Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Medicina Clínica 159 (2022) 262–267

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Original article

Clinical course of Covid-19 in a cohort of patients with Behçet disease

María Correa-Rodríguez[a,b,*], José-Luis Callejas-Rubio[b,c], Blanca Rueda-Medina[a,b], Raquel Ríos-Fernández[b,c], Javier de la Hera-Fernández[b,c], Norberto Ortego-Centeno[b,d]

[a] Department of Nursing, Faculty of Health Sciences, University of Granada, Spain
[b] Instituto de Investigación Biosanitaria ibs.GRANADA, Granada, Spain
[c] Systemic Autoimmune Diseases Unit, San Cecilio University Hospital, Granada, Spain
[d] Department of Medicine, Faculty of Medicine, University of Granada, Granada, Spain

ARTICLE INFO

Article history:
Received 17 August 2021
Accepted 12 November 2021

Keywords:
Behçet disease
Covid-19
Colchicine
Tumor necrosis factor alpha inhibitor
Glucocorticoids

ABSTRACT

Objective: The implications of Covid-19 in patients with Behçet's disease (BD) are unknown. Patients with BD usually take long-term therapy with therapeutic agents that have been tested in Covid-19 patients. We aimed to assess the prevalence of Covid-19 in a cohort of patients with BD and investigate whether those patients with a long-term treatment with colchicine, tumor necrosis factor inhibitors (TNFi) or glucocorticoids are at reduced or increased prevalence of Covid-19 related clinical outcomes.
Methods: A retrospective study was conducted among 244 patients with BD (86.1% females; mean age 43.95 ± 11.11 years). Each participant completed an online questionnaire regarding demographics, medical conditions, dispensed colchicine, TNFi or oral glucocorticoids, Covid-19 infection, clinical symptoms and recovery.
Results: The prevalence of Covid-19 infection was 14.75%. Regarding dose of colchicine, the presence of ageusia was lower in patients taking 0.5 mg/day of colchicine compared to those taking 1.5 mg/day ($p = 0.021$). The prevalence of dyspnea was significantly higher in patients taking TNFi compared with those without therapy ($p = 0.032$). With regards to oral glucocorticoids, no significant differences were found.
Conclusions: The prevalence of Covid-19 among patients with BD seems to be higher than that among the general population in Spain. Continuous TNFi therapy might increase the prevalence of worse clinical outcomes such as dyspnea; oral glucocorticoids and colchicine apparently provided no protection against the Covid-19 related clinical outcomes of patients with BD.

Evolución clínica de la Covid-19 en una cohorte de pacientes con enfermedad de Behçet

Palabras clave:
Enfermedad de Behçet
COVID-19
Colchicina
Inhibidor del factor de necrosis tumoral alfa
Glucocorticoides

RESUMEN

Objetivo: Se desconocen las implicaciones de la Covid-19 en pacientes con enfermedad de Behçet (EB). Los pacientes con EB generalmente tienen tratamiento de larga duración con agentes terapéuticos que se han probado en pacientes con Covid-19. Nuestro objetivo fue evaluar la prevalencia de la Covid-19 en una cohorte de pacientes con EB e investigar si los pacientes con un tratamiento de larga duración con colchicina, inhibidores del factor de necrosis tumoral (TNFi) o glucocorticoides tienen una prevalencia reducida o aumentada en los resultados clínicos de la Covid-19.
Métodos: Se realizó un estudio retrospectivo en 244 pacientes con EB (86,1% mujeres; edad media, 43,95 ± 11,11 años). Cada participante completó un cuestionario en línea sobre datos demográficos, afecciones médicas, tratamiento con colchicina, TNFi o glucocorticoides orales, infección por Covid-19, síntomas clínicos y recuperación.

* Corresponding author.
E-mail address: macoro@ugr.es (M. Correa-Rodríguez).

Resultados: La prevalencia de la infección por Covid-19 fue del 14,75%. En cuanto a la dosis de colchicina, la presencia de ageusia fue menor en los pacientes que tomaban 0,5 mg/día de colchicina en comparación con los que tomaban 1,5 mg/día (p = 0,021). La prevalencia de disnea fue significativamente mayor en los pacientes que tomaban TNFi en comparación con aquellos sin terapia (p = 0,032). Con respecto a los glucocorticoides orales, no se encontraron diferencias significativas.
Conclusiones: La prevalencia de Covid-19 en pacientes con EB parece ser superior a la de la población general en España. La terapia continua con TNFi podría aumentar la prevalencia de peores resultados clínicos como la disnea; los glucocorticoides orales y la colchicina aparentemente no proporcionan protección contra los resultados clínicos relacionados con la Covid-19 en pacientes con EB.

