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ORIGINAL ARTICLE

Sociodemographic and clinical factors associated with poor COVID-19 outcomes in patients with rheumatic diseases: data from the SAR-COVID Registry

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Abstract

Background/objective This study aims to describe the course and to identify poor prognostic factors of SARS-CoV-2 infection in patients with rheumatic diseases.

Methods Patients ≥ 18 years of age, with a rheumatic disease, who had confirmed SARS-CoV-2 infection were consecutively included by major rheumatology centers from Argentina, in the national, observational SAR-COVID registry between August 13, 2020 and July 31, 2021. Hospitalization, oxygen requirement, and death were considered poor COVID-19 outcomes.

Results A total of 1915 patients were included. The most frequent rheumatic diseases were rheumatoid arthritis (42%) and systemic lupus erythematosus (16%). Comorbidities were reported in half of them (48%). Symptoms were reported by 95% of the patients, 28% were hospitalized, 8% were admitted to the intensive care unit (ICU), and 4% died due to COVID-19. During hospitalization, 9% required non-invasive mechanical ventilation (NIMV) or high flow oxygen devices and 17% invasive mechanical ventilation (IMV). In multivariate analysis models, using poor COVID-19 outcomes as dependent variables, older age, male gender, higher disease activity, treatment with glucocorticoids or rituximab, and the presence of at least one comorbidity and a greater number of them were associated with worse prognosis. In addition, patients with public health insurance and Mestizos were more likely to require hospitalization.

Conclusions In addition to the known poor prognostic factors, in this cohort of patients with rheumatic diseases, high disease activity, and treatment with glucocorticoids and rituximab were associated with worse COVID-19 outcomes. Furthermore, patients with public health insurance and Mestizos were 44% and 39% more likely to be hospitalized, respectively.

Study registration This study has been registered in ClinicalTrials.gov under the number NCT04568421.

Key Points

- *High disease activity, and treatment with glucocorticoids and rituximab were associated with poor COVID-19 outcome in patients with rheumatic diseases.*
- *Some socioeconomic factors related to social inequality, including non-Caucasian ethnicity and public health insurance, were associated with hospitalization due to COVID-19.*

Extended author information available on the last page of the article

Keywords Argentina · COVID-19 · Rheumatic diseases · SARS-CoV-2

Introduction

Since the outbreak of COVID-19 worldwide, rheumatologists have focused their efforts on trying to understand its impact on patients with rheumatic diseases and how to improve management and treatment in case they got infected. Among rheumatic diseases, systemic autoimmune diseases are usually associated with a greater predisposition to viral infections due to the intrinsic risk of the pre-existing disease and to the iatrogenic effect of immunosuppressive drugs used for their treatments [1–3]. They also have a higher prevalence of comorbidities, like cardiovascular and pulmonary disease, which have been associated with poor COVID-19 outcomes [4]. On the other hand, glucocorticoids and some disease-modifying anti-rheumatic drugs (DMARDs) have been used to treat inflammation caused by SARS-CoV-2 [5].

Most of the renowned severity risk factors, like male gender, older age, and the presence of comorbidities, are non-modifiable [6]. However, high disease activity and some treatments, including glucocorticoids, rituximab, azathioprine, and cyclophosphamide, which have been associated with poor COVID-19 outcomes in patients with rheumatic diseases are potentially adjustable [7, 8]. The latter must be taken into consideration by rheumatologists when making therapeutic decisions and highlights the importance of a strict control of these patients during the COVID-19 pandemic.

Most of the information regarding the effect of COVID-19 in patients with rheumatic diseases comes from cohorts from other parts of the world and they do not necessarily apply to the Argentine population, considering its sociodemographic and economic characteristics. In this context, and emphasizing the importance of having local data to improve patient management, the Argentine Society of Rheumatology (SAR) developed a national registry of COVID-19 in patients with rheumatic diseases (SAR-COVID).

The aim of this study was to evaluate sociodemographic, clinical characteristics, and outcomes of SARS-CoV-2 infection in patients with rheumatic diseases from the SAR-COVID registry. Furthermore, we wanted to identify poor prognostic factors of COVID-19.

Methods

The SAR-COVID registry has been previously described [9]. Briefly, it is a national, multicenter, observational registry including consecutive adult patients with a rheumatic disease and confirmed SARS-CoV-2 infection. COVID-19 diagnosis was made with a positive RT-PCR test from nasopharyngeal or oropharyngeal swab, or positive serology in patients previously diagnosed according to symptoms and close contact with a confirmed patient. A total of 140 independent rheumatologists from all over Argentina registered to participate. All variables were collected by self-report, clinical and laboratory examination, and/or medical records review, performed by the rheumatologist during patient hospitalization due to COVID-19, or at the patient control visit (virtual or face-to-face) performed after SARS-CoV-2 infection, depending on availability.

At baseline, sociodemographic data including age, gender, ethnicity, socioeconomic level according to the Graffar scale [10], formal education and health insurance, as well as comorbidities, rheumatic treatment, symptoms, and outcomes regarding SARS-CoV-2 infection were recorded. Rheumatic disease activity was stratified into categories based on the treating physician's criteria (remission, low, moderate, or high disease activity). This analysis comprises the first visit of patients enrolled between August 13, 2020 and July 31, 2021.

Regarding SARS-CoV-2 infection, date, place, and diagnostic method used were registered. Furthermore, symptoms, laboratory findings, pharmacological treatments, and medical interventions, like oxygen therapy, were recorded for all patients. For this study, the following were considered poor COVID-19 outcomes: hospitalization in general ward or admission to the ICU; severe oxygen requirements according to the ordinal scale for clinical improvement from WHO [11], high-flow oxygen devices or non-invasive mechanical ventilation (NIMV) or invasive mechanical ventilation (IMV); and death due to COVID-19.

Ethical considerations

This study was approved by an independent ethics committee and was conducted in accordance with Good Clinical Practice (GCP) guidelines, the International Conference on Harmonization (ICH), the ethical principles established in the Declaration of Helsinki, the law 3301/09, and the guidelines of the local ethics committee. Personal identification data was kept anonymous and protected according to international and national regulations in order to guarantee confidentiality, in accordance with the Law on Protection of Personal Data No. 25.326/2000.

Statistical analysis

Overall comparisons were performed using descriptive statistical analysis of sociodemographic, clinical

characteristics, laboratory, and COVID-19 outcomes data. The distribution of continuous variables was evaluated using boxplot, histogram visual inspection, and Shapiro–Wilk test, and they are presented as mean and standard deviation for normal distributions, or median and interquartile range otherwise. Categorical variables are summarized as frequencies and percentages.

To compare associations between sociodemographic and clinical variables and COVID-19 outcomes, chi-square test was used, and if assumptions were not fulfilled, categories were grouped applying Fisher exact test. For continuous variables, Student's *t* test, Mann–Whitney *U* test, or ANOVA were used as appropriate. Finally, all variables with a *p* value less than 0.10 in the univariate analysis and those that, according to the investigator's criteria, were considered relevant were included in multiple regression models (logit link function), using each poor COVID-19 outcome as a dependent variable. Later, variable selection was made using a stepwise method.

A p value < 0.05 was considered statistically significant. All statistical analyses and model development were performed using R version 4.0.0 (Free Software Foundation, Inc., Boston, USA).

Results

A total of 1915 patients with rheumatic diseases and SARS-CoV-2 infection were included; most of them were female (80.9%), with a mean age of 51.4 years (SD 14.2). The predominant ethnic groups were Caucasian and Mestizo, 48.6% and 44.1%, respectively. Most of the patients (78.1%) had some type of health insurance different from public health, and regarding socioeconomic level, 50% were classified as middle class. Comorbidities were reported in half of them (Table 1).

