



SCIENTIFIC ARTICLE

Clinical characteristics of Chilean patients with rheumatic diseases and COVID-19: data from the Covid-19 Global Rheumatology Alliance physician-reported registry

Características clínicas de pacientes chilenos con enfermedades reumáticas y COVID19: datos del registro informado por médicos de La Alianza Global de Reumatología COVID-19

Características clínicas de pacientes chilenos com doenças reumáticas e COVID19: dados do registro relatado por médicos da Aliança Global de Reumatologia COVID-19

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BRIEF REPORT

Clinical characteristics of Chilean patients with rheumatic diseases and COVID-19: data from the Covid-19 Global Rheumatology Alliance physician-reported registry

Abstracts

In English

Objective

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), has registered more than 234 million confirmed cases and more than 4.7 million deaths throughout the world until October 2, 2021. During the last few months, a significant number of reports of COVID-19 in patients with rheumatic diseases have been published. In this study the objective is to report the clinical characteristics of Chilean patients with rheumatic diseases and COVID-19 reported in the "Global Rheumatology Alliance" (GRA) physician registration platform.

Material and Method

Chilean patients with rheumatic diseases and COVID-19 were included in the Covid-19 GRA physician-reported registry.

Results

54 patients were included. The most common primary rheumatic disease was rheumatoid arthritis (RA) with 28 cases (51.9%). 30 patients (55.6%) used corticosteroids, of which 20 (66.7%) used a dose of 10 mg or less. 33 patients (61.1%) only used conventional DMARDs, 4 (7.4%) only biological, and 6 (11.1%) the combination. A total

of 35 patients (64.8%) had to be hospitalized. 2 patients (3.7%) died. 26 patients of the 35 hospitalized (74.2%) required some type of ventilatory support, of which 5 (19.2%) required non-invasive and 8 (30.8%) invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO).

Conclusion

Most of included Chilean rheumatic patients were hospitalized, with a low mortality rate but with a high percentage of patients requiring at least non-invasive mechanical ventilation.

Keywords

Rheumatic Disease, Pandemia, Covid-19, Brief Report



Abstracts

In Spanish

Objetivo

La pandemia por coronavirus 2019 (COVID-19), causada por el síndrome respiratorio agudo severo coronavirus 2 (SARS-Cov-2), ha registrado más de 234 millones de casos confirmados y más de 4,7 millones de muertes en todo el mundo hasta el 2 de octubre de 2021. Durante los últimos meses se han publicado un número importante de reportes de COVID-19 en pacientes con enfermedades reumáticas. En este estudio el objetivo es reportar las características clínicas de los pacientes chilenos con enfermedades reumáticas y COVID-19 reportados en la plataforma de registro de médicos "Global Rheumatology Alliance" (GRA).

Material y Método

Los pacientes chilenos con enfermedades reumáticas y COVID-19 fueron incluidos en el registro informado por médicos COVID-19 GRA.

Resultados

Se incluyeron 54 pacientes. La enfermedad reumática más frecuente fue la artritis reumatoide (AR) con 28 casos (51,9%). 30 pacientes (55,6%) utilizaron corticosteroides, de los cuales 20 (66,7%) utilizaron una dosis de 10 mg o menos. 33 pacientes (61,1%) solo utilizaron

FAME convencionales, 4 (7,4%) solo biológicos y 6 (11,1%) la combinación. Un total de 35 pacientes (64,8%) tuvieron que ser hospitalizados. Fallecieron 2 pacientes (3,7%). 26 pacientes de los 35 hospitalizados (74,2%) requirieron algún tipo de soporte ventilatorio, de los cuales 5 (19,2%) precisaron ventilación mecánica no invasiva y 8 (30,8%) invasiva u oxigenación por membrana extracorpórea (ECMO).

Conclusión

La mayoría de los pacientes reumáticos chilenos incluidos fueron hospitalizados, con una baja tasa de mortalidad pero con un alto porcentaje de pacientes que requirieron al menos ventilación mecánica no invasiva.

Palabras clave

Enfermedad reumática, Pandemia, Covid-19, Reporte



Abstracts

In Portuguese

Objetivo

A pandemia da doença coronavírus 2019 (COVID-19), causada pela síndrome respiratória aguda grave coronavírus 2 (SARS-Cov-2), registrou mais de 234 milhões de casos confirmados e mais de 4,7 milhões de mortes em todo o mundo até 2 de outubro, 2021. Nos últimos meses, foi publicado um número significativo de notificações de COVID-19 em pacientes com doenças reumáticas. Neste estudo o objetivo é relatar as características clínicas de pacientes chilenos com doenças reumáticas e COVID-19 relatadas na plataforma de registro de médicos "Global Rheumatology Alliance" (GRA).

