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therapies. Trial designs need to rest on better evidence of the pathophysiology of severe COVID-19 and ensure stratification by phenotype to select patients who have evidence of hyperinflammation and who are therefore more likely to benefit. Equally, such trial designs need to consider where immunosuppression might plausibly cause harm. For example, it has been postulated that in some patients with severe COVID-19, persistence of viral RNA drives the inflammatory responses,[11] and the host needs a robust immune system to clear the virus and viral products.

The COVID-19 pandemic has shown the importance of multispecialty collaboration. Further prospective trials of IL-1 pathway antagonism are needed, and rheumatologists should be central to the design of such trials to ensure thoughtful stratification of patients to maximise benefit and minimise harm.

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*Rachel S Tattersall, Dennis McGonagle, Jessica J Manson
rachel.tattersall@nhs.net

Department of Rheumatology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK (RST); Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of Leeds, Leeds, UK (DM); Department of Rheumatology, University College London Hospitals NHS Foundation Trust, London, UK (JJM)

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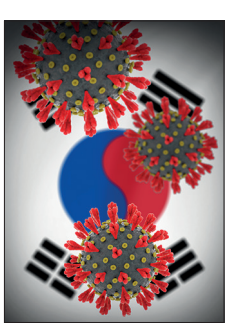
First data on COVID-19 morbidity and mortality in patients with rheumatic disease from South Korea

Whether patients with autoimmune inflammatory rheumatic diseases constitute a more vulnerable, higher-risk population liable to contract SARS-CoV-2 infection and whether these patients have poorer clinical outcomes remain unclear.[1] Of particular concern for rheumatologists are the potential risk factors associated with autoimmune rheumatic diseases, such as reduced lung function and comorbidities, including cardiovascular disease, which have been identified as risk factors for worse clinical outcomes for COVID-19.[2,3]

The widespread use of immunomodulatory or immunosuppressive medications in these patients has been a central issue during the COVID-19 pandemic because their use was of concern to rheumatologists who initially had scarce evidence as to whether these medications increase patients' risk of infection, and because certain drugs soon gained attention as potential treatments for COVID-19-related hyperinflammation.[4]

Several epidemiological studies have investigated COVID-19 in patients with autoimmune inflammatory rheumatic diseases, including infectivity, disease course, role of medications, and patients' self-protection strategies.[5,6] Data from 3729 patients with autoimmune rheumatic diseases included in the COVID-19 Global Rheumatology Alliance physician-reported registry showed that older age, male sex, and cardiovascular and chronic lung disease were associated with COVID-19-related death.[7] In these cohort studies, disease-specific factors, such as moderate-to-high disease activity and certain medications (eg, rituximab, sulfasalazine, and immunosuppressants) were also associated with COVID-19-related death.[7]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In *The Lancet Rheumatology*, Youn Ho Shin and colleagues report a population-based study from South Korea that provides further real-world evidence of the association between autoimmune rheumatic disease, the drugs used to treat these diseases, and COVID-19.[8] The group used a South Korean national health insurance claims-based database, which was linked to general health examination records, and included 133 609 South Korean patients aged 20 years or older who underwent SARS-CoV-2 testing between Jan 1 and May 30, 2020, providing an excellent nationwide cohort.

The study included 8297 patients with autoimmune inflammatory rheumatic diseases, including inflammatory arthritis (ie, rheumatoid arthritis, psoriatic arthritis, and spondyloarthritis) and connective tissue diseases, including systemic lupus erythematosus, Sjögren's syndrome, systemic sclerosis, polymyalgia rheumatica, mixed connective tissue diseases, dermatomyositis or polymyositis, polyarteritis nodosa, or vasculitis, based on International Classification of Diseases (tenth revision) codes. After exposure-driven propensity score matching, patients with autoimmune rheumatic diseases showed an increased likelihood of testing positive for SARS-CoV-2 (adjusted odds ratio 1·19, 95% CI 1·03–1·40; p=0·026), severe COVID-19 outcomes (1·26, 1·02–1·59; p=0·041), and COVID-19-related death (1·69, 1·01–2·84; p=0·046), compared with the general population. Patients who were treated with any dose of systemic corticosteroids or disease-modifying antirheumatic drugs (DMARDs) were not associated with COVID-19-related outcomes, but those receiving a dose of 10 mg per day or more of systemic corticosteroids had an increased likelihood of testing positive for SARS-CoV-2 (adjusted odds ratio 1·47, 95% CI 1·05–2·03; p=0·022), severe COVID-19 outcomes (1·76, 1·06–2·96; p=0·031), and COVID-19-related death (3·34, 1·23–8·90; p=0·017).