Introduction

Coronavirus disease 2019 (Covid-19) is a global pandemic caused by the respiratory droplet transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that is responsible for many deaths worldwide. Severe disease induces an exaggerated inflammatory response known as the "cytokine storm". Behçet's disease (BD) is a chronic multisystemic inflammatory disorder characterized by recurrent skin mucosa lesions and uveitis.[1] The pathogenesis is unclear but it has been established that immunological aberrations might play a main role in the BD development.[2] To date, there is limited evidence regarding the susceptibility and severity of Covid-19 infection is patients displaying BD[3,4] and only case series studies have explored the characteristics and outcomes of BD patients with Covid-2019.[5,6]

Since the clinical manifestations of BD are heterogeneous, the treatment has to be individualized and depends on organ damage, severity of the disease, and patient's characteristics. Immunosuppressive therapy along with colchicine have been recommended for mucocutaneous and joint involvement.[7] Evidence suggests that tumor necrosis factor inhibitors (TNFi) are important agents in the treatment of patients with severe and resistant BD. Thus, patients with BD usually take long-term therapy with colchicine, TNFi and glucocorticoids, that have been tested in Covid-19 patients with conflicting results. The potential preventive effect of continuous treatment with colchicine, an anti-inflammatory and immunomodulator that has been used as chronic treatments in certain rheumatological diseases, on Covid-19 related outcomes remains poorly characterized.[8–10] Previous studies stated that colchicine treatment helped prevent a "cytokine storm" phenomenon and reduced Covid-19 complications[11–18] whereas others reported that colchicine may not be beneficial in patients with Covid-19 since its effects of increasing cytosolic pH and preventing cytokine storms are very weak.[19] The use of glucocorticoids in the treatment of Covid-19 patients was initially regarded with caution due to their immunosuppressive function but recent research found that systemic glucocorticoids in patients with severe Covid-19 are associated with lower mortality.[20–22] Moreover, trials to assess the efficacy of biologic agents such as TNFi therapies to improve outcomes in patients with Covid-19 are ongoing.[23] Initially it was proposed that cytokine inhibition may worsen Covid-19 related outcomes via general immune suppression but more recently it has been suggested that inhibition of a cytokine storm may be beneficial.[24]

Data on Covid-19 in patients with BD are limited.[5,6] Further progress in understanding the implications of Covid-19 in patients with BD, an immune-mediated inflammatory disease, and the effects of anti-inflammatory, immunosuppressive or immunomodulatory therapies on a long-term basis on Covid-19 related outcomes, is urgently needed to help clinicians caring for patients with this condition. In this context, we aimed to assess the prevalence of Covid-19 in a cohort of patients with BD and investigate whether those patients with a long-term treatment with colchicine, TNFi or oral glucocorticoids are at reduced or increased prevalence of Covid-19 related clinical outcomes.

Methods

A retrospective study was conducted among a population of patients with BD that were recruited from an online systemic autoimmune disease association of Spain. A total of 2356 patients with BD were registered in this system and were invited to participate. Patients ≥ 18 years of age who had been previously diagnosed with BD by a professional and met the International Study Group for BD diagnosis criteria[25] were invited to answer an online questionnaire about possible Covid-19 infection. Each participant completed an ad-hoc structured questionnaire regarding demographics, body mass index (BMI), medical conditions, dispensed and prescribed colchicine, TNFi or oral glucocorticoids, confirmed Covid-19 infection, clinical symptoms and full recovery, defined as a total absence of symptoms 6 months after the onset of Covid-19. The questionnaire has been included as supplementary material (Appendix 1). Patients were required during January 2021. Finally, a total of 244 patients were included in the study after giving written informed consent (86.1% females; mean age 43.95 ± 11.11 years).

SPSS® Statistics version 21.0 (SPSS, Chicago, IL, USA) was used for all analyses. Continuous variables were presented as mean ± standard deviation and categorical variables as frequencies and percentages. Fisher's exact tests and Student's *t*-test were used for data analysis. *p* values of <0.05 were considered statistically significant.