The most frequent immune-mediated diseases were rheumatoid arthritis (42.0%), systemic lupus erythematosus (16.0%), and spondyloarthritis (9.7%). At the time of COVID-19 infection, most were in remission or minimal/low disease activity (78%). In relation to treatment, 36% were receiving glucocorticoids, 37.3% methotrexate, 18.9% antimalarials, 17% biologic DMARDs, and 4% JAK inhibitors (Table 1).

After infection, patients were followed for a median time of 62.0 days (Q1, Q3 30.8, 141.0). COVID-19 symptoms were present in 95% of the patients and were mostly fever, cough, and headache (Fig. 1). During infection, 29.8% received some pharmacological treatment, dexamethasone being the most frequently used. A quarter (26.8%) of the patients were hospitalized and 8% were admitted to the ICU. Among hospitalized patients, 8.9% required high-flow oxygen devices or NIMV and 16.6% IMV. Median hospital

Table 1 Baseline characteristics of patients with SARS-CoV-2 infection from the SAR-COVID registry

Variables	All patients ($n = 1915$)
Female gender *n* (%)	1549 (80.9)
Age (years) mean (SD)	51.4 (14.2)
Ethnicity	
Caucasian *n* (%)	931 (48.6)
Mestizo *n* (%)	844 (44.1)
Other *n* (%)	55 (2.9)
Unknown *n* (%)	85 (4.4)
Socioeconomic level	
High *n* (%)	39 (2)
Medium–high *n* (%)	328 (17.1)
Medium *n* (%)	958 (50)
Medium–low *n* (%)	391 (20.4)
Low *n* (%)	136 (7.1)
Unknown *n* (%)	63 (3.3)
Education (years) mean (SD)	13.2 (3.8)
Health worker *n* (%)	126 (6.6)
Health insurance	929 (48.5)
Social security *n* (%)	467 (24.4)
Private health *n* (%)	100 (5.2)
Private health + social security *n* (%)	396 (20.7)
Public health *n* (%)	23 (1.2)
Unknown *n* (%)	
Rheumatic disease	
Rheumatoid arthritis *n* (%)	808 (42.2)
Systemic lupus erythematosus *n* (%)	308 (16.1)
Spondyloarthritis *n* (%)	186 (9.7)
Sjögren's syndrome *n* (%)	102 (5.3)
Systemic sclerosis *n* (%)	81 (4.2)
Vasculitis *n* (%)	65 (3.4)
Antiphospholipid syndrome *n* (%)	48 (2.5)
Inflammatory myopathy *n* (%)	51 (2.7)
Osteoarthritis *n* (%)	141 (7.4)
Fibromyalgia *n* (%)	72 (3.8)
Disease duration (years) mean (SD)	8.6 (7.6)
Disease activity	
Remission *n* (%)	634 (33.3)
Low disease activity *n* (%)	748 (39.3)
Moderate disease activity *n* (%)	319 (16.7)
High disease activity *n* (%)	63 (3.3)
Unknown/not applicable *n* (%)	151 (7.9)
Treatment	
Glucocorticoid dose	
0 mg/day *n* (%)	1208 (63.8)
≤5 mg/day *n* (%)	591 (31.2)
>5 mg/day *n* (%)	91 (4.8)
Unknown dose *n* (%)	3 (0.2)
Conventional DMARDs	
Methotrexate *n* (%)	714 (37.3)
Antimalarials *n* (%)	361 (18.9)
Leflunomide *n* (%)	148 (7.7)
Sulfasalazine *n* (%)	15 (0.8)
Immunosuppressants *n* (%)	
Mycophenolate mofetil *n* (%)	94 (4.9)
Azathioprine *n* (%)	79 (4.1)

Table 1 (continued)

Variables	All patients ($n = 1915$)
Cyclophosphamide *n* (%)	6 (0.3)
Cyclosporine *n* (%)	1 (0.06)
Biologic DMARDs	
TNF α inhibitors *n* (%)	204 (10.7)
Rituximab *n* (%)	38 (2)
IL-6 inhibitors *n* (%)	24 (1.2)
Abatacept *n* (%)	24 (1.2)
IL-17 inhibitors *n* (%)	24 (1.2)
IL-23 or IL-12/23 inhibitors *n* (%)	8 (0.4)
Belimumab *n* (%)	7 (0.4)
Targeted synthetic DMARDs	
JAK inhibitors *n* (%)	84 (4.4)
Apremilast *n* (%)	2 (0.1)
Comorbidities *n* (%)	883 (47.9)
Arterial hypertension *n* (%)	464 (25.3)
Obesity *n* (%)	262 (14.3)
Dyslipidemia *n* (%)	241 (13.2)
Lung disease *n* (%)	185 (10.1)
Diabetes *n* (%)	144 (7.9)
Cardiovascular disease *n* (%)	60 (3.3)
Cancer *n* (%)	42 (2.3)
Chronic kidney failure *n* (%)	34 (1.9)
Cerebrovascular disease *n* (%)	17 (0.9)
Smoking status	106 (5.6)
Current smoker *n* (%)	382 (20.3)
Past smoker *n* (%)	1211 (64.4)
Never *n* (%)	216 (11.3)
Unknown *n* (%)	
SARS-CoV-2 diagnostic method	1680 (87.7)
RT-PCR *n* (%)	259 (13.5)
Serology *n* (%)	
SARS-CoV-2 diagnostic place	871 (45.5)
Outpatient facility *n* (%)	627 (32.7)
Emergency department *n* (%)	260 (13.6)
Home/community detection *n* (%)	160 (8.4
Inpatient/hospital *n* (%)	6 (0.3)
Nursing home or assisted living facility *n* (%)	7 (0.4)
Unknown *n* (%)	
SARS-CoV-2 contagion	1084 (56.6)
Contact with confirmed/possible case *n* (%)	726 (37.9)
Community contagion *n* (%)	66 (3.4)
Other *n* (%)	
Symptoms *n* (%)	1819 (95)
Fever *n* (%)	1069 (55.8)
Headache *n* (%)	799 (41.7)
Cough *n* (%)	813 (42.5)
Myalgia *n* (%)	739 (38.6)
General discomfort *n* (%)	715 (37.3)
Anosmia *n* (%)	650 (33.9)
Odynophagia *n* (%)	559 (29.2)
Dyspnea *n* (%)	437 (22.8)
Arthralgia *n* (%)	406 (21.2)
Dysgeusia *n* (%)	456 (23.8)
Pharmacological treatment* *n* (%)	570 (29.8)

Table 1 (continued)

Variables	All patients ($n = 1915$)
Dexamethasone *n* (%)	353 (18.4)
Azithromycin *n* (%)	297 (15.5)
Anticoagulation *n* (%)	133 (7)
Oral glucocorticoids *n* (%)	130 (6.8)
Plasma from recovered patients *n* (%)	54 (2.8)
Antimalarials *n* (%)	22 (1.2)
Ivermectin *n* (%)	36 (1.9)
Complications *n* (%)	171 (9)
ARDS *n* (%)	11 (6)
Sepsis *n* (%)	37 (1.9)
Cytokine storm *n* (%)	11 (0.6)
Hospitalization *n* (%)	512 (26.8)
Hospitalization time (days) median (Q1, Q3)	10.0 (6.0, 15.0)
ICU admission *n* (%)	153 (8)
ICU time (days) median (Q1, Q3)	**8.0** (5.0, 14.0)
O2 treatment *n* (%)	
Supplemental oxygen *n* (%)	220 (43.5)
NIMV/high-flow O_2 *n* (%)	45 (8.9)
IMV *n* (%)	84 (16.6)
Ventilation, unknown *n* (%)	2 (0.4)
Unknown *n* (%)	2 (0.4)
Death due to COVID-19 *n* (%)	83 (4.4)

n number, *SD* standard deviation, *DMARDs* disease-modifying anti-rheumatic drugs, *TNF* tumor necrosis factor, *IL* interleukin, *RT-PCR* reverse transcription–polymerase chain reaction, *ARDS* acute respiratory distress syndrome, *Q* quartile, *ICU* intensive care unit, O_2 oxygen, *NIMV* non-invasive mechanical ventilation, *IMV* invasive mechanical ventilation

*Excludes analgesics and non-steroidal anti-inflammatory drugs

stay was 10.0 days (Q1, Q3 6.0, 15.0). Complications were reported in 9%, being acute respiratory distress syndrome the most frequent (6%). A total of 83 (4.4%) patients died due to COVID-19 during follow up.