Materiais e Métodos

Pacientes chilenos com doenças reumáticas e COVID-19 foram incluídos no registro Covid-19 GRA de relatórios médicos.

Resultados

54 pacientes foram incluídos. A doença reumática primária mais comum foi a artrite reumatoide (AR) com 28 casos (51,9%). 30 pacientes (55,6%) faziam uso de corticoide, dos quais 20 (66,7%) usavam dose igual ou inferior a 10 mg. 33 pacientes (61,1%) usavam apenas

DMARDs convencionais, 4 (7,4%) apenas biológicos e 6 (11,1%) a combinação. Um total de 35 pacientes (64,8%) teve que ser hospitalizado. 2 pacientes (3,7%) morreram. Dos 35 pacientes hospitalizados (74,2%), 26 necessitaram de algum tipo de suporte ventilatório, sendo 5 (19,2%) de ventilação mecânica não invasiva e 8 (30,8%) invasiva ou oxigenação por membrana extracorpórea (ECMO).

Conclusão

A maioria dos pacientes reumáticos chilenos incluídos foi hospitalizada, com uma baixa taxa de mortalidade, mas com uma alta porcentagem de pacientes necessitando, pelo menos, de ventilação mecânica não invasiva.

Palavras-chave:

Doença Reumática, Pandemia, Covid-19, Relatório breve



Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), has registered more than 234 million confirmed cases and more than 4.7 million deaths throughout the world until October 2, 2021, according to data published by the Johns Hopkins University (1). In Latin America, according to the World Health Organization, by October 2, 2021, almost 47 million cases had been registered, with approximately 1.5 million deaths (2), while Chile reported a total of 1.6 million cases with 37 thousand deaths from COVID-19 (3).

COVID-19 can generate a severe and aggressive illness, requiring hospitalization and ventilatory support, and potentially resulting in death. During the last few months, a significant number of case series and reports of COVID-19 in patients with rheumatic diseases have been published; one of the most important being the registry of the "COVID-19 Global Rheumatology Alliance" (GRA), the response of the rheumatology community to the global pandemic of COVID-19 (4). Since its launch in March 2020, more than 19,000 cases have been reported worldwide through its European and World-wide registries. Most of the GRA reports establish that the risk factors associated with hospitalization in rheumatic patients are the same as those in the general population and there does not seem to be a clear relationship between the activity indices

of rheumatic disease and the evolution of COVID-19 or worsening of underlying rheumatic disease secondary to COVID-19. Caution is necessary with some medications such as Rituximab, Sulfasalazine or doses of corticosteroids.

In this study the objective is to report the clinical characteristics of Chilean patients with rheumatic diseases and COVID-19 reported in the GRA physician registration platform..

Material and methods

Chilean patients with rheumatic diseases and COVID-19 were included in the GRA physician registry between April 2020 and August 2021. GRA is the collaborative work of an international group of rheumatologists, researchers and patient partners, surveying people with rheumatic diseases to better understand their experience during the COVID-19 pandemic and explore risk factors for developing COVID-19. 19. All health centers nationwide that wanted to participate in the study could do so, it was voluntary. The study included a single survey asking about medical history and the medications you take to treat your rheumatic disease. The selected patients were adults over 18 years of age with previously diagnosed rheumatic disease and confirmed COVID-19 who attended the emergency services. COVID-19 infection was defined as those individuals who presented suggestive symptoms and/or with compatible polymerase chain reaction (PCR) + or CT Scan



compatible.

COVID-19 diagnostic method as well as sociodemographic information, including age, sex, smoking status, rheumatic diagnosis, disease activity, comorbidities, and pre-COVID-19 medications were recorded. Medications prior to COVID-19 were classified as conventional synthetic disease-modifying antirheumatic drugs (DMARDs), biological DMARDs, synthetic plus biological DMARDs, and use of corticosteroids. Regarding COVID-19, the duration of symptoms, the status of the infection (resolved or not resolved at the time of the report, or unknown), the use of a specific drug treatment for COVID-19, the need for ventilatory support, infection outcome [death, hospitalization, complications such as acute respiratory distress syndrome (ARDS), sepsis, myocarditis / heart failure, secondary infection, cytokine storm] were also recorded.