Results

Table 1 shows the descriptive characteristics and co-morbidities of the study population stratified according to Covid-19 positive and negative patients. In this study cohort involving 244 patients with BD, we identified 36 patients with Covid-19 infection. Thus, the prevalence of Covid-19 was 14.75%. Most patients were females (86.1%), and the population had a mean age of 43.95 ± 11.11 years. The mean time since diagnosis of BD was 9.72 ± 8.69 years. In the overall study population, 66.8%, 37.9% and 24.2% of patients were receiving long-term therapy with colchicine, oral glucocorticoids and TNFi, respectively. Note that 12% of patients were receiving colchicine, oral glucocorticoids and TNFi simultaneously and 4% were not taking any of these. Seventeen percent of patients had hypertension, 12% ischemic heart disease, 9.5% chronic kidney disease, 21.1% stroke, 23.6% diabetes mellitus and 11.5% chronic obstructive pulmonary disease.

Clinical outcomes of the patients with BD infected by Covid-19 stratified according to the long-term use of colchicine are list in Table 2. No significant difference was found in any clinical outcome. Regarding dose of colchicine, the presence of ageusia was lower in patients taking 0.5 mg/day of colchicine compared to those taking 1.5 mg/day ($p = 0.021$). Table 3

Table 1
Descriptive characteristics and co-morbidities of the BD patients stratified according to Covid-19 infection.

Characteristics	Covid-19 infection		Total ($n = 244$)	p-Value
	Positive ($n = 36$)	Negative ($n = 208$)		
Sex, female	30 (83.3)	180 (87.0)	210 (86.1)	0.598
Age (years)	43.17 ± 9.49	44.09 ± 11.38	43.95 ± 11.11	0.603
Time since diagnosis (years)	8.66 ± 10.25	9.90 ± 8.41	9.72 ± 8.69	0.497
Body mass index (kg/m²)	25.15 ± 6.03	25.87 ± 4.89	25.76 ± 5.07	0.503
Co-morbidities				
Hypertension	6 (16.7)	37 (17.9)	43 (17.7)	1.000
Ischemic heart disease	6 (16.7)	23 (11.1)	29 (11.9)	0.401
Chronic kidney disease	4 (11.1)	19 (9.2)	23 (9.5)	0.757
Stroke	10 (27.8)	41 (19.9)	51 (21.1)	0.276
Diabetes mellitus	6 (16.7)	51 (24.8)	57 (23.6)	0.395
Chronic obstructive pulmonary disease	1 (2.8)	27 (13.0)	28 (11.5)	0.091
Long-term medications				
Colchicine	24 (66.7)	139 (67.1)	163 (66.8)	1.000
Oral glucocorticoids	14 (38.9)	78 (37.7)	92 (37.9)	0.896
Tumor necrosis factor inhibitors	7 (20.0)	52 (27.5)	50 (24.2)	0.410

Data are expressed as mean and frequency and percentage.

Table 2
Descriptive characteristics of the BD patients infected by Covid-19 stratified according to the long-term use of colchicine.

Characteristics	Long-term use of colchicine		Total ($n = 36$)	p-Value
	Yes ($n = 24$)	No ($n = 12$)		
Sex, female	21 (87.5)	9 (75.0)	30 (83.3)	0.378
Age (years)	42.08 ± 9.94	45.33 ± 8.50	43.17 ± 9.49	0.217
Body mass index (kg/m²)	25.84 ± 7.10	23.77 ± 2.68	25.15 ± 6.03	0.340
Clinical outcomes				
Asymptomatic	4 (16.7)	2 (18.2)	6 (17.1)	1.000
Fever	17 (70.8)	6 (50.0)	23 (63.9)	0.281
Headache	20 (80.3)	10 (83.3)	30 (83.3)	1.000
Fatigue	24 (100)	10 (83.3)	34 (94.3)	0.111
Cough	20 (83.3)	7 (63.6)	27 (77.1)	0.226
Dyspnea	12 (50.0)	5 (41.7)	17 (47.2)	0.454
Ageusia	16 (66.7)	5 (41.7)	21 (58.3)	0.175
Anosmia	14 (60.9)	5 (41.7)	19 (54.3)	0.311
Diarrhea	18 (78.3)	5 (41.7)	23 (65.7)	0.059
Pneumonia	1 (4.3)	–	1 (2.9)	1.000
Oxygen therapy	1 (4.3)	–	1 (2.9)	1.000
Hospitalization	1 (4.3)	–	1 (2.9)	1.000
Full recovery*	11 (45.8)	5 (41.7)	16 (44.4)	1.000

Data are expressed as mean and frequency and percentage. Full recovery, total absence of symptoms 6 months after the onset of Covid-19.