Older patients, male gender, and the presence of comorbidities were associated with worse COVID-19 outcomes. In the univariate analysis, men were more frequently hospitalized and were more likely to require oxygen than females. Patients who were hospitalized, had severe oxygen requirements, or died were significantly older than those without these outcomes. Similarly, the presence and number of comorbidities was associated with all three outcomes. Individually, every comorbidity was more frequent in patients with poor COVID-19 outcomes (Tables 2, 3, and 4). After adjusting for sociodemographic and clinical variables, male gender remained significantly associated with hospitalization, and older age with all three outcomes. The presence of at least one comorbidity was associated with a higher likelihood of being hospitalized compared to patients without comorbidities, and two or more comorbidities was more commonly associated with severe oxygen therapy.

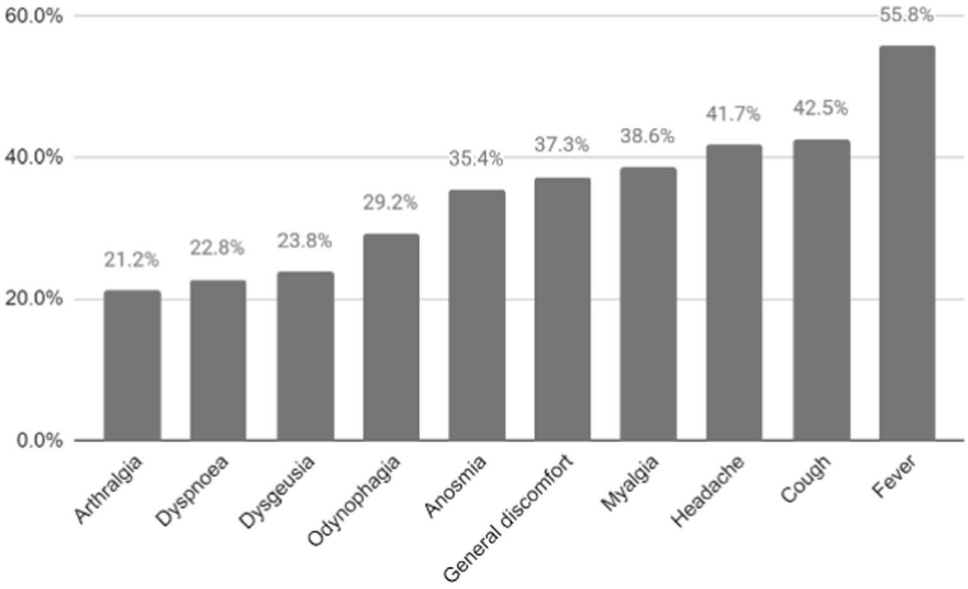


Fig. 1 COVID-19 symptoms most frequently reported in the SAR-COVID registry

Furthermore, obesity and pulmonary disease were associated with hospitalization; diabetes and chronic renal disease with severe oxygen requirements and death; and cardiovascular disease with death (Fig. 2A–C).

Regarding socioeconomic status, hospitalized patients were more frequently non-Caucasians, had public health insurance, and had lower socioeconomic status. Likewise, patients who died had more frequently social security and less frequently private health insurance. Moreover, fewer years of schooling was associated with poor COVID-19 outcomes (Tables 2–4). In multivariable analysis, after adjusting for other demographic and clinical risk factors, being non-Caucasian and having public health insurance were still associated with hospitalization (Fig. 2A–C).

Patients with vasculitis were more frequently hospitalized, required severe oxygen therapy, and were more likely to die from COVID-19. Those with systemic sclerosis and inflammatory myopathy were more frequently hospitalized, whereas spondyloarthritis was associated with less hospitalizations and deaths. Nonetheless, high disease activity was associated with all three poor outcomes. Regarding rheumatic disease treatment, glucocorticoids and rituximab were more frequently used among patients who were hospitalized, required severe oxygen treatment, and died. In addition, cyclophosphamide and azathioprine were more commonly used in hospitalized patients, and the latter also in those with severe oxygen treatment. On the contrary, treatment with methotrexate or TNF inhibitors was associated with outpatient care and antimalarials with no severe oxygen requirement (Tables 2–4).

In multivariate analysis, treatment with rituximab was associated with a 2.5-fold increase of hospitalization, sixfold increase of severe oxygen requirement, and eightfold increase of death due to COVID-19. Even 5 mg/day or less of prednisone was associated with hospitalization and death. On the contrary, patients in remission and with low or moderate disease activity had better COVID-19 outcomes compared to those with high disease activity (Fig. 2A–C).

Finally, to assess factors associated with poor COVID-19 outcomes in a more balanced population, we decided to perform a sensitivity analysis including only data from three major clinics, where physicians thoroughly assessed all patients with rheumatic disease and SARS-CoV-2 infection. From a total of 320 patients studied, 21 (6.6%) were hospitalized. Similar to the general cohort, hospitalized patients were older (OR 1.03, 95% CI 1.00–1.06), had more comorbidities (OR 1.6, 95% CI 1.2–2.1), more frequently vasculitis (OR 6.6, 95% CI 2.2–18.7), moderate and high disease activity (ref. remission OR 5.3, 95% CI 1.5–21.5 and OR 26.5, 95% CI 6.6–120.0, respectively), and treatment with glucocorticoids (≤ 5 mg/day: OR 8.6, 95% CI 2.2–42.1 and >5 mg/day: OR 12.9, 95% CI 3.9–58.1) and rituximab (OR 10.4, 95% CI 1.3–66.4).

Discussion

This is the first report of poor COVID-19 outcomes, including hospitalization, severe oxygen requirements, and death, in Argentine patients with rheumatic diseases from the SAR-COVID registry. Demographic and clinical variables were analyzed as well as socioeconomic characteristics. Particularly, male sex, older age, the presence of comorbidities, high disease activity, and treatment with glucocorticoids and rituximab were associated with poor COVID-19 outcomes. In addition, Mestizos and those with public health insurance were more likely to be hospitalized.

