EPIDEMIOLOGICAL SCIENCE

Risk factors for hospital admissions related to COVID-19 in patients with autoimmune inflammatory rheumatic diseases

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ABSTRACT

Objectives To describe patients with autoimmune inflammatory rheumatic diseases (AIRD) who had COVID-19 disease; to compare patients who required hospital admission with those who did not and assess risk factors for hospital admission related to COVID-19.

Methods An observational longitudinal study was conducted during the pandemic peak of severe acute respiratory syndrome coronavirus 2 (1 March 2020 to 24 April). All patients attended at the rheumatology outpatient clinic of a tertiary hospital in Madrid, Spain with a medical diagnosis of AIRD and with symptomatic COVID-19 were included. The main outcome was hospital admission related to COVID-19. The covariates were sociodemographic, clinical and treatments. We ran a multivariable logistic regression model to assess risk factors for the hospital admission.

Results The study population included 123 patients with AIRD and COVID-19. Of these, 54 patients required hospital admission related to COVID-19. The mean age on admission was 69.7 (15.7) years, and the median time from onset of symptoms to hospital admission was 5 (3–10) days. The median length of stay was 9 (6–14) days. A total of 12 patients died (22%) during admission. Compared with outpatients, the factors independently associated with hospital admission were older age (OR: 1.08; p=0.00) and autoimmune systemic condition (vs chronic inflammatory arthritis) (OR: 3.55; p=0.01). No statistically significant findings for exposure to disease-modifying antirheumatic drugs were found in the final model.

Conclusion Our results suggest that age and having a systemic autoimmune condition increased the risk of hospital admission, whereas disease-modifying antirheumatic drugs were not associated with hospital admission.

Key messages

What is already known about this subject?

- The epidemiological scenario is changing daily. There is little evidence for risk factors of poor outcome with COVID-19 specific to autoimmune inflammatory rheumatic diseases.

What does this study add?

- Patients with an autoimmune systemic condition have a higher risk of hospital admission related to COVID-19 compared with those with chronic inflammatory arthritis.
- Disease-modifying agents were not associated with a higher risk of hospital admission related to COVID-19.

How might this impact on clinical practice or future developments?

- Our data show that, in a real-world setting, a high percentage of patients with autoimmune inflammatory rheumatic diseases and COVID-19 required hospital admission. The patients were mainly elderly, with comorbidities and a systemic autoimmune condition.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes a myriad of clinical signs and symptoms, together with typical laboratory abnormalities, that manifest as the disease COVID-19.[1]

Since the confirmation of the first patient infected with SARS-CoV-2 in Spain in January 2020, the current COVID-19 outbreak has had a considerable impact, especially in the Madrid region, where the highest incidence of COVID-19 cases has been recorded, with more than 41 304 patients admitted to the hospital until the first week of May.[2]

The incidence and severity of COVID-19 disease seem to be higher in patients with risk factors, such as advanced age and associated comorbidities, mainly hypertension, diabetes, heart disease and previous respiratory diseases.[3] It is not clear whether patients with rheumatic diseases are more susceptible to SARS-CoV-2 infection, or, when they are infected, whether they have more severe disease or a poorer outcome. Previous outbreaks caused by coronaviruses did not yield overwhelming evidence that patients with rheumatic diseases are at an increased risk,[4] although some patients are candidates for a higher number of infections owing to their rheumatic disease (predominantly systemic) or the treatment they are receiving for rheumatic diseases.[5] Preliminary experiences in patients with COVID-19 show that those with chronic arthritis treated with synthetic conventional or targeted synthetic/biologic disease-modifying antirheumatic

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drugs (DMARDs) do not seem to be at a greater risk of respiratory or life-threatening complications from SARS-CoV-2 than the general population.[6 7]

The epidemiological scenario is changing, and evidence on the risk factors of poor outcome with COVID-19 specific to inflammatory rheumatic disease is scarce. In addition, there are little data on how the hospital admissions of these patients with severe COVID-19 infection have evolved.[8]

The aim of our study was to describe patients with autoimmune inflammatory rheumatic diseases (AIRD) who had COVID-19 during the pandemic peak. We also explored possible risk factors associated with hospital admission related to COVID-19 disease in patients with AIRD from a tertiary hospital in Madrid, Spain.