What do these data add to the existing literature? This study is the first to report COVID-19-related outcomes in patients with rheumatic diseases from South Korea and indicates an increased risk of testing positive for SARS-CoV-2, severe COVID-19 outcomes, and COVID-19-related death compared with the general South Korean population. Absolute comparisons with cohorts from different parts of the world are difficult to make due to differences in study designs. However, potential future meta-analyses might include these data for pooled analyses. This is relevant, as non-White ethnicity has been associated with a higher risk of COVID-19-related hospitalisation and mortality in previous studies.[9] An important factor to take into consideration when reading the study by Shin and colleagues is the timing of patient enrolment into the presented cohort, in that these patients were treated before any of the results on effective treatments (including dexamethasone) were published from the major COVID-19 studies. The standard of care at the beginning of the pandemic compared with now has considerably changed, adding yet another variable into the equation and making comparisons between cohorts even more difficult.

At the beginning of the pandemic, there was a concern among rheumatologists globally that patients with rheumatic diseases might be at particular risk for increased morbidity and mortality related to COVID-19. 15 months into the pandemic, the published data consistently show that the main drivers for adverse clinical outcomes in the general population and in patients with rheumatic diseases are age, male sex, and comorbidities such as cardiovascular disease. The main questions that arises from these data from South Korea is whether and to what degree patients with rheumatic diseases treated with DMARDs will respond to the available vaccinations. Emerging data suggest that patients with rheumatic and muskuloskeletal diseases treated with conventional or biological DMARDs exert an immune response to COVID-19 vaccines;[10] however, further data on larger cohorts are urgently needed to identify whether and to which extent the individual rheumatic and muskuloskeletal diseases, and their associated treatments, affect the immune response to the individual COVID-19 vaccines. There is work ahead for the rheumatology community.

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Karen Schreiber, Oliver Hendricks
kschreiber@danskgigthospital.dk

Danish Hospital for Rheumatic Diseases, University of Southern Denmark, Sønderborg 6400, Denmark (KS, OH); Institute of Regional Health Research (IRS), University of Southern Denmark, Odense, Denmark (KS, OH); Thrombosis and Haemophilia, Guy's and St Thomas' NHS Foundation Trust, London, UK (KS)

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Effect of the COVID-19 pandemic on patients with systemic rheumatic diseases

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The effect of the COVID-19 pandemic on people with inflammatory or autoimmune rheumatic diseases remains unclear. Risk factors associated with severe COVID-19 outcomes include older age (>65 years), male sex, and pre-existing comorbidities (hypertension, diabetes, obesity, cardiovascular diseases, and chronic respiratory diseases).[1] Additionally, immune-compromised individuals, including people with systemic rheumatic diseases, are at increased risk of infection, including by SARS-CoV-2.[2]

The prevalence of COVID-19 and its association with rheumatic diseases and immunosuppressive medications have been evaluated in large population-based studies in the first phase of pandemic, from February to August, 2020. Some studies have shown a high prevalence of COVID-19 in people with inflammatory or autoimmune rheumatic diseases compared with the general population.[3] Furthermore, a protective role of some immunomodulatory drugs (eg, hydroxychloroquine) has been suggested by other observational studies in patients with rheumatic diseases; some of these drugs have been proposed as treatments in patients with COVID-19 who develop hyperinflammation, which is associated with severe COVID-19 outcomes.[4] Conflicting results, however, were initially reported in the literature about both the risk of COVID-19, and the effects of immunomodulatory drugs in patients with inflammatory or autoimmune rheumatic diseases.

More recently, increased prevalence of COVID-19 in patients with rheumatic disease has been shown by large observational and meta-analysis studies.[5] Notably, differences in prevalence have been reported according to types of rheumatic disease, with patients with connective tissue diseases showing a higher prevalence of COVID-19 than patients with chronic arthritis.[6] Moreover, COVID-19 is more prevalent in patients with pre-existing interstitial lung disease than in those without,[6] and interstitial lung disease is associated with a more severe COVID-19 pneumonia, and a worse prognosis. Thus, the risks of COVID-19 in people with rheumatic diseases are complex and varied, as are the challenges faced in deciding how to reduce the risk of infection by SARS-CoV-2.

In *The Lancet Rheumatology*, Jonathan S Hausmann and colleagues[7] report the results of the COVID-19 Global Rheumatology Alliance Patient Experience Survey, an international online survey designed to investigate the effects of the COVID-19 pandemic on patients with rheumatic diseases worldwide. Survey questions were disseminated through websites, social media, and patient support organisations. The questionnaire included information about demographics, rheumatic disease diagnosis, COVID-19 diagnosis, protective behavioural measures adopted to reduce COVID-19 exposure, health-care access and communication with rheumatologists, medication access and changes, and changes in employment.

Responses from 9300 adult patients with rheumatic diseases were included from more than 90 countries (mean age 46·1 years [SD 12·8];