Male gender, older age, and comorbidities were associated with poor COVID-19 outcomes. Men were twice more

Table 2 Sociodemographic and clinical variables associated with COVID-19 hospitalization

Variables	Not hospitalized $n=1403$	Hospitalized $n=512$	p value	OR (95% CI)
Female gender *n* (%)	1155 (82.3)	394 (77.0)	0.010	1.39 (1.09, 1.78)
Age (years) mean (SD)	49.3 (13.5)	57.2 (14.4)	< 0.001	1.04 (1.03, 1.05)
Ethnicity				
Caucasian *n* (%)	722 (51.5)	209 (40.8)	< 0.001	Ref: Caucasian
Mestizo *n* (%)	603 (43)	241 (47.1)		1.38 (1.11, 1.71)
Others *n* (%)	32 (2.3)	23 (4.5)		2.48 (1.41, 4.32)
Unknown *n* (%)	46 (3.3)	39 (7.6)		–
Socioeconomic level				
High *n* (%)	34 (2.5)	5 (1)	< 0.001	Ref: High
Medium–high *n* (%)	85 (6.3)	51 (10.2)		1.71 (0.70, 5.15)
Medium *n* (%)	262 (19.4)	66 (13.3)		2.41 (1.02, 7.10)
Medium–low *n* (%)	707 (52.2)	251 (50.4)		3.20 (1.33, 9.49)
Low *n* (%)	266 (19.6)	125 (25.1)		4.08 (1.62, 12.5)
Unknown *n* (%)	49 (3.5)	14 (2.7)		–
Education (years) mean (SD)	13.5 (3.7)	12.4 (3.9)	< 0.001	0.93 (0.90, 0.96)
Health insurance				
Social security *n* (%)	678 (48.3)	251 (49.0)	0.003	Ref: Social security
Private health *n* (%)	367 (26.2)	100 (19.5)		0.74 (0.56, 0.96)
Private health + social security *n* (%)	76 (5.42)	24 (4.7)		0.85 (0.52, 1.36)
Public health *n* (%)	264 (18.8)	132 (25.8)		1.35 (1.05, 1.74)
Unknown *n* (%)	18 (1.3)	5 (1.0)		–
Rheumatic disease				
Rheumatoid arthritis *n* (%)	591 (42.1)	217 (42.4)	0.961	1.01 (0.82, 1.20)
Systemic lupus erythematosus n(%)	228 (16.3)	80 (15.6)	0.795	0.95 (0.72, 1.25)
Spondyloarthritis *n* (%)	149 (10.6)	37 (7.2)	0.033	0.66 (0.44, 0.94)
Sjögren's syndrome *n* (%)	75 (5.4)	27 (5.3)	1.000	0.99 (0.62, 1.53)
Systemic sclerosis *n* (%)	51 (3.6)	27 (5.3)	0.044	1.65 (1.03, 2.60)
Vasculitis *n* (%)	34 (2.4)	31 (6.1)	< 0.001	2.60 (1.57, 4.27)
Antiphospholipid syndrome *n* (%)	36 (2.6)	12 (2.3)	0.912	0.91 (0.45, 1.72)
Inflammatory myopathy *n* (%)	30 (2.1)	21 (4.1)	0.028	1.96 (1.10, 3.43)
Osteoarthritis *n* (%)	108 (7.7)	33 (6.5)	0.407	0.83 (0.54, 1.22)
Fibromyalgia *n* (%)	58 (4.1)	14 (2.7)	0.197	0.65 (0.35, 1.15)
Disease duration (years) mean (SD)	8.4 (7.4)	9.3 (8.3)	0.111	1.01 (1.00, 1.03)
Disease activity				
Remission *n* (%)	506 (38.7)	128 (27.9)	< 0.001	Ref: Remission
Low disease activity *n* (%)	561 (43)	187 (40.8)		1.32 (1.02, 1.70)
Moderate disease activity *n* (%)	211 (16.2)	108 (23.6)		2.02 (1.49, 2.74)
High disease activity *n* (%)	28 (2.1)	35 (7.6)		4.94 (2.91, 8.48)
Unknown/not applicable *n* (%)	97 (6.9)	54 (10.5)		–
Treatment				
Glucocorticoid dose				
0 mg/day *n* (%)	961 (69.2)	247 (49.0)	< 0.001	Ref: 0 mg/day
≤ 5 mg/day *n* (%)	382 (27.5)	209 (41.5)		2.13 (1.71, 2.65)
> 5 mg/day *n* (%)	43 (3.10)	48 (9.52)		4.34 (2.81, 6.73)
Dose unknown	3 (0.216)	0 (0)		–
Conventional DMARDs				
Methotrexate *n* (%)	545 (38.8)	169 (33)	0.022	0.78 (0.63, 0.96)
Antimalarials *n* (%)	278 (19.8)	83 (16.2)	0.086	0.78 (0.60, 1.02)
Leflunomide *n* (%)	106 (7.6)	42 (8.2)	0.709	1.09 (0.75, 1.58)
Sulfasalazine *n* (%)	10 (0.7)	5 (1)	0.563	1.37 (0.43, 3.89)
Immunosuppressants				
Mycophenolate mofetil *n* (%)	65 (4.6)	29 (5.7)	0.421	1.24 (0.78, 1.92)
Azathioprine *n* (%)	47 (3.4)	32 (6.3)	0.007	1.92 (1.20, 3.04)
Cyclophosphamide *n* (%)	2 (0.1)	4 (0.8)	0.047	5.52 (1.07, 39.9)
Cyclosporine *n* (%)	1 (0.1)	0 (0)	1.000	–

Table 2 (continued)

Variables	Not hospitalized $n=1403$	Hospitalized $n=512$	p value	OR (95% CI)
Biological DMARDs				
TNF-α inhibitors *n* (%)	170 (12.1)	34 (6.6)	< 0.001	0.52 (0.35, 0.75)
Rituximab *n* (%)	17 (1.2)	21 (4.1)	< 0.001	3.49 (1.83, 6.75)
IL-6 inhibitors *n* (%)	17 (1.2)	7 (1.4)	0.969	1.13 (0.43, 2.64)
Abatacept *n* (%)	16 (1.1)	8 (1.6)	0.615	1.38 (0.55, 3.15)
IL-17 inhibitors *n* (%)	21 (1.5)	3 (0.6)	0.176	0.39 (0.09, 1.13)
IL-23 or IL-12/23 inhibitors *n* (%)	6 (0.4)	2 (0.4)	1.000	0.91 (0.13, 3.98)
Belimumab *n* (%)	6 (0.4)	1 (0.2)	0.683	0.46 (0.02, 2.68)
Targeted synthetic DMARDs				
JAK inhibitors *n* (%)	59 (4.2)	25 (4.9)	0.607	1.15 (0.70, 1.83)
Apremilast *n* (%)	0 (0)	2 (0.4)	0.071	–
Comorbidities *n* (%)	534 (39.5)	349 (70.8)	< 0.001	3.71 (2.98, 4.65)
Arterial hypertension *n* (%)	257 (19.1)	207 (42.2)	< 0.001	3.09 (2.47, 3.87)
Obesity *n* (%)	133 (9.9)	110 (22.9)	< 0.001	2.70 (2.04, 3.56)
Dyslipidemia *n* (%)	139 (10.4)	102 (21.6)	< 0.001	2.38 (1.79, 3.15)
Lung disease *n* (%)	81 (6.1)	104 (21.4)	< 0.001	4.22 (3.10, 5.79)
Diabetes *n* (%)	69 (5.2)	75 (15.4)	< 0.001	3.36 (2.38, 4.75)
Cardiovascular disease *n* (%)	25 (1.9)	75 (15.4)	< 0.001	4.16 (2.47, 7.10)
Cancer *n* (%)	27 (2)	16 (3.3)	0.152	1.66 (0.87, 3.08)
Chronic kidney failure *n* (%)	12 (0.9)	22 (4.5)	< 0.001	5.24 (2.62, 11.0)
Cerebrovascular disease *n* (%)	6 (0.4)	11 (2.3)	< 0.001	5.18 (1.96, 15.10)
Smoking status				
Current smoker *n* (%)	83 (6.60)	23 (5.2)	< 0.001	Ref: Current smoker
Past smoker *n* (%)	240 (19.1)	142 (32.2)		2.14 (1.31, 3.61)
Never *n* (%)	935 (74.3)	276 (62.6)		1.07 (0.67, 1.76)
Unknown *n* (%)	145 (10.3)	71 (13.9)		–

