: Infliximab, LEF: Leflunomide, MMF: Mycophenolate mofetil, MTX: Methotrexate, TOC: Tocilizumab, COVID-19: Coronavirus disease-2019

A patient who had a mild COVID-19 disease had pulmonary thromboembolism 2 weeks after the infection, and his symptoms resolved after starting anticoagulation. No deaths were observed related to COVID-19 among TAK patients.

DISCUSSION

This study describes the largest cohort of COVID-19 cases in TAK patients. Among TAK patients that were followed up in our clinic, 15 of them had a confirmed diagnosis of SARS-CoV-2 infection. Of these 15 patients, all were using an immunosuppressive medication except one patient, and 7 of them were using bDMARDs. Two of the patients were hospitalized, and all of them had full recovery from the infection. Tomelleri et al. (8) reported 2 TAK patients with COVID-19 with no hospitalization or death. Comarmond et al. (9) reported 4 TAK patients with COVID-19, and only one of them with multiple comorbidities died, and the other 3 patients had a full recovery.

The effect of immunosuppression on the course of COVID-19 is unknown. In the first report of COVID-19 Global Rheumatology Alliance registry including 600 patients, bDMARD monotherapy was associated with a lower risk of hospitalization (11).

In the second report of COVID-19 Global Rheumatology Alliance registry, including 3,729 patients, treatment with bDMARDs, except for rituximab were not associated with a higher risk of death compared with methotrexate monotherapy. However, azathioprine and mycophenolate were related to a higher risk

of death than methotrexate monotherapy (7). Glucocorticoid exposure of ≥10 mg/day was associated with an increased risk of a worse prognosis of COVID-19 (7,11). In our cohort, only 2 patients were taking prednisone ≥10mg/day, and both of them had mild COVID-19 disease. Also, despite the use of csDMARD and bDMARD therapies in TAK patients, there is no mortality related to COVID-19, but our sample size is limited to make a definitive comment on this issue.

Recent studies reported that the major risk factors for severe COVID-19 in patients with rheumatic diseases are comorbidities and older age (7,11), similar to the general population (12,13). In our cohort, the patient hospitalized for one month was 60 years old and had multiple comorbidities. Also, both the patients who were hospitalized had obesity. Despite the limited number of patients, this could be interpreted as the risk factors for severe COVID-19 in TAK patients are similar to the general population. Furthermore, 14 of the 15 patients were under 65 years of age, which can be a reasonable explanation for the lower severity of COVID-19 in this study.

In our cohort, 2 of the 15 TAK patients (13.3%) had required hospitalization due to COVID-19. In one of the largest studies from Turkey, which investigated the outcomes of COVID-19 in patients with iRMD, 30% of the patients had required hospitalization and oxygen support, 13% of the patients were treated in the ICU, and 10% of the patients had died (14). Also, our tertiary center was one of the biggest pandemic hospitals in Istanbul. During the second wave of pandemic between November 2020 and April 2021, the hospitalization rate among all PCR-positive patients admitted to the hospital was 22.4% (unpublished observation). In a study assessing COVID-19 infection among patients with Behçet's syndrome, no greater risk of severe infection was found compared with the general population (15). It seems like there is a lower hospitalization rate in TAK patients compared to the general population in our region, but there is a need for a more detailed comparison with age, sex, and comorbidity-matched cohorts.

Study Limitations

This study has several limitations. We had a limited number of patients to make definitive comments on the risk factors for severe COVID-19 in TAK patients. We could only contact 118 of the 201 TAK patients (58.7%) who followed up at our clinic; therefore, we might have missed some patients that had COVID-19 infection. Also, due to the retrospective study design, we could not assess the patients' disease activity during infection. However, this is the largest cohort to report the characteristics and outcomes of COVID-19 in TAK patients.

Despite the limited number of patients, our data suggest that there is no increased risk for mortality related to COVID-19 in patients with TAK. Further studies must fully understand the clinical characteristics and prognosis of COVID-19 in TAK patients.