METHODS

Setting, study design and patients

The study was performed in a public tertiary hospital, Hospital Clínico San Carlos (HCSC), in Madrid, Spain. The catchment area is home to almost 400 000 people.

We performed a prospective observational study from 1 March 2020 (when our health area had the first hospital admission related to COVID-19) to 24 April 2020. We preselected all patients attended at the rheumatology outpatient clinic of our centre during the study period whose data were recorded in the electronic clinical history of our department (HCR Penelope). The inclusion criteria were age >16 years, a medical diagnosis (according to International Classification of Diseases (ICD-10)) of inflammatory rheumatic disease and symptomatic COVID-19 disease assessed by medical diagnosis or confirmed with a positive SARS-CoV-2 PCR diagnostic test.

Patient data were obtained during routine clinical practice. The study was conducted in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice and was approved by the HCSC Ethics Committee (approval number 20/268-E-BS).

Variables

The primary outcome was admission to hospital with a medical diagnosis of COVID-19 and/or a positive PCR result between 1 March and 15 April compared with outpatients with symptomatic COVID-19 disease.

The covariables recorded were as follows: (1) sociodemographic baseline characteristics including sex, age and rheumatic disease duration. (2) Type of AIRD, including systemic autoimmune conditions (polymyalgia rheumatica, mixed connective tissue disease, systemic sclerosis, Sjogren's syndrome, vasculitis, Raynaud phenomenon, polymyositis, polychondritis, sarcoidosis, antiphospholipid syndrome, autoinflammatory syndromes and systemic lupus erythematosus) and chronic inflammatory arthritis (rheumatoid arthritis, inflammatory polyarthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, uveitis and inflammatory bowel disease). (3) Baseline comorbid conditions, including hypertension, dyslipidaemia, depression, diabetes mellitus, smoking habit, kidney disease, chronic liver disease, respiratory diseases (chronic obstructive pulmonary disease and interstitial lung disease), thyroid disease, heart disease (valve disease, arrythmias, cardiomyopathy, heart failure and pericarditis), ischaemic vascular disease (stroke, cardiovascular and peripheral vascular disease), venous thrombosis/lung embolism and cancer. (4) Treatment for inflammatory rheumatic disease: (a) glucocorticoids, (b) nonsteroidal anti-inflammatory drugs (NSAIDs), (c) conventional synthetic disease-modifying antirheumatic drugs (csDMARDs): antimalarials (hydroxychloroquine and chloroquine), azathioprine, cyclophosphamide, cyclosporine, colchicine, leflunomide, methotrexate, mycophenolate mofetil/mycophenolic acid and sulfasalazine; (d) targeted synthetic/biologic DMARDs (ts/bDMARDs) including: (1) antitumour necrosis factor (TNF)-alpha drugs (infliximab, adalimumab, etanercept, certolizumab and golimumab); (2) other biologics: anti-interleukin (IL)-6 (tocilizumab and sarilumab); rituximab; abatacept; belimumab; anti-IL-17/23; anti-IL-17 (ustekinumab, ixekizumab and secukinumab); (3) Janus kinase (JAK) inhibitors (tofacitinib and baricitinib).

Treatment had to start at least 1 month before the beginning of the study and continue during the study period until the end of the study or hospital admission for antimalarial therapy, glucocorticoids, sulfasalazine, NSAIDs or colchicine. Regarding csDMARDs and ts/bDMARDs, treatment had to start at least 1 month before the beginning of the study and continue until at least 21st March, the end of the study or hospital admission. In the case of rituximab, the last infusion had to be at least in January.

Data sources

Patient sociodemographic, clinical, laboratory and data on treatment of rheumatic disease were obtained through HCR Penelope.

