COVID-19 and Its Potential Effect on Patients With Rheumatic Diseases in Latin America

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Abstract: The COVID-19 (coronavirus disease 2019) pandemic has dramatically affected the entire world. Because of significant disparity levels in Latin American countries with deficient health care access and significant poverty, their population may end up among the most severely impacted. Patients with chronic conditions such as rheumatic diseases are quite vulnerable because of their high flaring risks and subsequent poor outcomes. Additionally, an overuse of antimalarials for the treatment of COVID-19 could lead to shortages in our region. Telemedicine, personal protective equipment use by patients and providers, web conferences, and comprehensive care are tools that will contribute to reduce the risk of infections and other complications in rheumatic disease patients, as well as to improve the knowledge and experience of rheumatologists at a global level.

Key Words: COVID-19, coronavirus disease 2019, rheumatic diseases

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First recognized in Wuhan, China, in December 2019, the coronavirus disease 2019 (COVID-19), an infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),[1] rapidly spread globally. The World Health Organization declared it to be a pandemic on March 11, given its alarming levels of dissemination and severity. By May 26, more than 5.5 million cases have been confirmed, and there have been almost 350,000 deaths worldwide. In Latin America (LA), the most affected countries are Brazil (with >374,800 cases), Peru (with >123,900 cases), Chile and Mexico (with>71,000), and Ecuador (with >37,300 cases). Similarly, Brazil has more than 23,400 deaths; Peru, 3600; Mexico, almost 6700; and Ecuador, more than 3200 (https://coronavirus.jhu.edu/map.html, accessed on May 26).

With regard to physiopathology, the involvement of the lower airways in patients with severe COVID-19 is due not only to the infection per se but also to the occurrence of an uncontrolled immune-mediated inflammatory response. T lymphocytes are the main target cells in SARS due to COVID-19; this triggers a cytokine storm with subsequent exhaustion of the immune response[2,3] and an increased probability of a fatal outcome.[2,4] Under these circumstances, the use of cytokine blockers such as interleukins 6 and 1 blockers, tocilizumab and anakinra, respectively,[5] seems a reasonable option. In addition, biomarkers of disease progression in COVID-19 resemble markers of the macrophage activation syndrome such as high ferritin, low platelets, and high alanine transaminase (ALT).[2,4] Furthermore, there is certainly a complexity in the contribution of type I interferons regarding early and late responses in COVID-19. The former may restrict virus replication through induction of interferon-stimulated genes, whereas the latter can exacerbate disease by enhancing the recruitment and function of macrophages and other innate immune cell.[6]

Even though the number of cases and deaths are lower in LA than in the United States, Europe, or China, it is important to point out that it is one of the world regions with most significant levels of socioeconomic disparities, particularly in terms of health care access.[7] As it has been previously reported, availability is one of the main determinants of access to treatment and constitutes a huge problem in LA as only 3 of its 20 countries invest more than 6% of their gross domestic product in health-related expenses. In addition, 10 of those 20 LA countries do not have at least 25 physicians and nurses per 10,000 population. Furthermore, in several countries, there is a huge difference between the health workforce (physicians, nurses, and midwives) concentrated in large cities, in contrast to their limited availability in the rural areas.[8] Given this reality, many countries are using a combination of containment and mitigation actions aimed at delaying major surges of patients and leveling the demand for hospital beds, while protecting the most vulnerable (i.e., older individuals and those with preexistent comorbidities) from being infected. These varied initiatives are based on national risk assessments that many times include the estimated numbers of patients requiring hospitalization and the availability of hospital beds and ventilation resources.[9] As commendable and necessary as this is, it is important to note that these activities will, nevertheless, reduce the access of patients with chronic conditions,[10] including those with rheumatic diseases and increasing, as a result, the risk of flares and of long-term poor outcomes. Moreover, the number of tests being conducted in LA is exceedingly low; in fact, 9 of the 20 countries in the world with the fewest tests per million persons are in LA and the Caribbean region; thus, by not identifying the infected persons, the chain of transmission continues, and the number of cases increases exponentially. Consequently, the underreporting will be further magnified, which will likely cause an underallocation of emergency resources, which will further compound the problem.[11]

As rheumatologists, we identify 2 main issues in need of urgent consideration. First, what will happen to patients with rheumatic disease if they develop COVID-19? Will they have a more serious clinical condition compared to those who do not have a rheumatic disease? The latest National Health Service guide for the management of patients with rheumatic diseases during this pandemic points out that the majority of such patients are at high or very high risk of acquiring a COVID-19 infection.[12] Additionally, the Hospital for Special Surgery, one of the major academic health centers in New York City, indicates that individuals with rheumatic disease may be at greater risk of developing more severe infections, although there is no critical evidence for that at this point.[13] Whether background immunosuppressive medications place individuals with rheumatic disease at an increased or Large COVID-19 studies on autoimmune diseases are not available as of now; however, the international rheumatology community has been mobilized at an unprecedented pace to create the