Table 3
Descriptive characteristics of the BD patients infected by Covid-19 with long-term use of colchicine stratified according to the dose.

	Dose of colchicine ($n = 24$)		p-Value
	0.5 mg/day ($n = 7$)	1 mg/day ($n = 17$)	
Sex, female	7 (100.0)	14 (82.4)	0.530
Age (years)	39.00 ± 10.67	43.35 ± 9.67	0.372
Body mass index (kg/m²)	28.94 ± 10.46	24.57 ± 5.04	0.326
Clinical outcomes			
Asymptomatic	3 (42.9)	1 (5.9)	0.059
Fever	3 (42.9)	14 (82.4)	0.134
Headache	5 (71.4)	15 (88.2)	0.552
Fatigue	7 (100.0)	17 (100.0)	–
Cough	6 (85.7)	14 (82.4)	1.000
Dyspnea	4 (57.1)	8 (47.1)	1.000
Ageusia	2 (28.6)	14 (82.4)	0.021
Anosmia	2 (28.6)	12 (70.6)	0.162
Diarrhea	5 (71.4)	13 (81.3)	0.621
Pneumonia	–	1 (6.3)	1.000
Oxygen therapy	–	1 (6.3)	1.000
Hospitalization	–	1 (6.3)	0.292
Full recovery	1 (14.3)	10 (58.8)	0.078

Data are expressed as mean and frequency and percentage. Full recovery, total absence of symptoms 6 months after the onset of Covid-19.

Table 4
Descriptive characteristics of the BD patients infected by Covid-19 stratified according to the long-term use of tumor necrosis factor inhibitors.

Characteristics	Long-term use of tumor necrosis factor inhibitors		Total ($n=36$)	p-Value
	Yes ($n=7$)	No ($n=27$)		
Sex, female	6 (86.7)	23 (82.1)	29 (82.9)	1.000
Age (years)	44.71 ± 9.46	42.61 ± 9.75	43.17 ± 9.49	0.613
Clinical outcomes				
Body mass index (kg/m^2)	27.58 ± 9.87	24.74 ± 4.76	25.15 ± 6.03	0.485
Asymptomatic	2 (28.6)	4 (14.8)	6 (17.6)	0.580
Fever	6 (85.7)	16 (57.1)	22 (62.9)	0.220
Headache	7 (100.0)	22 (78.6)	29 (82.9)	0.311
Fatigue	7 (100.0)	26 (92.9)	32 (94.1)	1.000
Cough	7 (100.0)	19 (70.4)	26 (76.5)	0.160
Dyspnea	6 (85.7)	10 (35.7)	16 (45.7)	0.032
Ageusia	4 (57.1)	16 (59.3)	20 (57.1)	1.000
Anosmia	4 (57.1)	15 (53.6)	19 (55.9)	0.672
Diarrhea	6 (85.7)	16 (59.3)	22 (64.7)	0.378
Pneumonia	–	1 (3.7)	1 (2.9)	1.000
Oxygen therapy	–	1 (3.7)	1 (2.9)	1.000
Hospitalization	–	1 (3.7)	1 (2.9)	0.206
Full recovery	5 (71.4)	14 (51.85)	19 (55.9)	0.415

Data are expressed as mean and frequency and percentage. Full recovery, total absence of symptoms 6 months after the onset of Covid-19.

Table 5
Descriptive characteristics of the BD patients infected by Covid-19 stratified according to the long-term use of oral glucocorticoids.

Characteristics	Long-term use of oral glucocorticoids		Total ($n=36$)	p-Value
	Yes ($n=14$)	No ($n=22$)		
Sex, female	10 (71.4)	20 (90.9)	30 (83.3)	0.181
Age (years)	45.40 ± 10.09	41.68 ± 9.01	43.17 ± 9.49	0.260
Body mass index (kg/m^2)	27.01 ± 7.56	23.97 ± 4.62	25.15 ± 6.03	0.191
Clinical outcomes				
Asymptomatic	3 (21.4)	3 (14.3)	6 (17.1)	0.664
Fever	7 (50.0)	16 (72.7)	23 (63.9)	0.286
Headache	11 (78.6)	19 (86.4)	30 (80.3)	0.658
Fatigue	12 (85.7)	21 (95.5)	33 (94.3)	1.000
Cough	12 (85.7)	15 (71.4)	27 (77.1)	0.431
Dyspnea	8 (57.1)	9 (40.9)	17 (47.2)	0.495
Ageusia	9 (64.3)	12 (54.5)	21 (58.3)	0.732
Anosmia	7 (50.0)	12 (54.5)	19 (54.3)	1.000
Diarrhea	9 (64.3)	14 (66.7)	23 (63.9)	1.000
Pneumonia	1 (7.7)	–	1 (2.9)	1.000
Oxygen therapy	1 (7.7)	–	1 (2.9)	0.371
Hospitalization	1 (7.7)	–	1 (2.9)	0.371
Full recovery	7 (50.0)	9 (40.9)	16 (44.4)	0.734