n number, *SD* standard deviation, *ref* reference, *DMARDs* disease-modifying anti-rheumatic drugs, *TNF* tumor necrosis factor, *IL* interleukin

likely to be hospitalized or to require at least high-flow oxygen therapy. Moreover, every extra year beyond 18 years of age represented a 4%, 6%, and 7% increased risk of hospitalization, severe oxygen requirement, and death, respectively. Similar results were observed by Schönfeld et al. [6] studying the general Argentine population; male gender was associated with ICU admission and death with an OR of 1.49 (95% CI 1.43–1.56) and individuals over 60 years old were almost five times more likely to reach this composite outcome. Likewise, arterial hypertension, diabetes, obesity, pulmonary disease, heart failure, malignancy, and chronic renal disease were identified as poor prognostic factors [6]. These factors have also been associated with hospitalization and death during SARS-CoV-2 infection in patients with rheumatic diseases [7, 8].

Univariate analysis showed that variables related to social inequality, like lower socioeconomic status, less education, and public health insurance, were more frequent among patients with worse COVID-19 outcomes. Also, Mestizos and other non-Caucasian ethnicities were more frequently hospitalized and required more severe oxygen therapy. It could be argued that patients with lower socioeconomic status have higher disease activity as a result of having less access to medical care and treatments; however, even after adjusting for clinical variables, patients with public health insurance and Mestizos were 44% and 39% more likely to be hospitalized, respectively. Likewise, data from one of the most affected areas with COVID-19 of Argentina, Buenos Aires City, showed that neighborhoods with higher mortality rates had more households with unsatisfied needs (UBN) compared to districts with lower mortality. In addition, two items included in the UBN index, particularly overcrowding and homes without bathrooms, could have a direct relationship with the spread of the virus [12]. The association between mortality due to COVID-19 and poor socioeconomic status was also described in other South American countries, like Brazil and Chile [13, 14]. This could be related to less social distancing measures, insufficient testing, poor public health interventions, test result delays, and higher fatality rates in the lower end of the socioeconomic spectrum [15]. On the other hand, data provided by the COVID-19 Global Rheumatology Alliance (GRA) showed that ethnicity was associated with different COVID-19 outcomes. Particularly, after adjusting for poor prognostic factors, Latins were almost twice more likely to be hospitalized and die due to SARS-CoV-2 infection [16].

Table 3 Sociodemographic and clinical variables associated with severe oxygen requirements due to COVID-19

Variables	No severe O_2 requirement $n=1784$	Severe O_2 requirement $n=131$	*p* value	OR (95% CI)
Female gender *n* (%)	1458 (81.7)	91 (69.5)	< 0.001	1.97 (1.32, 2.89)
Age (years) mean (DE)	50.6 (14.0)	61.6 (13.6)	< 0.001	1.06 (1.05, 1.08)
Ethnicity				
Caucasian *n* (%)	872 (48.9)	59 (45)	0.012	Ref: Caucasian
Mestizo *n* (%)	791 (44.3)	53 (40.5)		2.20 (1.05, 4.21)
Others *n* (%)	47 (2.6)	8 (6.1)		0.99 (0.67, 1.45)
Unknown *n* (%)	74 (4.1)	11 (8.4)		–
Socioeconomic level				
High *n* (%)	36 (2)	3 (2.3)	0.308	Ref: High
Medium–high *n* (%)	312 (18.1)	16 (12.8)		0.62 (0.19, 2.74)
Medium *n* (%)	897 (51.9)	61 (48.8)		0.82 (0.28, 3.45)
Medium–low *n* (%)	358 (20.7)	33 (26.4)		1.11 (0.37, 4.76)
Low *n* (%)	124 (7.2)	12 (9.6)		1.16 (0.35, 5.30)
Unknown *n* (%)	57 (3.2)	6 (4.6)		–
Education (years) mean (SD)	13.3 (3.75)	12.5 (4.17)	0.066	0.95 (0.90, 1.00)
Health insurance				
Social security *n* (%)	856 (48.)	73 (55.7)	0.382	Ref: Social security
Private health *n* (%)	441 (24.7)	26 (19.8)		1.17 (0.75, 1.87)
Private health + social security *n* (%)	95 (5.3)	5 (3.8)		0.81 (0.46, 1.41)
Public health *n* (%)	369 (20.7)	27 (20.6)		0.72 (0.24, 1.77)
Unknown *n* (%)	23 (1.3)	0 (0)		–
Rheumatic disease				
Rheumatoid arthritis *n* (%)	751 (42.1)	57 (43.5)	0.822	1.06 (0.74, 1.51)
Systemic lupus erythematosus *n* (%)	293 (16.4)	15 (11.5)	0.170	0.66 (0.36, 1.11)
Spondyloarthritis *n* (%)	176 (9.9)	10 (7.6)	0.497	0.76 (0.37, 1.40)
Sjögren's syndrome *n* (%)	100 (5.6)	2 (1.5)	0.071	0.26 (0.04, 0.84)
Systemic sclerosis *n* (%)	76 (4.3)	5 (3.8)	0.985	0.89 (0.31, 2.04)
Vasculitis *n* (%)	47 (2.6)	18 (13.7)	< 0.001	5.89 (3.24, 10.30)
Antiphospholipid syndrome *n* (%)	45 (2.5)	18 (2.3)	1.000	0.91 (0.22, 2.52)
Inflammatory myopathy *n* (%)	47 (2.6)	4 (3.0)	0.775	1.16 (0.35, 2.92)
Osteoarthritis *n* (%)	131 (7.3)	10 (7.6)	1.000	1.04 (0.50, 1.94)
Fibromyalgia *n* (%)	70 (3.9)	2 (1.5)	0.231	0.38 (0.06, 1.23)
Disease duration (years) mean (SD)	8.5 (7.5)	10.7 (9.1)	0.007	1.03 (1.01, 1.06)
Disease activity				
Remission *n* (%)	700 (42.5)	48 (41.7)	< 0.001	Ref: Remission
Low disease activity *n* (%)	293 (17.8)	26 (22.6)		8.29 (4.08, 16.5)
Moderate disease activity *n* (%)	609 (36.9)	25 (21.7)		1.67 (1.03, 2.78)
High disease activity *n* (%)	47 (2.9)	16 (12.2)		2.16 (1.22, 3.82)
Unknown/not applicable *n* (%)	135 (7.6)	16 (12.2)		–
Treatment				
Glucocorticoid dose				
0 mg/day *n* (%)	1155 (65.5)	53 (41.1)	< 0.001	Ref: 0 mg/day
≤ 5 mg/day *n* (%)	535 (30.3)	56 (43.4)		2.28 (1.54, 3.37)
> 5 mg/day *n* (%)	71 (4.0)	20 (15.5)		6.14 (3.42, 10.70)
Unknown dose *n* (%)	3 (0.2)	0 (0)		–
Conventional DMARDs				
Methotrexate *n* (%)	676 (37.9)	38 (29.0)	0.053	0.67 (0.45, 0.98)
Antimalarials *n* (%)	347 (19.5)	14 (10.7)	0.018	0.50 (0.27, 0.84)
Leflunomide *n* (%)	144 (8.1)	4 (3.1)	0.057	0.36 (0.11, 0.87)
Sulfasalazine *n* (%)	13 (0.7)	2 (1.5)	0.274	2.11 (0.33, 7.75)
Immunosuppressants				
Mycophenolate mofetil *n* (%)	87 (4.9)	7 (5.3)	0.977	1.10 (0.45, 2.27)
Azathioprine *n* (%)	67 (3.8)	12 (9.2)	0.006	2.58 (1.30, 4.74)