Patients with COVID-19 were detected by warning calls to our rheumatologists or nurses or via routine telephone consultation. Other infected patients were detected through their sick leave forms for COVID-19. The results of SARS-CoV-2 PCR diagnostic assays were obtained from the microbiology/infectious service of HCSC. In addition, our Hospital Central Services registered all medical admissions to HCSC. This information was provided from 1 March to 15 April.

The researchers carried out an exhaustive review of the clinical histories of admitted patients to identify COVID-19 cases and rule out patients admitted for other reasons. Once the COVID-19 cases were identified, we collected clinical, laboratory and treatment data during admission until the end of admission (either discharge or death) in order to describe the progress of the disease. The review was performed until 24th April in order to include follow-up data from patients admitted to the hospital with COVID-19.

Statistical analysis

Patient characteristics are expressed as mean and SD or median and IQR for continuous variables; categorical variables are expressed as percentages. Statistical tests were performed to compare characteristics between patients admitted with COVID-19 and those without hospital admissions. Continuous variables were analysed using the Mann-Whitney test or t-test, and discrete variables were analysed using the χ^2 or Fisher exact test. Univariable logistic regression analyses were performed to assess differences between hospital admissions related to COVID-19 risk and covariates. Multivariable logistic regression models (adjusted for age, sex and comorbidity) were run in a stepwise manner to examine the possible effect of sociodemographic, clinical and therapeutic factors on hospital admissions related to COVID-19 The model also included csDMARDs and all other variables with a $p<0.2$ from the simple regression analysis. The results were expressed as the OR with its respective 95% CI.

All analyses were performed in Stata V.13 statistical software (Stata Corp). A two-tailed p value <0.05 was considered to indicate statistical significance.

RESULTS

A total of 123 patients with AIRD with symptomatic COVID-19 disease were included in the study (table 1). The tests were performed as an exploratory measure of the association between a variable and the outcome.

Most of the patients were women, with a mean age of 59.88 (14.9) years and a mean time since diagnosis of 10.65 (8.31) years. The main diagnosis was rheumatoid arthritis (40.65%), followed by axial spondyloarthritis (14.63%). Many patients had at least one baseline comorbid condition, the most prevalent being hypertension, dyslipidaemia and lung disease. Most patients were taking csDMARDs (71.54%). Half of the patients were taking glucocorticoids (49.59%), a quarter were taking NSAIDs (24.39%) and 21.14% were taking ts/bDMARDs, of which adalimumab was the most frequently prescribed (6.50%), followed by rituximab (4.07%). Only one patient was taking a JAK inhibitor. Interestingly, 14.63% of the patients taking ts/bDMARDs were taking the drug in combination with a csDMARD.

A total of 54 patients had to be admitted to the hospital because of COVID-19. Of these, 51 were evaluated in the HCSC Emergency Department (49 were admitted to HCSC and 2 were transferred to the Institucion Ferial de Madrid (IFEMA) support hospital owing to the lack of capacity in our hospital at that time). The remaining three patients were evaluated and admitted to other hospitals in the Autonomous Community of Madrid. Table 2 presents data for the 51 patients admitted to HCSC.

Of the patients admitted to our hospital, 59.2% were women, with a mean age at admission of 69.7 (15.7) years and median lag time from the onset of symptoms to the admission of 5 (3–10) days. The median length of stay was 9 (6–14) days (table 2).

At admission, the median haemoglobin was 12.9 (12.4–13.8) g/dL and the median total lymphocyte count was 700 (500–1200) ng/mL. The median D-dimer value was 727 (487–1091) ng/mL. In 10% of patients, median interleukin (IL)-6 levels were 213 (43–383) pg/mL. Patients received various antibiotics (mainly azithromycin, levofloxacin and third-generation cephalosporins).