Data are expressed as mean and frequency and percentage. Full recovery, total absence of symptoms 6 months after the onset of Covid-19.

Table 4 shows the clinical outcomes of patients infected by Covid-19 stratified according to the long-term use of TNFi. The prevalence of dyspnea was significantly higher in patients taking TNFi compared with those without long-term therapy ($p=0.032$). With regards to long-term use of oral glucocorticoids, there were no statistically significant differences between the clinical outcomes of Covid-19 for those patients with versus without treatment (Table 5).

Discussion

In the present study, for the first time, we reported that the prevalence of Covid-19 in a cohort of patients with BD was 14.75% and investigate whether those patients with a long-term treatment with colchicine, TNFi or oral glucocorticoids are at reduced or increased prevalence of Covid-19 related clinical outcomes. We found that that the prevalence of ageusia, a Covid-19 related symptom was higher in patients taking 1 mg/day of colchicine compared to those taking 0.5 mg/day. Regarding the long-term use of TNFi, the prevalence of dyspnea was significantly higher in patients taking TNFi compared with those without therapy. These findings might not support the potential beneficial effect of colchicine on recovery for Covid-19 and might suggest that the baseline use of biologic treatments might not be related to worse Covid-19 outcomes in BD patients. In addition, we observed that the clinical outcomes were not significantly different between the long-term oral glucocorticoid's treatment and nontreatment groups. Given the study design and the limited sample size, our preliminary results should be interpreted with caution. However, by generating information such as what we presented in this study, we provide a first glance on the characteristics of BD patients with Covid-19 infection.

In this study involving patients with BD, a chronic multisystemic inflammatory vasculitis, from Spain the prevalence of Covid-19 infection was 14.75%. In that mean-time, the official Spanish rate of infection in Spain was 5.8% of the whole population. Thus, our novel data suggest that the prevalence of Covid-19 among patients with BD seems be higher than that among the general population in Spain reported by the Databases and graphics of the Europa Press Agency (https://www.epdata.es). However, the results should be interpreted cautiously because our study based on the online response to a questionnaire implies an inclusion bias related to motivation to participate. Of note, a clinical case series study in Spain reported that all patients with BD had a Covid-19 clinical picture resembling the general population[5] whereas other case series

study conducted in Istanbul supported that BD patients appear to have increased risk for severe outcome when infected with Covid-19 compared to the general population.[6]

Concerning the potential protective role of long-term colchicine therapy against Covid-19 infection, available literature reports contrasting findings.[8,9,14] Results from a population-based prospective cohort in patients chronically exposed to chloroquine/hydroxychloroquine indicated that did not differ in risk of Covid-19 nor hospitalization, compared with controls.[10] A study conducted in a cohort of familial Mediterranean fever (FMF) patients with a long-term treatment by colchicine also concluded that those patients whit this immunity disorder, have no additional risk factor for severe Covid-19 infection compared with the general population.[8] Similarly, a retrospective study based on a large healthcare database indicated that no significant difference in terms of rates of usage of hydroxychloroquine or colchicine between subjects who were found positive for Covid-19 and those who were found negative.[9] Among the same line, our findings might not support the potential beneficial effect of colchicine on recovery for Covid-19 in BD patients. Nonetheless, Kobak et al. reported that a patient with FMF with Covid-19 infection under treatment with colchicine had only mild symptoms of the disease but without fever or pneumonia development, supporting that colchicine may prevent a severe form of the disease.[14] Therefore, these contradictory findings warrant further investigation to clarify the effect of colchicine on Covid-19 infection in patients BD.