CONCLUSION

Our data suggest that there is no increased risk for morbidity or mortality related to COVID-19 in TAK patients. Further studies with a larger sample size are needed to confirm these results.

NOTE: The study was accepted as a poster in the EULAR 2022 congress and the abstract was published with the DOI number "10.1136/annrheumdis-2022-eular.4528".

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from Marmara University Clinical Research Ethics Committee (no: 09.2021.850, date no: 02.07.2021).

Informed Consent: All patients provided consent for the use of their clinical and demographic data.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: G.S., S.K.A., K.Y.A., A.A., H.D., F.A.Ö., Concept: G.S., H.D., F.A.Ö., Design: G.S., H.D., F.A.Ö., Data Collection or Processing: G.S., S.K.A., K.Y.A., A.A., H.D., F.A.Ö., Analysis or Interpretation: G.S., H.D., F.A.Ö., Literature Search: G.S., S.K.A., K.Y.A., A.A., Writing: G.S., H.D., F.A.Ö.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Falagas ME, Manta KG, Betsi GI, Pappas G. Infection-related morbidity and mortality in patients with connective tissue diseases: a systematic review. Clin Rheumatol 2007;26:663-70.
2. Gabriel SE, Michaud K. Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases. Arthritis Res Ther 2009;11:229.
3. Gianfrancesco MA, Hyrich KL, Gossec L, et al. Rheumatic disease and COVID-19: initial data from the COVID-19 Global Rheumatology Alliance provider registries. Lancet Rheumatol 2020;2:e250-e3.
4. Sanchez-Piedra C, Diaz-Torne C, Manero J, et al. Clinical features and outcomes of COVID-19 in patients with rheumatic diseases treated with biological and synthetic targeted therapies. Ann Rheum Dis 2020;79:988-90.
5. Haberman RH, Castillo R, Chen A, et al. COVID-19 in patients with inflammatory arthritis: a prospective study on the effects of comorbidities and disease-modifying antirheumatic drugs on clinical outcomes. Arthritis Rheumatol 2020;72:1981-9.

6. FAI2R /SFR/SNFMI/SOFREMIP/CRI/IMIDIATE consortium and contributors. Severity of COVID-19 and survival in patients with rheumatic and inflammatory diseases: data from the French RMD COVID-19 cohort of 694 patients. Ann Rheum Dis 2021;80:527-38.

7. Strangfeld A, Schäfer M, Gianfrancesco MA, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis 2021;80:930-42.

8. Tomelleri A, Sartorelli S, Campochiaro C, Baldissera EM, Dagna L. Impact of COVID-19 pandemic on patients with large-vessel vasculitis in Italy: a monocentric survey. Ann Rheum Dis 2020;79:1252-3.

9. Comarmond C, Leclercq M, Leroux G, et al. Correspondence on 'Impact of COVID-19 pandemic on patients with large-vessels vasculitis in Italy: a monocentric survey'. Ann Rheum Dis 2020;annrheumdis-2020-219407. doi: 10.1136/annrheumdis-2020-219407.

10. T.C. Sağlık Bakanlığı. COVID-19 Bilgilendirme Platformu. Available from URL: https://covid19.saglik.gov.tr. (cited 15 April 2021).

11. Gianfrancesco M, Hyrich KL, Al-Adely S, et al. 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. 2020;79:859-66.

12. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature 2020;584:430-6.

13. Docherty AB, Harrison EM, Green CA, et al. Features of 20133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ 2020;369:m1985. doi: 10.1136/bmj.m1985.

14. Esatoglu SN, Tascilar K, Babaoğlu H, et al. COVID-19 Among patients with inflammatory rheumatic diseases. Front Immunol 2021;12:651715. doi: 10.3389/fimmu.2021.651715.

15. Mattioli I, Bettiol A, Silvestri E, et al. Prevalence and clinical course of SARS-CoV-2 infection in patients with Behçet's syndrome. Clin Exp Rheumatol 2021;39 Suppl 132:47-50.