Most patients were treated with hydroxychloroquine during admission (86%). About half received glucocorticoids (52%). Eighteen were treated with lopinavir/ritonavir and 3 received the anti-IL-6R antibody tocilizumab (table 2).FEDER

A total of 20 patients (44%) developed relevant complications during admission, the most frequent being myocarditis, thrombosis and kidney failure. Only two patients were admitted to the intensive care unit during admission. The first was a patient in 50s with mixed connective tissue disease and associated comorbidities who developed acute respiratory insufficiency and bilateral pneumonia. The patient was treated with antibiotic therapy, lopinavir/ritonavir, hydroxychloroquine and β-interferon. Finally, the patient was extubated 40 days later and is recovering. The other was a young adult patient with systemic lupus erythematosus treated with methotrexate, rituximab, hydroxychloroquine and glucocorticoids, who, days after being diagnosed with COVID-19 (PCR+), developed an erythematous rash and generalised urticaria requiring hospitalisation in the intensive care unit owing to general clinical and laboratory worsening (elevated D-dimer values). The patient was treated with methylprednisolone, heparin and a cephalosporin. A few days later, the patient's condition improved and he recovered completely at discharge.

Of the 49 patients admitted to HCSC, 5 were sent to another care centre (converted-hotel hospital/IFEMA support hospital) when their condition improved. A further 29 patients (53.7%) were discharged home to continue self-isolation after improvement. At the end of the study, five patients remained in hospital (9.26%). A total of 12 patients died (22%) during admission (6 men and 6 women), with a median age of 81 (76.5–87) years. Of the patients who died, 87% had relevant comorbidity (diabetes mellitus, pulmonary disease, ischaemic vascular disease, hypertension, venous thrombosis/lung embolism, lung disease and or liver disease). The main diagnoses were rheumatoid arthritis (6), followed by spondyloarthritis (2), polymyalgia rheumatica (2), vasculitis (1) and Sjogren's syndrome (1).

The results of the univariable analysis are shown in table 3. Older age, systemic autoimmune conditions (vs chronic inflammatory arthritis) (OR: 2.65; 95% CI 1.22–5.7, p=0.014), hypertension, diabetes mellitus, lung disease, heart disease and glucocorticoids were associated with statistically significant greater risk of admission to the hospital. Female sex, NSAIDs and anti-TNF drugs (vs non-use) were associated with a statistically significant lower risk. The differences reported for the remaining variables did not reach statistical significance.

The multivariable analysis was adjusted for gender, age and comorbidities related to COVID-19. These comorbidities were diabetes mellitus, pulmonary disease, ischaemic vascular disease, hypertension, venous thrombosis/lung embolism, lung disease and/or liver disease (table 4). Age and systemic autoimmune conditions had more probability of hospital admissions, regardless of other factors. Differences in exposure to glucocorticoids were not statistically significant. The type of exposed DMARDs did not reach statistical significance in the multivariate model. In fact, long-term treatment with antimalarials (OR: 0.76; 95% CI 0.26–2.53; p=0.66), other csDMARDs (including methotrexate, leflunomide and azathioprine) (OR: 0.95; 95% CI 0.36–2.51; p=0.9) and NSAIDs (OR: 1.49; 95% CI 0.42–5.23; p=0.5) dropped from the final model. The variable ts/bDMARDs was also eliminated from the final model (anti-TNF vs none: OR: 0.29; 95% CI 0.05–1.66; p=0.16; and non-anti-TNF vs none: OR: 2.21; 95% CI 0.47–10.2; p=0.3).

DISCUSSION

Our study aims to shed light on rheumatologists' concerns regarding their patients. We found that, in a real-world setting, 44% of patients with AIRD and COVID-19 required hospital admission. These were mainly elderly patients, with more comorbidities and systemic autoimmune conditions. Our data show that patients exposed to disease-modifying agents do not seem to be at higher risk of hospital admission related to COVID-19.

Of the 123 patients included in the study with COVID-19, 54 required hospital admission. Comparison of the characteristics of patients admitted to hospital because of COVID-19 and those who did not require hospital admission were as follows: admitted patients had a median age close to 70 years, that is, more than 15 years older than patients who were not admitted. Moreover, those who were admitted more frequently had baseline comorbidities and systemic autoimmune conditions. As for therapy, admitted patients were less frequently exposed to antimalarial and anti-TNF-alpha agents.