With regards to continuous TNFi treatment, although we cannot draw any definitive conclusion from our observations, we found that the prevalence of dyspnea was significantly higher in patients taking TNFi compared with those without therapy, supporting the hypothesized that TNFi long-term usage might increase the risk of worse clinical outcomes such as dyspnea in BD patients with Covid-19. On the contrary, a prospective case series involving patients with immune-mediated inflammatory disease (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, psoriasis, inflammatory bowel disease, or related conditions) who were receiving anticytokine biologics when confirmed or highly suspected symptomatic Covid-19 developed, found an incidence of hospitalization among patients with immune-mediated inflammatory disease that was consistent with that among patients with Covid-19 in the general population.[26] Similarly, a large comparative cohort study performed on adult patients who were diagnosed with Covid-19 found that patients with recent TNFi exposure do not have increased hospitalization or mortality compared with patients with COVID-19 without recent TNFi exposure.[23] In contrast, anti-TNF exposure was associated with a decreased odds of hospitalization in patients with rheumatic disease and Covid-19.[27] Based on our results, it can be suggested that the risk associated with continuous TNFi is low and other factors that were not considered in this study might play a main role in the prevalence of worse outcomes in BD patients.

There has been a long debate about the impact of corticosteroid use on Covid-19 evolution since some studies suggest that glucocorticoids early in infection are harmful[27,28] and others suggest a significant benefit later during the Covid-19 course.[29] In this investigation conducted in patients with BD infected by Covid-19, we failed to detect a potential worse effect of continuous oral glucocorticoids. Similarly, a recent systemic review and meta-analysis concluded that increased glucocorticoids had no significant correlation with hospitalization risk in patients with rheumatic diseases and that the risk of severe Covid-19 in the this population was similar to that observed in the reference population.[30] Nonetheless, Gianfranceso et al. in a study cohort involving patients with rheumatic disease and Covid-19 showed that glucocorticoid exposure of $\geq$10 mg/day was associated with a higher odds of hospitalization in[27] and Montero et al. also indicated that glucocorticoids dose $\geq$5 mg/day was associated with increased risk of hospitalization in patients with rheumatic and musculoskeletal disease and immunosuppressive therapies with Covid-19.[28] Due to limited and contradictory data, more research is needed to evaluate specific immunosuppressive medication.

This study has some limitations that must be acknowledged. Firstly, as the study cohort was recruited from an online survey, it could imply an inclusion bias related to motivation to participate. Although 2356 patients were registered in the online platform, only the 10.35% participated in this study. We cannot discard that patients who have not had COVID-19 infection may be less likely to respond. Also, note that the high prevalence of women reported in our study cohort could be explained by differences in motivation. In fact, a recent systemic review reported that gender differences in social network sites usage were observed to be the product of differences in motivation.[31] Secondly, the small sample, the short period study and the fact that the clinical variables were collected only as present or absent might limit more conclusive results. Therefore, our findings should be considered as preliminary and future prospective, randomized, placebo-controlled studies are warranted to analyze the potential benefit of continuous colchicine, TNF-i and glucocorticoids treatments in COVID-19. Furthermore, the methodology of the study, which is based on an online survey might be incomplete since we did not have information regarding the daily doses of TNFi and oral glucocorticoids per patient, and the dose could also influence the results. Likewise, there is no information regarding the use of medications in other classes, which may affect the results of the study. Furthermore, the risk of Covid-19 infection is also influenced by environmental characteristics, which have not been controlled. Despite its limitations, this pilot investigation provides novel information on the characteristics of BD patients with Covid-19 infection.

In conclusion, our novel data suggest that the prevalence of Covid-19 among patients with BD seems to be higher than that among the general population in Spain. Continuous TNFi therapy might increase the prevalence of worse clinical outcomes such as dyspnea and oral glucocorticoids and colchicine apparently provided no protection against the Covid-19 related clinical outcomes of patients with BD. This study is an initial approach to know how Covid-19 infection behave in patients with BD and provides novel information. Since this study is based on the online response that implies an inclusion bias, future research is warranted to support these preliminary findings.

Authors' contributions

Conceptualization, MCR, JLCR and NORC; Data curation, BRM, RFR and JHF; Formal analysis, MCR and NOC; Methodology, MCR, BRM, NOC; Project administration, MCR and JFH; Supervision, JLCR and NOC; Validation, BRM and RRF; Visualization, BRM and JHF; Writing – original draft, MCR; Writing – review & editing, BRM and NOC. All authors read and approved the final manuscript.

Ethical conduct of research

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained for all participants.

Funding

Not applicable.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgments

The authors thank the participating BD patients.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.medcli.2021.11.009.