Statistical analysis: The mean and standard deviation (SD) were calculated for the variables with normal distribution, and the median and interquartile range (IQR) were calculated for the variables without normal distribution. All analyzes were performed using the IBM SPSS Statistics version 24 program for Macintosh.

Ethical Considerations: This study was approved by the Department of Academic Development and Research and the Scientific Ethics Committee of the "Clinica Alemana-Universidad del Desarrollo" Medicine Faculty.

Results

54 patients were included, from April 2020 to August 2021. The mean age of the patients was 53.4 years (SD 14.6), and 36 patients (66.7%) were women. The most common primary rheumatic disease was rheumatoid arthritis (RA) with 28 cases (51.9%), followed by lupus (LES) with 7 cases (13%). At the time of COVID-19 diagnosis, 30 patients (55.6%) were in remission or had minimal or low activity of their underlying rheumatic disease, 8 patients (14.8%) had moderate activity and 8 (14.8%) severe activity, according to the physician appreciation. 30 patients (55.6%) used corticosteroids, of which 20 (66.7%) used a dose of 10 mg or less, and in 18 (60%) the dose was increased after COVID-19 diagnosis. 33 patients (61.1%) used only conventional DMARDs, the most used DMARDs were hydroxychloroquine, 20 patients (37%) and Methotrexate 17 patients (31.5%), 4 patients (7.4%) only biologics, and 6 (11.1%) the combination. No patients were reported using targeted synthetic DMARDs.

DMARDs were stopped in 22 patients (51.2%) after COVID-19 diagnosis, methotrexate is the that most frequently stopped with 7 patients (31.8%). Regarding comorbidities, 28 patients (51.9%) were hypertensive, 9 (16.7%) had underlying lung disease, 7 (13%) had diabetes, 1 (1.9%), 13 patients (24.1%) had ever smoked. Regarding COVID-19 in 47 (87%) patients the diagnosis was confirmed by polymerase chain reaction (PCR), 4 cases (7.4%) were diagnosed only by symptoms and 3 cases (5.6%) by a compatible CT scan. 52 cases (96.3%) were symptomatic, the main symptoms being fever

in 29 patients (53.7%), cough also in 29 (53.7%), and dyspnea in 27 cases (50%) (Table 1).

Specific drug treatment for COVID-19 was used in 30 patients (55.6%), of these, 16 (29.6%) received corticosteroids, 8 (14.8%) received azithromycin, 6 (11.1%) antimalarials, and 1 (1.9%) received tocilizumab. In 18 of the 30 patients (60%) who used corticosteroids before the diagnosis of COVID-19, the dose was increased after the diagnosis. At the time of registering, 40 patients (76.9%) had resolved symptoms. The duration of symptoms in these patients was a median of 21 days (interquartile range (IQR) 10-31.5). A total of 35 patients (64.8%) had to be hospitalized. 2 patients (3.7%) died. Among the 35 hospitalized patients, 26 (74.2%) required some type of ventilatory support, 13 (24.1%) at least non-invasive mechanical ventilation and of these 8 (14.8%) patients required invasive mechanical ventilation (IMV) or extracorporeal membrane oxygenation (ECMO). None of the registered patients presented a cytokine storm like syndrome.

Discussion

Since the COVID-19 pandemic began, the question has arisen as to whether patients with pre-existing inflammatory diseases mediated by the immune system, such as rheumatic diseases, are at increased risk of SARS CoV2 infection or severe COVID-19 outcomes. The first GRA report was published in May 2020 (5), where the factors associated with

hospitalization were examined in 600 rheumatic patients with COVID-19 from 40 countries, of which 46% (277 patients) required hospitalization. Both, advanced age, and the presence of previous comorbidities were factors associated with hospitalization (as in the general population). The use of high-dose glucocorticoids (≥ 10 mg per day of prednisone equivalent) was associated with an increased risk of hospitalization. The study also included a preliminary analysis of biological DMARD exposure and found that compared to patients who were not receiving biological DMARDs, they were less like to be hospitalized, regardless of the presence of other risk factors. In the Chilean registry the inclusion of hospitalized patients was favored, and the number of registered cases was low, so performing analysis of associations of risk for hospitalization and worse outcome of infection did not seem appropriate to us. The median of days from onset to resolution of symptoms was 13 days in the global report, while in Chilean patients it was 21 days.

In September 2020 another GRA (6) study was published comparing the characteristics of 74 patients with rheumatic diseases and COVID-19 reported in Latin America with 583 from the rest of the world. Mortality was similar in both groups (12% in Latin America vs 11% in the rest of the world). However, the Latin American registry included a higher percentage of hospitalized patients (61% in Latin America vs 45% in the rest of the world) and a high percentage needed at least non-invasive ventilation. This was like our Chilean report, but

the reported mortality was higher in the Latin American cohort.