The median lag time from onset of symptoms to admission was 5 days, and almost 90% of patients had pneumonia at admission. The baseline laboratory results for admitted patients in our study are consistent with those published elsewhere[9–12] and are characterised by lymphopenia and elevated acute-phase reactants. In fact, 75% of the patients had elevated D-dimers (normal, <500) and elevated IL-6 (normal, <7 pg/mL). Treatment during admission varied widely as the disease proved

Table 1 Baseline demographic and clinical characteristics of patients with AIRD and with COVID-19 (admitted vs no admitted at the hospital)

Variable	AIRD–COVID-19 patients (N=123)	AIRD–COVID non-admitted patients (N=69)	AIRD–COVID admitted patients (N=54)	P value
Women, n (%)	86 (69.92)	54 (78.26)	32 (59.26)	0.02
Age (years), mean (SD)	59.88 (14.90)	52.91 (9.58)	68.78 (15.79)	0.0001
Time since diagnosis (years), mean (SD)	10.65 (8.31)	10.37 (7.99)	11 (8.77)	0.8
PCR test, n (%)				0
Positive	58(47)	17(25)	41(76)	
Negative	3 (2)	0	3 (5)	
Not performed	62(51)	52(75)	10 (19)	
Smoking habit (active vs none)	4 (3.25)	1 (1.45)	3 (5.56)	0.31
Diagnosis (AIRD), n (%)				0.01
Rheumatoid arthritis	50 (40.65)	32 (46.38)	18 (33.33)	
Axial spondyloarthritis	18 (14.63)	11 (15.94)	7 (12.96)	
Polymyalgia rheumatica	6 (4.88)	0	6 (11.11)	
Psoriatic arthritis	6 (4.88)	3 (4.35)	3 (5.56)	
Systemic lupus erythematosus	8 (6.50)	6 (8.70)	2 (3.70)	
Mixed connective tissue disease	6 (4.88)	2 (2.90)	4 (7.41)	
Sjogren's syndrome	9 (7.32)	5 (7.25)	4 (7.41)	
Vasculitis	2 (1.63)	0	2 (3.70)	
Uveitis	1 (0.81)	1 (1.45)	0	
Systemic sclerosis	1 (0.81)	0	1 (1.85)	
Inflammatory polyarthritis	8 (6.50)	6 (8.70)	2 (3.20)	
Polychondritis	1 (0.81)	0	1 (1.85)	
Polymyositis	1 (0.81)	0	1 (1.85)	
Raynaud phenomenon	3 (2.44)	0	3 (5.56)	
Other*	3 (2.44)	3 (4.35)	0	
Comorbidities, n (%)				
Hypertension	40 (32.52)	14 (20.29)	26 (48.15)	0.002
Dyslipidaemia	27 (21.95)	12 (17.35)	15 (27.38)	0.19
Depression	9 (7.32)	8 (11.59)	1 (1.85)	0.039
Diabetes mellitus	17 (13.82)	4 (5.80)	13 (24.07)	0.007
Heart disease	15 (12.20)	5 (7.25)	10 (18.52)	0.09
Vascular disease	8 (6.50)	2 (2.90)	6 (11.11)	0.13
Liver disease	7 (5.69)	3 (4.35)	4 (7.41)	0.69
Kidney disease	6 (4.88)	0	6 (11.11)	0.006
Lung disease (ILD/COPD)	19 (15.45)	6 (8.70)	13 (24.07)	0.02
Cancer	5 (4.07)	1 (1.45)	4 (7.41)	0.16
Venous thrombosis/lung embolism	3 (2.44)	0	3 (5.56)	0.08
Thyroid disease	17 (13.8)	12 (17.39)	5 (9.26)	0.29
NSAIDs, n (%)	30 (24.39)	22 (31.88)	8 (14.81)	0.03
Glucocorticoids, n (%)	61 (49.59)	29 (42.03)	32 (59.26)	0.07
csDMARDs, n (%)				
Methotrexate–leflunomide–azathioprine	68 (55.28)	40 (57.97)	28 (51.85)	0.49
Sulfasalazine	9 (7.32)	5 (7.25)	4 (7.41)	0.97
Antimalarials	27 (21.95)	18 (26.09)	9 (16.67)	0.21
Ts/bDMARDs, n (%)	26 (21.14)	19 (27.54)	7 (12.96)	0.04
Anti-TNF-alpha agent	17 (13.82)	15 (21.74)	2 (3.70)	0.004
Other biologics	9 (7.32)	4 (5.80)	5 (9.26)	0.4
Abatacept	1 (0.81)	1 (1.45)	0	0.99
Tocilizumab	2 (1.63)	1 (1.45)	1 (1.85)	0.99
Belimumab	1 (0.81)	1 (1.45)	0	0
Rituximab	5 (4.07)	1 (1.45)	4 (7.41)	0.16
JAKi, n (%)	1 (0.89)	0	1 (2)	0.43