References

1. Tong B, Liu X, Xiao J, Su G. Immunopathogenesis of Behcet's disease. Front Immunol. 2019;10:665, http://dx.doi.org/10.3389/fimmu.2019.00665.
2. Leccese P, Alpsoy E. Behçet's disease: an overview of etiopathogenesis. Front Immunol. 2019;10:1067, http://dx.doi.org/10.3389/fimmu.2019.01067.
3. Dursun R, Temiz SA, Özer İ, Daye M, Ataseven A. Management of patients with Behçet's disease during the COVID-19 pandemic. Dermatol Ther. 2020;33:e14063, http://dx.doi.org/10.1111/dth.14063.
4. Elmas ÖF, Demirbaş A, Bağcıer F, Türsen Ü, Atasoy M, Dursun R, et al. Treatment considerations for Behçet disease in the era of COVID-19: a narrative review. Dermatol Ther. 2021;34:e14507, http://dx.doi.org/10.1111/dth.14507.
5. Espinosa G, Araujo O, Amaro S, Bodro M, Moreno PJ, Moreno R, et al. COVID-19 and Behçet's disease: clinical case series. Ann Rheum Dis. 2021:80, http://dx.doi.org/10.1136/annrheumdis-2020-217778.
6. Yurttaş B, Oztas M, Tunc A, Balkan İİ, Tabak OF, Hamuryudan V, et al. Characteristics and outcomes of Behçet's syndrome patients with Coronavirus Disease 2019: a case series of 10 patients. Intern Emerg Med. 2020;15:1567–71, http://dx.doi.org/10.1007/s11739-020-02427-8.
7. Hatemi G, Christensen R, Bang D, Bodaghi B, Celik AF, Fortune F, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis. 2018;77:808–18, http://dx.doi.org/10.1136/annrheumdis-2018-213225.
8. Bourguiba R, Delplanque M, Vinit C, Ackermann F, Savey L, Grateau G, et al. Clinical course of COVID-19 in a cohort of 342 familial Mediterranean fever patients with a long-term treatment by colchicine in a French endemic area. Ann Rheum Dis. 2021;80:539–40, http://dx.doi.org/10.1136/annrheumdis-2020-218707.
9. Gendelman O, Amital H, Luigi N, Watad A. Continuous hydroxychloroquine or colchicine therapy does not prevent infection with SARS-CoV-2: insights from a large healthcare database analysis. Autoimmun Rev. 2020;19:102566, http://dx.doi.org/10.1016/j.autrev.2020.102566.
10. Vivanco-Hidalgo RM, Molina I, Martinez E, Roman-Viñas R, Sánchez-Montalvá A, Fibla J, et al. Incidence of COVID-19 in patients exposed to chloroquine and hydroxychloroquine: results from a population-based prospective cohort in Catalonia. Spain, 2020. Euro Surveill. 2021;26, http://dx.doi.org/10.2807/1560-7917.ES.2021.26.9.2001202, pii=2001202.
11. Montealegre-Gómez G, Garavito E, Gómez-López A, Rojas-Villarraga A, Parra-Medina R. Colchicine: a potential therapeutic tool against COVID-19. Experience of 5 patients. Reumatol Clin. 2020;17:371–5, http://dx.doi.org/10.1016/j.reuma.2020.05.001.
12. Lopes MI, Bonjorno LP, Giannini MC, Amaral NB, Menezes PI, Dib SM, et al. Beneficial effects of colchicine for moderate to severe COVID-19: a randomised, double-blinded, placebo-controlled clinical trial. RMD Open. 2021;7:e001455, http://dx.doi.org/10.1136/rmdopen-2020-001455.
13. Sandhu T, Tieng A, Chilimuri S, Franchin G. A case control study to evaluate the impact of colchicine on patients admitted to the hospital with moderate to severe covid-19 infection. Can J Infect Dis Med Microbiol. 2020:2020, http://dx.doi.org/10.1155/2020/8865954.
14. Kobak S. COVID-19 infection in a patient with FMF: does colchicine have a protective effect. Ann Rheum Dis. 2021:80, http://dx.doi.org/10.1136/annrheumdis-2020-217882.
15. Scarsi M, Piantoni S, Colombo E, Airó P, Richini D, Miclini M, et al. Association between treatment with colchicine and improved survival in a single-centre cohort of adult hospitalised patients with COVID-19 pneumonia and acute respiratory distress syndrome. Ann Rheum Dis. 2020;79:1286–9, http://dx.doi.org/10.1136/annrheumdis-2020-217712.