Table 3 (continued)

Variables	No severe O_2 requirement $n=1784$	Severe O_2 requirement $n=131$	*p* value	OR (95% CI)
Cyclophosphamide *n* (%)	4 (0.2)	2 (1.5)	0.058	6.90 (0.95, 35.70)
Cyclosporine *n* (%)	1 (0.1)	0 (0)	1	–
Biological DMARDs				
TNF-α inhibitors *n* (%)	195 (10.9)	9 (6.9)	0.191	0.60 (0.28, 1.14)
Rituximab *n* (%)	26 (1.5)	12 (9.2)	< 0.001	6.82 (3.25, 13.60)
IL-6 inhibitors *n* (%)	22 (1.2)	2 (1.5)	0.678	1.24 (0.20, 4.28)
Abatacept *n* (%)	22 (1.2)	2 (1.5)	0.678	1.24 (0.20, 4.28)
IL-17 inhibitors *n* (%)	24 (1.4)	0 (0)	0.404	–
IL-23 or IL-12/23 inhibitors *n* (%)	7 (0.4)	1 (0.8)	0.433	1.95 (0.10, 11.1)
Belimumab *n* (%)	6 (0.3)	1 (0.8)	0.392	2.28 (0.12, 13.5)
Targeted synthetic DMARDs				
JAK inhibitors *n* (%)	78 (4.4)	6 (4.6)	1	1.04 (0.40, 2.24)
Apremilast *n* (%)	2 (0.1)	0 (0)	1	–
Comorbidities *n* (%)	784 (45.7)	99 (77.3)	< 0.001	4.06 (2.69, 6.31)
Arterial hypertension *n* (%)	401 (23.5)	63 (49.6)	< 0.001	3.20 (2.22, 4.62)
Obesity *n* (%)	228 (13.4)	34 (26.8)	< 0.001	2.46 (1.58, 3.73)
Dyslipidemia *n* (%)	209 (12.4)	32 (26.4)	< 0.001	2.55 (1.64, 3.88)
Lung disease *n* (%)	155 (9.1)	30 (23.8)	< 0.001	3.11 (1.97, 4.79)
Diabetes *n* (%)	113 (6.7)	31 (24.4)	< 0.001	4.53 (2.86, 7.02)
Cardiovascular disease *n* (%)	44 (2.6)	16 (13.1)	< 0.001	5.64 (3.00, 10.10)
Cancer *n* (%)	36 (2.1)	7 (5.6)	0.0025	2.72 (1.09, 5.88)
Chronic kidney failure *n* (%)	22 (1.3)	12 (9.5)	< 0.001	7.95 (3.73, 16.20)
Cerebrovascular disease *n* (%)	14 (0.8)	3 (2.4)	0.106	2.95 (0.67, 9.18)
Smoking status				
Current smoker *n* (%)	97 (6.1)	9 (8)	0.02	Ref: Current smoker
Past smoker *n* (%)	346 (21.8)	36 (32.1)		1.12 (0.54, 2.55)
Never *n* (%)	1144 (72.1)	67 (59.8)		0.63 (0.32, 1.39)
Unknown *n* (%)	197 (11)	19 (14.5)		–

n number, *SD* standard deviation, *Ref* reference, *DMARDs* disease-modifying anti-rheumatic drugs, *TNF* tumor necrosis factor, *IL* interleukin

In addition, an analysis including over 14,000 patients from 23 countries proved that countries with low socioeconomic status, environmental exposures, scarce medical resources, and few government-imposed containment measures were independently associated with higher odds of death attributed to COVID-19 in patients with rheumatic diseases [17]. These results highlight the importance of public health approaches to reduce the consequences of socioeconomic inequalities in order to improve SARS-CoV-2 detection and prompt access to the healthcare system.

Regarding rheumatic diseases, and in concordance with data from the COVID-19 GRA and other European cohorts [7, 8, 18, 19], high disease activity and treatment with glucocorticoids and rituximab were associated with all three poor outcomes. In this study, patients taking at least 5 mg/day of prednisolone or rituximab were almost four and eight times more likely to die from COVID-19, respectively. Similarly, Strangfeld et al. showed that patients with rheumatic diseases taking rituximab and glucocorticoids over 10 mg/day and those with high disease activity were 4.0, 1.7, and 1.9 times more likely to die due to COVID-19, respectively [7]. In addition, the same group also described the association between immunosuppressants and JAK inhibitors with poor outcomes [7, 19, 20]. Here, although the use of azathioprine and cyclophosphamide was more frequent among patients with severe COVID-19, it did not reach statistical significance in the multivariable analysis, probably because of the small sample size of this group. In relation to JAK inhibitors, we did not find differences in our study.

Although some studies have shown that patients with rheumatic diseases have more severe COVID-19 compared to the general population, existing data is conflicting [21–26]. The design of our study only allowed for indirect comparisons with a population without rheumatic conditions. According to the report of July 31, 2021 from the Ministry of Health (cut-off date of this analysis), 4,929,764 cases of SARS-CoV-2 infection had been confirmed, of which 4,569,552 patients had recovered and 105,721 (2.1%) had

Table 4 Sociodemographic and clinical variables associated with death due to COVID-19