*Others: inflammatory bowel disease, antiphospholipid syndrome, juvenile idiopathic arthritis, autoinflammatory syndromes and sarcoidosis.
†Heart disease: arrhythmias,valve disease, cardiomyopathy and heart failure. Ischaemic vascular disease: stroke, cardiovascular and peripheral vascular disease.
AIRD, autoimmune inflammatory rheumatic disease; Anti-TNF, tumour necrosis factor-alpha; COPD, chronic obstructive pulmonary disease; csDMARD, conventional synthetic disease-modifying antirheumatic drug; ILD, interstitial lung disease; JAKi, JAK inhibitor; ts/bDMARDs, target synthetic/biologic disease-modifying antirheumatic drug.

Table 2 Hospital admissions related to COVID-19 among patients with AIRD

Variable	Value
Admissions, n	54
Lag time from onset of symptoms to admission (days), median (IQR)	5 (3–10)
Pneumonia at admission, n (%)	47 (87)
Systemic autoimmune conditions, n (%)	24 (44.4)
Laboratory data at admission, median (IQR)	
Haemoglobin (g/dL)	12.9 (12.4–13.8)
D-dimer (ng/mL)	727 (487–1091)
Neutrophil count (×10^9/L)	4500 (3500–5700)
Lymphocyte count (×10^9/L)	700 (500–1200)
CRP (mg/dL)	9.19 (2.9–14.6)
LDH (U/L)	618 (489–919)
Platelet count (×10^9/L)	199 000 (158 000–267 000)
Creatinine (mg/dL)	0.86 (0.76–1.28)
Ferritine (ng/mL)	319 (151–885)
COVID-19-related treatments during admission*, n (%)	
Azithromycin	17 (34)
Other antibiotics	29 (58)
Glucocorticoids	26 (52)
Lopinavir/ritonavir	18 (6)
Remdesivir	0
Darunavir/cobicistat	4 (8)
Tocilizumab	3 (6)
Interferon	4 (8)
HCQ	43 (86)
Immunoglobulin	0
Admitted by intensive care unit during hospital admission	
No	52 (96.29)
Yes	2 (3.71)
Length of stay (days), median (IQR)	9 (6–14)
Discharge reason, n (%)	
Improvement, home isolation	29 (53.70)
Other care centre (medicalised hotel/IFEMA hospital)	8 (14.82)
Death	12 (22.22)
End of study (no discharge)	5 (9.26)

*Data for 50 patients (4 patients were treated in other support centres after referral or admission in other centres).
CRP, C reactive protein; HCQ, hydroxychloroquine; LDH, lactate dehydrogenase.