In January 2021, a publication derived from the GRA (7) registry determined the factors associated with death related to COVID-19 in people with rheumatic disease. Of 3729 patients, 1739 (49%) was hospitalized, 187 (6.2%) required invasive ventilation and 390 (10.5%) died. Death was associated with known general factors and disease-specific factors (disease activity and specific medications). The association with moderate/high disease activity highlights. Caution may be required with rituximab, sulfasalazine, glucocorticoid dosages and some immunosuppressants. Mortality was higher, but the percentage of hospitalized patients was lower in this study than that reported in the Chilean registry (10.5% vs 3% deaths, 49% vs 64% hospitalized patients).

A more recent publication from the GRA (8), with a total of 1,324 patients, concluded that African American, Latinos, and Asian patients were more likely to require hospitalization compared to white patients. Latino patients were also 3 times more likely to require ventilatory support. We think these differences may be due in large part to a bias in the registry, clearly in Chile the registry of hospitalized patients was favored. No differences in mortality were found based on race / ethnicity. The results of this study are like the Chilean data in terms of mortality and the use of at least non-invasive mechanical ventilation reported, even though in Chile the registration of hospitalized patients was favored (64% Chile vs

36% Global).

Conclusions

This study had some limitations, such as the difficulty in data collection, due to medical exhaustion, the increased care load in the health centers selected to carry out the study, constant changes in the treatment paradigm, therefore, the number of patients included is low compared to those affected by COVID-19 in Chile. Therefore, we did not perform any further association analysis, as it would not reflect the reality of what happened. It is evident that the median number of symptoms is higher than that reported in other studies. This may be because the patients with more days of symptoms were those who attended the health centers and were hospitalized, and these were the patients who were included in the study, which also explains the high percentage of hospitalized patients when compared with the rest of the world. It is possible that there is an underreporting of mortality due to patients who did not consult the emergency services, and this would explain the low mortality rate with respect to the global data. In Chilean rheumatic patients, the symptoms of COVID-19 were the classic symptoms described for the disease, a low percentage manifested arthralgia and no activation of the rheumatic disease was reported. There is evidence of less use of corticosteroids and greater use of biological DMARDs in rheumatic patients from the rest of



the world compared to Chilean patients, possibly related to accessibility due to economic factors and health policies in each region. Regarding specific treatment for COVID-19, some patients were treated with therapies that were initially believed to work, but later evidence showed that they did not, such as hydroxychloroquine or azithromycin. Only one patient received tocilizumab, probably at the time of registration (early in the pandemic). If we compare the data of patients with rheumatic disease vs the total number of patients with COVID-19 in Chile for the dates of data collection, a higher percentage of hospitalization is evidenced for patients with rheumatic disease 64% vs 9.3%, in relation to mortality are similar 3% vs 2.4%, the reason for the greater number of patients requiring hospitalization may be due to what was previously mentioned and is that only patients who consulted the emergency room were included in the study, and that therefore it is understood they had more severe symptoms of COVID-19. It is not mentioned if the patients were vaccinated because when the data collection began it was

not yet available, and Chile started the vaccination process in patients with comorbidities in February 2021, and after that very few patients were registered.

It is concluded that most of the Chilean rheumatic patients included were hospitalized with a low mortality rate, although with a high percentage of patients who required at least non-invasive mechanical ventilation. No worsening of arthralgias or activation of

rheumatic disease was reported at the time of diagnosis of COVID-19

Conflict of Interest

The authors of this brief report have no conflict of interest.

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Table 1. Demographic characteristics of patients with rheumatological diseases and COVID 19 (n = 54)

Women, n(%)	36 (66.7)
Age (SD)	53.4 (14.6)
Primary rheumatologic diagnosis, n (%)	
RA	28 (51.9)
SLE	7 (13)
Spondyloarthritis	4 (7.4)
Sjogren's syndrome	3 (5.6)
Inflammatory myopathies	3 (5.6)
Other	7 (12.9)
Comorbidities, n (%)	
HT	28 (51.9)
Lung disease	9 (16.7)
Diabetes	7 (13)
Cancer	3 (5.6)
CVA	3 (5.6)
Ever smokers, n (%)	13 (24.1)
COVID-19 diagnostic method, n (%)	
PCR	47 (87)
Based on symptoms	4 (7.4)
CT scan	3 (5.6)