Variables	Alive $n=1832$	Death $n=83$	p value	OR (95% CI)
Female gender *n* (%)	1489 (81.3)	60 (72.3)	0.058	1.66 (1.00, 2.69)
Age (years) mean (DE)	50.9 (14)	63 (13.1)	< 0.001	1.07 (1.05, 1.09)
Ethnicity				
Caucasian *n* (%)	891 (50.8%)	40 (53.3)	0.388	Ref: Caucasian
Mestizo *n* (%)	813 (46.3%)	31 (41.3)		2.31 (0.98, 4.88
Others *n* (%)	51 (2.91%)	4 (5.3)		0.85 (0.52, 1.37
Unknown *n* (%)	77 (4.2%)	8 (9.6)		1.75 (0.51, 4.55
Socioeconomic level				
High *n* (%)	39 (2.2)	0 (0)	0.418	0.00 (0.00, 6,16)
Medium–high *n* (%)	316 (17.8)	12 (15.2)		0.70 (0.28, 1.92)
Medium *n* (%)	920 (51.9)	38 (48.1)		0.76 (0.35, 1.89)
Medium–low *n* (%)	369 (20.8)	22 (27.8)		1.10 (0.48, 2.83)
Low *n* (%)	129 (7.3)	7 (8.1)		Ref: Low
Unknown *n* (%)	59 (3.2)	4 (4.8)		–
Education (years) mean (SD)	13.3 (3.8)	11.6 (3.8)	< 0.001	0.89 (0.83, 0.95)
Health insurance				
Social security *n* (%)	877 (47.9)	52 (62.7)	0.04	Ref: Social security
Private health *n* (%)	456 (24.9)	11 (13.3)		0.41 (0.20, 0.76)
Private health + social security *n* (%)	98 (5.4)	2 (2.4)		0.34 (0.06, 1.13)
Public health *n* (%)	378 (20.6)	18 (21.7)		0.80 (0.45, 1.37)
Unknown *n* (%)	23 (1.3)	0 (0)		–
Rheumatic disease				
Rheumatoid arthritis *n* (%)	774 (42.2)	34 (41)	0.906	0.95 (0.60, 1.48)
Systemic lupus erythematosus *n* (%)	298 (16.3)	10 (12)	0.384	0.71 (0.34, 1.32)
Spondyloarthritis *n* (%)	185 (10.1)	1 (1.2)	0.0.13	0.11 (0.01, 0.49)
Sjögren's syndrome *n* (%)	101 (5.5)	1 (1.2)	0.127	0.21 (0.01, 0.96)
Systemic sclerosis *n* (%)	75 (4.1)	6 (7.2)	0.160	1.83 (0.69, 4.00)
Vasculitis *n* (%)	51 (2.8)	14 (16.9)	< 0.001	7.09 (3.62, 13.10)
Antiphospholipid syndrome *n* (%)	45 (2.5)	3 (3.6)	0.462	1.49 (0.36, 4.19)
Inflammatory myopathy *n* (%)	46 (2.5)	5 (6)	0.067	2.49 (0.85, 5.89)
Osteoarthritis *n* (%)	138 (7.5)	3 (3.6)	0.262	0.46 (0.11, 1.25)
Fibromyalgia *n* (%)	70 (3.8)	2 (2.4)	0.767	0.62 (0.10, 2.03)
Disease duration (years) mean (SD)	8.6 (7.6)	10.2 (8.9)	0.080	1.03 (1.00, 1.05)
Disease activity				
Remission *n* (%)	618 (36.6)	16 (21.3)	< 0.001	Ref: Remission
Low disease activity *n* (%)	722 (42.7)	26 (34.7)		11.0 (5.04, 24.00)
Moderate disease activity *n* (%)	300 (17.8)	19 (25.3)		1.39 (0.75, 2.67)
High disease activity *n* (%)	49 (2.9)	14 (18.7)		2.45 (1.24, 4.88)
Unknown/not applicable *n* (%)	143 (7.8)	8 (9.6)		–
Treatment				
Glucocorticoid dose				
0 mg/day *n* (%)	1182 (65.2)	26 (32.1)	< 0.001	Ref: 0 mg/day
…… ≤ 5 mg/day *n* (%)	549 (30.3)	42 (51.9)		3.48 (2.12, 5.80)
> 5 mg/day *n* (%)	78 (4.3)	13 (16)		7.58 (3.65, 15.10)
> Unknown dose *n* (%)	3 (0.2)	0 (0)		–
Conventional DMARDs				
Methotrexate *n* (%)	690 (37.7)	24 (28.9)	0.135	0.67 (0.41, 1.08)
Antimalarials *n* (%)	350 (19.1)	11 (13.3)	0.234	0.65 (0.32, 1.18)
Leflunomide *n* (%)	146 (8)	2 (2.4)	0.100	0.29 (0.05, 0.92)
Sulfasalazine *n* (%)	15 (0.8)	0 (0)	1.000	–
Immunosuppressants				
Mycophenolate mofetil *n* (%)	88 (4.8)	6 (7.2)	0.296	1.54 (0.59, 3.37)
Azathioprine *n* (%)	74 (4)	5 (6)	0.388	1.52 (0.52, 3.52)
Cyclophosphamide *n* (%)	6 (0.3)	0 (0)	1.000	–
Cyclosporine *n* (%)	1 (0.1)	0 (0)	1.000	–

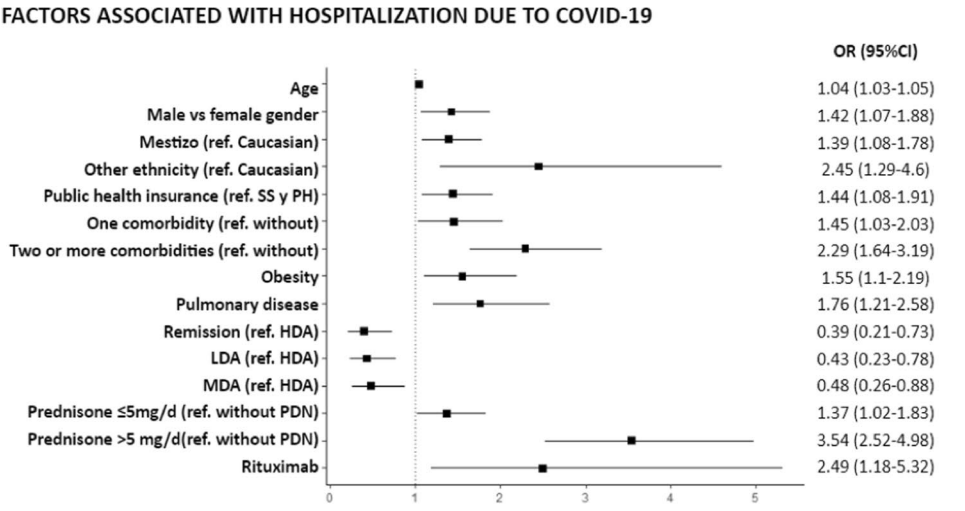
Table 4 (continued)

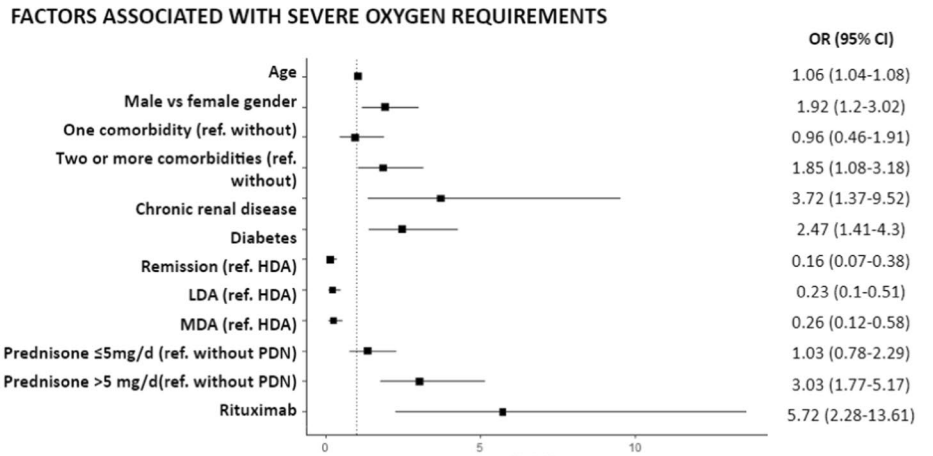
Variables	Alive $n=1832$	Death $n=83$	p value	OR (95% CI)
Biological DMARDs				
TNF-α inhibitors *n* (%)	199 (10.9)	5 (6)	0.224	0.53 (0.18, 1.19)
Rituximab *n* (%)	29 (1.6)	9 (10.8)	<0.001	7.56 (3.27, 16.00)
IL-6 inhibitors *n* (%)	24 (1.3)	0 (0)	0.622	–
Abatacept *n* (%)	22 (1.2)	2 (2.4)	0.279	2.03 (0.32, 7.06)
IL-17 inhibitors *n* (%)	24 (1.3)	0 (0)	0.622	–
IL-23 or IL-12/23 inhibitors *n* (%)	8 (0.4)	0 (0)	1.000	–
Belimumab *n* (%)	6 (0.3)	1 (1.2)	0.267	3.71 (0.20, 22.10)
Targeted synthetic DMARDs				
JAK inhibitors *n* (%)	81 (4.4)	3 (3.6)	1.000	0.80 (0.19, 2.20)
Apremilast *n* (%)	2 (0.1)	0 (0)	1.000	–
Comorbidities *n* (%)	819 (46.4)	64 (80)	<0.001	4.62 (2.72, 8.33)
Arterial hypertension *n* (%)	424 (24.2)	40 (50.6)	<0.001	3.22 (2.04, 5.08)
Obesity *n* (%)	243 (13.9)	19 (24.1)	0.018	2.23 (1.27, 3.74)
Dyslipidemia *n* (%)	224 (12.9)	17 (23)	0.020	2.01 (1.12, 3.45)
Lung disease *n* (%)	162 (9.3)	23 (29.5)	<0.001	4.09 (2.41, 6.75)
Diabetes *n* (%)	124 (7.1)	20 (25.3)	<0.001	4.43 (2.53, 7.48)
Cardiovascular disease *n* (%)	46 (2.7)	14 (18.4)	<0.001	8.29 (4.20, 15.50)
Cancer *n* (%)	38 (2.)	5 (6.4)	0.034	3.08 (1.04, 7.39)
Chronic kidney failure *n* (%)	23 (1.3)	11 (13.9)	<0.001	12.1 (5.49, 25.40)
Cerebrovascular disease *n* (%)	15 (0.9)	2 (2.6)	0.160	3.07 (0.48, 11.10)
Smoking status				
Current smoker *n* (%)	104 (6.4)	2 (2.9)	0.012	Ref: Current smoker
Past smoker *n* (%)	357 (21.9)	25 (36.8)		3.64 (1.06, 22.9)
Never *n* (%)	1170 (71.7)	41 (60.3)		1.82 (0.55, 11.3)
Unknown *n* (%)	201 (11)	15 (18.1)		–