16. Pelechas E, Drossou V, Voulgari PV, Drosos AA. Anti-rheumatic drugs for the fight against the novel coronavirus infection (SARSCoV-2): what is the evidence? Mediterr J Rheumatol. 2020;31:259–67, http://dx.doi.org/10.31138/mjr.31.3.259.
17. Schlesinger N, Firestein BL, Brunetti L. Colchicine in COVID-19: an old drug new use. Curr Pharmacol Rep. 2020;6:137–45, http://dx.doi.org/10.1007/s40495-020-00225-6.
18. Vrachatis DA, Giannopoulos GV, Giotaki SG, Raisakis K, Kossyvakis C, Iliodromitis KE, et al. Impact of colchicine on mortality in patients with COVID-19: a meta-analysis. Hell J Cardiol. 2021, http://dx.doi.org/10.1016/j.hjc.2020.11.012. S1109-9666(20)30285-2.
19. Cumhur Cure M, Kucuk A, Cure E. Colchicine may not be effective in COVID-19 infection; it may even be harmful? Clin Rheumatol. 2020;39:2101–2, http://dx.doi.org/10.1007/s10067-020-05144-x.
20. Cheng W, Li Y, Cui L, Chen Y, Shan S, Xiao D, et al. Efficacy and safety of corticosteroid treatment in patients with COVID-19: a systematic review and meta-analysis. Front Pharmacol. 2020;11:571156, http://dx.doi.org/10.3389/fphar.2020.571156.
21. Han Y, Jiang M, Xia D, He L, Lv X, Liao X, et al. COVID-19 in a patient with long-term use of glucocorticoids: a study of a familial cluster. Clin Immunol. 2020;214:108413, http://dx.doi.org/10.1016/j.clim.2020.108413.
22. Singh AK, Majumdar S, Singh R, Misra A. Role of corticosteroid in the management of COVID-19: a systemic review and a Clinician's perspective. Diabetes Metab Syndr Clin Res Rev. 2020;14:971–8, http://dx.doi.org/10.1016/j.dsx.2020.06.054.
23. Yousaf A, Gayam S, Feldman S, Zinn Z, Kolodney M. Clinical outcomes of COVID-19 in patients taking tumor necrosis factor inhibitors or methotrexate: a multicenter research network study. J Am Acad Dermatol. 2021;84:70–5, http://dx.doi.org/10.1016/j.jaad.2020.09.009.
24. Feldmann M, Maini RN, Woody JN, Holgate ST, Winter G, Rowland M, et al. Trials of anti-tumour necrosis factor therapy for COVID-19 are urgently needed. Lancet. 2020;395:1407–9, http://dx.doi.org/10.1016/S0140-6736(20)30858-8.
25. International Study Group for Behçet's Disease. Criteria for diagnosis of Behcet's disease. Lancet. 1990;335:1078–80.
26. Haberman R, Axelrad J, Chen A, Castillo R, Yan D, Izmirly P, et al. Covid-19 in immune-mediated inflammatory diseases—case series from New York. N Engl J Med. 2020;383:85–8, http://dx.doi.org/10.1056/NEJMc2009567.
27. Gianfrancesco M, Hyrich KL, Hyrich KL, Al-Adely S, Al-Adely S, Carmona L, 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.
28. Montero F, Martínez-Barrio J, Serrano-Benavente B, González T, Rivera J, Molina Collada J, et al. Coronavirus disease 2019 (COVID-19) in autoimmune and inflammatory conditions: clinical characteristics of poor outcomes. Rheumatol Int. 2020;40:1593–8, http://dx.doi.org/10.1007/s00296-020-04676-4.
29. Ledford H. Coronavirus breakthrough: dexamethasone is first drug shown to save lives. Nature. 2020;582:469.
30. Wang Q, Liu J, Shao R, Han · Xiaopeng, Su C, Lu W. Risk and clinical outcomes of COVID-19 in patients with rheumatic diseases compared with the general population: a systematic review and meta-analysis. Rheumatol Int. 2021;1:851–61, http://dx.doi.org/10.1007/s00296-021-04803-9.
31. Mancinelli E, Bassi G, Salcuni S. Predisposing and motivational factors related to social network sites use: systematic review. JMIR Form Res. 2019;3:e12248, http://dx.doi.org/10.2196/12248.