Table 3 OR of hospital admission related to COVID-19 in patients with AIRD (univariable analysis)

Variable	OR	95% CI	P
Gender, women	0.4	0.18–0.988	0.02
Age (years)	1.09	1.05–1.14	0
Diagnosis (AIRD: one category vs the rest)*			
Rheumatoid arthritis	0.57	0.27–1.20	0.14
Inflammatory polyarthritis	0.4	0.07–2.08	0.27
Systemic lupus erythematosus	0.4	0.07–2.08	0.27
Psoriatic arthritis	1.29	0.25–6.68	0.7
Spondyloarthritis	0.78	0.28–2.18	0.64
MTCD	2.68	0.47–15.2	0.26
Sjogren syndrome	1.02	0.26–4.01	0.93
Disease duration	1.01	0.96–1.05	0.67
Smoking habit (active vs none)	3.99	0.40–39.58	0.23
Comorbidities (yes)			
Hypertension	3.64	1.65–8.06	0.001
Dyslipidaemia	1.82	0.77–4.32	0.17
Depression	0.14	0.01–1.18	0.07
Diabetes mellitus	5.15	1.5–16.8	0.007
Heart disease	2.9	0.93–9.09	0.06
Vascular disease	4.18	0.81–21.64	0.09
Liver disease	1.76	0.37–8.22	0.47
Kidney disease	1	–	–
Lung disease (ILD/COPD)	3.32	1.17–9.45	0.02
Cancer	5.4	0.58–50.1	0.13
Venous thrombosis/lung embolism	1	–	–
Thyroid disease	0.48	0.15–1.47	0.2
NSAIDs	0.37	0.15 –0.91	0.03
Glucocorticoids	2.01	0.97–4.13	0.05
csDMARDSs			
Methotrexate–leflunomide–azathioprine	0.78	0.38–1.59	0.49
Sulfasalazine	1.02	0.26–4.01	0.97
Antimalarial agents	0.56	0.23–1.38	0.21
Ts/bDMARDs	0.39	0.15–1.01	0.05
None	1	–	–
Anti-TNF agents	0.13	0.03–0.63	0.01
Other biologics	1.65	0.46–6.49	0.46
JAKis	1	–	–

Other biologics: anti-IL-6 (tocilizumab, sarilumab); rituximab (Rtx); anti-IL-17/23; anti-IL-17.
*Othercategories could not be represented: polymalgia rheumatica, systemicsclerosis, vasculitis, Raynaud phenomenon, polychondritis, Behçet disease,polymyositis, uveitis inflammatory boweldisease, antiphospholipid syndrome, juvenile idiopathic arthritis, autoinflammatorysyndromes and sarcoidosis.
AIRD, autoimmune inflammatory rheumatic disease; anti-TNF, tumour necrosis factor; csDMARD, Conventional synthetic disease-modifying antirheumatic drug; IL-6, interleukin-6; JAKi, JAK inhibitors; ts/bDMARDs, target synthetic/biologic disease-modifying antirheumatic drug.

challenging for specialists, who prescribed various combinations of drugs based on little published evidence. In this sense, the anti-IL-6R antibody tocilizumab has proven to be beneficial in patients with COVID-19.[12] Treatment may also be successful in the early stages of cytokine release syndrome, if it can effectively block the signal transduction pathway of IL-6; therefore, tocilizumab and sarilumab are likely to emerge as effective drugs for patients with moderate to severe COVID-19.[13 14] In our study, almost 10% of the patients were treated with tocilizumab.

The patients who eventually died had a median age of >80 years. This finding is in line with data for the general population, where over 95% of deaths occurred in persons >60 years and more than 50% of all deaths were in people aged ≥80 years.[7]

The multivariable regression model showed that only age (increasing by 8% per year) and systemic autoimmune conditions continued to be risk factors for hospital admission related to COVID-19.

As for the association between sex and risk of hospital admission, we did not find a higher risk of admission in women, despite the fact that rheumatic diseases are more prevalent in this group. The type of diagnosis seems to play an important role in the probability of hospital admission, and patients with systemic autoimmune conditions seem to have the highest risk compared with chronic inflammatory arthritis.