n number, *SD* standard deviation, *Ref* reference, *DMARDs* disease-modifying anti-rheumatic drugs, *TNF* tumor necrosis factor, *IL* interleukin

died (27). Overall mortality in our cohort was 4.4%. This difference can be due to several factors. First, the general population was younger and had a lower frequency of comorbidities, which have been identified as poor prognostic factors. Furthermore, our registry overrepresents COVID-19 patients with only 5% of asymptomatic patients and higher frequency of female sex. In addition, those with rheumatic diseases presented other factors that have been associated with a worse outcome of COVID-19, particularly disease activity and their treatments, whose impact has been observed in our cohort as well as in other registries in Latin America and the world [7, 8, 28–30]. As the latter are potentially modifiable factors, the role of the rheumatologist during the pandemic is of great relevance. Patients with rheumatic diseases should be encouraged to continue their medical check-ups in order to minimize disease activity and ensure early detection of disease flares. Moreover, rheumatologists should choose the best treatment possible considering risks and benefits of every drug and promote the vaccination of patients taking into account international recommendations [31, 32].

Given the observational design, there are some limitations to the registry. First, there could be an inclusion bias since the data is voluntarily reported by rheumatologists. Marketing campaigns by SAR are constantly being carried out to promote patient inclusion, and now almost 15% of SAR members are participating in this project. Most of them belong to the Buenos Aires metropolitan area, Córdoba and Santa Fe. However, this reflects the distribution of the population in our country and the areas with highest COVID-19 incidence [2]. Less populated provinces were also represented and, as expected, these provinces contributed fewer patients. This is the biggest cohort of patients with rheumatic diseases and SARS-CoV-2 infection in our country and data from patients from all over Argentina have been included, considering sociodemographic and economic characteristics. Second, patients with an immunosuppressive condition could have been hospitalized even without presenting moderate or severe SARS-CoV-2 infection, particularly at the beginning of the pandemic when information about their evolution and treatment was scarce. Notably, in this cohort, 43% of the hospitalized patients did not require oxygen supplementation. For this reason, more robust outcomes, like severe oxygen requirements and mortality, were also analyzed. Third, since only rheumatologists participated in this registry, no control group was included, only allowing indirect comparisons with the general population from





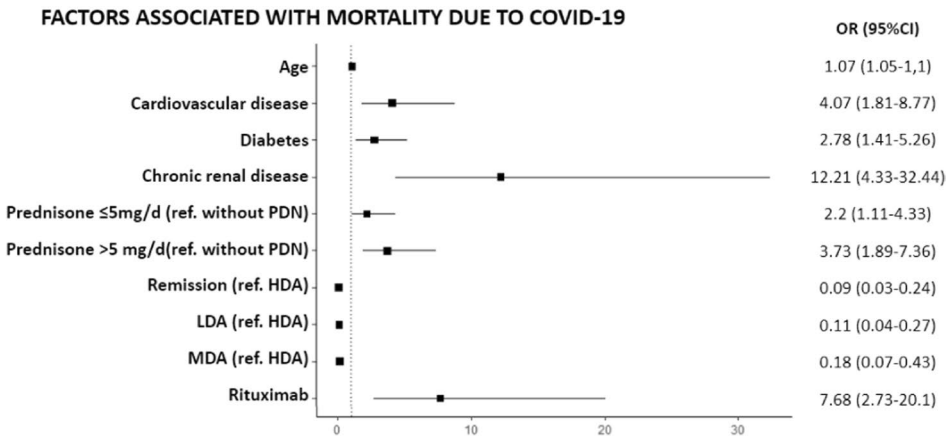


Fig. 2 Sociodemographic and clinical factors associated with **A** hospitalization, **B** severe oxygen requirements, and **C** death due to COVID-19. Only significant associations are shown. The models have been adjusted for the following variables: sex, age, ethnicity, socioeconomic level, health insurance, education, comorbidities, smoking status, rheumatic disease diagnostic, activity, and treatment. ref, reference; SS, social security; PH, private health; HDA, high disease activity; MDA, moderate disease activity; LDA, low disease activity; PDN, prednisone

previously published data. In addition, since some of the data was collected during the lockdown asymptomatic or mild cases could be underreported.

To conclude, unmodifiable, well-known risk factors like age and male gender, along with the presence of comorbidities, were related to poor COVID-19 outcomes in patients with rheumatic diseases. Hospitalizations were associated with socioeconomic factors related to social inequality, including ethnicity and public health insurance. Finally, patients with high disease activity and those receiving glucocorticoids or rituximab at the time of infection were more likely to have a poor COVID-19 outcome.

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Author contribution All authors listed in this manuscript made substantial contributions to the acquisition, analysis, or interpretation of data and were involved in drafting or revising this article critically for important intellectual content. All authors approved the final version to be published. A list of all the SAR-COVID registry sub-investigators is included in the Appendix.

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Data availability All data and materials generated and analyzed during the current study belong to the SAR-COVID registry and the Argentine Society of Rheumatology. They are available from the corresponding author on reasonable request. The authors declare that all relevant data is included in the article and its supplementary information files. More information about the registry is available in https://www.unisar.reumatologia.org.ar/registros_sarcovid.php.

Declarations

Ethics approval This study is being conducted in accordance with Good Clinical Practice (GCP) guidelines, the International Conference on Harmonization (ICH), the ethical principles established in the Declaration of Helsinki, the law 3301/09, and local guidelines. Personal identification data was kept anonymous. An independent ethics committee approved the protocol and the informed consent form (Comité de Ética Dr Claude Bernard – SARCOVID.20200526.16.PI, June 8, 2020).

Consent to participate All patients signed the corresponding informed consent form to participate in this registry.

Consent for publication Individuals provided consent for the publication of their data.

Conflict of interest The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: SAR-COVID is a multi-sponsor registry, where Pfizer, Abbvie, and Elea Phoenix provided unrestricted grants. None of them participated or influenced the development of the project, data collection, analysis, interpretation, or writing of the report. They do not have access to the information collected in the database.

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