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COVID-19 Global Rheumatology Alliance to capture information about data regarding rheumatic disease before COVID-19 infection and COVID-19–related illness.[15] Of note, however, a report of 86 New York city patients with known immune-mediated inflammatory disease (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, psoriasis, inflammatory bowel disease, or related conditions) who were receiving anticytokine biologics, other immunomodulatory therapies, or both with confirmed or highly suspected COVID-19 was assessed; the authors concluded that the incidence of hospitalization among patients with immune-mediated inflammatory disease was consistent with the rate of hospitalization for COVID-19 in the general population; these data suggest that the baseline use of biologics is not associated with worse COVID-19 outcomes.[16]

Second, COVID-19 is already disproportionally affecting ethnic minorities who, oftentimes, have a low socioeconomic status with limited to no health insurance. In addition, these individuals are also more likely to have a number of comorbidities who predispose them to a more severe COVID-19 infection, if and when they develop it. This has been clearly shown in the United States, the country with the highest number of individuals infected by COVID-19. The state of New York alone has surpassed the number of cases of the most affected European countries such as Italy and Spain. Furthermore, the disproportion in terms of the percent affected with COVID-19 and those succumbing to it is tilted toward the ethnic minorities in impoverished areas of New York City. Rates by borough show the Bronx and Queens as the most affected ones.[17] Similar disproportionate mortality has been registered in African American and minority communities in other states such as Michigan, Illinois, and Louisiana; this could be explained also because they are still riding public transportation in large numbers for people to go to work and less likely referred for testing, making it more difficult to stop the spread of the disease.[18] Unfortunately, in patients with autoimmune diseases, particularly lupus, nonwhite ethnicity and poverty, as well as the lack of or limited health insurance, have been recognized as predictive factors of a worse prognosis in studies from different US cohorts.[19–21] Taken together, this information suggests that nonwhite patients from low socioeconomic status are at a higher risk of developing more severe infections, with subsequent less favorable course and outcomes. Furthermore, in patients with overt inflammatory arthritis, infections are a major concern as they can contribute to disease flares.[22–24] As to systemic lupus erythematosus (SLE), underlying immune dysregulation contributes to propagate other diseases increasing the patient's risk of infection; likewise, treatment measures of SLE further increase this risk. Infectious agents have also been shown to play a role in SLE pathogenesis and increased disease activity.[25] In addition, chronic renal disease, cardiovascular morbidity, and chronic lung disease have been reported as risk factors for a more severe COVID-19,[26] and as these organs can be compromised in patients with autoimmune diseases, the risks of more serious disease course and less favorable outcomes obviously increase.

On the other hand, publications about treatment of cases of COVID-19 with medications that are indicated mainly for rheumatic diseases such as hydroxychloroquine (HCQ) have caused legitimate concern because of its abusive and nonregulated prescription. In addition, the approval for use in COVID-19, by agencies such as the Food and Drugs Administration,[27] without strong evidence for its efficacy is truly regrettable as it has led to shortage of HCQ in the United States[28]; this will limit its availability to patients with COVID-19, if efficacy is truly established, but also represents a real risk to patients with rheumatic diseases who depend on HCQ for their treatment and survival.[29] Based on that, several groups, such as the American College of Rheumatology,[30] the European League Against Rheumatism,[31] the Lupus Foundation of America,[32] and the COVID-19 Global Rheumatology Alliance,[33] have recommended an effort to ensure an adequate supply of antimalarials to all patients who need them. In LA, this shortage has not been reported yet, but as antimalarials have been approved in some countries for the treatment of COVID-19,[34,35] the most sensible recommendation would be to use them cautiously, particularly until more evidence about their efficacy is gathered.

The effect of the pandemic on patients with rheumatic diseases will not be seen for some time, probably months or even years. The impact of the COVID-19 on the global economy will also be a factor to consider; the levels of poverty overall and the limited availability of resources may result in worsening disease activity and damage accumulation in patients with rheumatic diseases. Additionally, to reduce the impact of COVID-19, rheumatologists may need to opt for telemedicine as an alternative to an in-person visit and must be reimbursed for these services. However, again, such virtual visits may not be accessible to the disenfranchised populations who may lack the tools to get connected.

In terms of infusion therapies, they should be administered very carefully; personal protective equipment should be used by patients and providers. Patients should be screened to determine if they may have any suggestions of COVID-19 before being infused. If fever or other symptoms are present, these patients should be rescheduled, and consideration be given to whether immunomodulatory therapy should be continued. Also, web conferences would allow us to share information as well as experience with experts worldwide.[36] Thanks to these measures, the potential risk of COVID-19 in our patients could be reduced substantially.

In conclusion, as rheumatologists, we should consider that our patients could be more affected by the COVID-19 infection, and we should improve the strategies for their treatment and follow-up. This is particularly important in LA.

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