As it has been reported elsewhere, comorbidities play an important role in the risk of hospital admission.[15] Clinical outcomes are poorer in patients with COVID-19 with a comorbid condition than in those without, and a greater number of comorbidities correlates with poorer clinical outcomes.[16] Diabetes is a major comorbidity in COVID-19, and patient's history of diabetes is an independent risk factor for morbidity and mortality in this condition.[17 18] Diabetes has been associated with admissions to

Table 4 Multivariable analysis. risk factors for hospital admission related to COVID-19 in patients with AIRD

Variable	OR	95% CI	P value
Gender, women	0.45	0.15–1.29	0.14
Age (years)	1.08	1.04–1.13	0
AIRD (systemic autoimmune conditions vs chronic inflammatory arthritis)	3.55	1.30–9.67	0.01
COVID comorbidities (yes)	1.82	0.69–4.80	0.22
Glucocorticoids	1.97	0.77–5.01	0.15

Systemic autoimmune conditions (polymyalgia rheumatica; mixed connective tissue disease, systemic sclerosis, Sjogren's syndrome, vasculitis, Raynaud, polymyositis polychondritis, sarcoidosis, antiphospholipid syndrome; autoinflammatory syndromes and systemic lupus erythematosus) vs chronic inflammatory arthritis (rheumatoid arthritis; inflammatory polyarthritis; juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, uvetis and inflammatory bowel disease). Comorbidities including the presence of at least one of the follows: hypertension, heart disease, vascular disease, diabetes mellitus, venous thrombosis/lung embolism, chronic kidney disease, liver disease and lung disease (ILD/COPD). AIRD, autoimmune inflammatory rheumatic disease; ;COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease.

the intensive care unit due to COVID-19 in recent series[19 20] and has been shown to increase mortality.[6] Therefore, we adjusted for comorbidity in the multivariable analysis.

Treatment with glucocorticoids lost its statistical significance in the multiple regression model. However, the dose was not reported in our data, and in the case of these agents, the risk could be dose-dependent. In a recent publication from a European registry, the authors found that exposure to >10 mg/day was associated with a greater probability of hospitalisation.[21]

The exposure to DMARDs, regardless of whether they were biological or synthetic, does not seem to be associated with a higher hospital admission related to COVID-19. Although we have to consider the limited number of patients in our study, our results are in concordance with data reported elsewhere.[8 20]

Our results should be interpreted taking into account other limitations. First, patients were included from a single centre. Second, of all the patients with COVID-19 19 who did not require admission, one-third contacted the rheumatology service to report the disease and the remainder were detected through the COVID-19 discharge reports sent to their primary care physician. Elderly persons and homemakers who did not contact us can be considered missing. Consequently, there may be some selection bias between those admitted and those not admitted, although this problem was addressed by adjusting for confounders in the multivariable analysis. Third, while it is acknowledged that clinical suspicion must be confirmed by PCR assay, almost 20% of patients admitted did not undergo PCR owing to the lack of tests or the extreme healthcare overload. Nevertheless, all cases included were clinically compatible and managed as COVID-19.

The key strength of our study is that it was performed in real-life conditions during then pandemic peak, with access to complete sociodemographic and clinical data from our rheumatology electronic clinical history, including thorough hospital admission data such as laboratory abnormalities and COVID-19 treatment data from the hospital computer services. Consequently, this has allowed us to analyse the risk of hospital admission related to COVID-19 adjusted for confounders, thus avoiding possible bias.

Although we are unable to modify the factors reported here, knowing them can help rheumatologists to treat and advise their patients during this new and challenging period. Results provided by our study are preliminary and should be corroborated with other real-life studies, but we consider our findings helpful to increase the knowledge in the management of patients with AIRD and COVID-19.

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Patient consent for publication Not required.

Ethics approval The study was approved by the Hospital Clínico San Carlos institutional ethics committee (approval number 20/268-E-BS). This study was conducted according to the principles of the Declaration of Helsinki.

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