Symptoms, n (%)	
Fever	29 (53.7)
Cough	29 (53.7)
Dyspnoea	27 (50)
Myalgia	25 (46.3)
Headache	22 (40.7)
Diarrhea, nausea, vomiting	16 (29.6)
Odynophagia	14 (25.9)
Anosmia	13 (24.1)
Dysgeusia	12 (22.2)
Arthralgia	2 (3.7)
Rheumatic disease activity	
Remission	7 (13)
Minimal or low disease activity	23 (42.6)
Moderate disease activity	8 (14.8)
Severe or high disease activity	8 (14.8)
Unknown	8 (14.8)
Received specific treatment for COVID-19, n (%)	30 (55.6)
Corticosteroids	16 (53.3)
Azithromycin	8 (26.7)
Antimalarials	6 (20)



SD: Standard deviation
RA: Rheumatoid arthritis
SLE: Systemic lupus erythematosus
HT: Arterial hypertension
CVA: Cerebrovascular accident
BMI: Body mass index
PCR: Hain reaction
CT: Computerized axial tomography
DMARD: Conventional synthetic disease-modifying antirheumatic drugs

Figure 2. Source(s) of information utilized by patients with knee OA in our Latin American cohort.

	Chile	Latin America	World May 2020	World Jan 2021	World March 2021
Number of patients	54	74	600	3729	1324
Most frequent rheumatological pathology (%)	Rheumatoid arthritis 51.9	Rheumatoid arthritis 35	Rheumatoid arthritis 38	Rheumatoid arthritis 37.4	Rheumatoid arthritis 39
Age (SD)	53.4 (14.6)	53.5 (15.6)	56	57 (15.7)	NR
Women (%)	66.7	73	71	68	72 (White race)
Use of corticosteroids pre-Covid-19 (%)	55.6	51	32	34.6	23 (White race)
Use of biological DMARDs alone or in combination with synthetic DMARDs (%)	18.5	16	38.5	37.7	45.5 (White race)
Hospitalized patients (%)	64	61	46	49	36
Need for mechanical ventilation (%)	24.1	31	NR	6.2	26
Death (%)	3	12	9	10.5	6

References

1. Johns Hopkins University. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University [Available from: <https://coronavirus.jhu.edu/map.html>]. Accessed October 2, 2021.
2. World Health Organization. Global Health Observatory Data [Available from: https://www.who.int/gho/publications/world_health_statistics/en/]. Accessed October 2, 2021.
3. <https://www.minsal.cl/nuevo-coronavirus-2019-nCoV/cases-confirmados-en-chile-covid-19/>. Accessed October 2, 2021.
4. Gianfrancesco MA, Hyrich KL, Gossec L, Strangfeld A, Carmona L, Mateus EF, et al. Rheumatic disease and COVID-19: initial data from the COVID-19 Global Rheumatology Alliance provider registries. *Lancet Rheumatol*. mayo de 2020;2(5):e250.
5. Gianfrancesco M, Hyrich KL, Al-Adely S, Carmona L, Danila MI, Gossec 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*. julio de 2020;79(7):859-66.
6. Ugarte-Gil MF, Marques CDL, Alpizar-Rodriguez D, Pons-Estel GJ, Xibille-Friedmann D, Paiva E, et al. Characteristics associated with Covid-19 in patients with Rheumatic Disease in Latin America: data from the Covid-19 Global Rheumatology Alliance physician-reported registry. *Glob Rheumatol* [Internet]. 15 de septiembre de 2020 [citado 14 de diciembre de 2021]; Disponible en: <https://www.globalrheumpanlar.org/node/254>
7. Strangfeld A, Schäfer M, Gianfrancesco MA, Lawson-Tovey S, Liew JW, Ljung L, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 1 de julio de 2021;80(7):930.
8. Gianfrancesco MA, Leykina LA, Izadi Z, Taylor T, Sparks JA, Harrison C, et al. Association of Race and Ethnicity With COVID-19 Outcomes in Rheumatic Disease: Data From the COVID-19 Global Rheumatology Alliance Physician Registry. *Arthritis Rheumatol*. marzo de 2021;73(3):374-80.
9. Informe epidemiológico N° 147. Enfermedad por SARS-CoV-2 (COVID-19). Chile 23/08/202. [Available from: <https://www.minsal.cl/wp-content/uploads/2021/08/Informe-Epidemiol%C3%B3gico-148.pdf>]. Accessed February 8, 2022.



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