



Rheumatic disease and COVID-19: initial data from the COVID-19 Global Rheumatology Alliance provider registries

Individuals with inflammatory rheumatic disease require special consideration with regard to coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Many of these individuals are considered at-risk for serious infections due to their immunocompromised state resulting from their underlying immune conditions and use of targeted immune-modulating therapies such as biologics.¹⁻⁴ However, some disease-modifying drugs commonly used to treat rheumatic diseases, such as hydroxychloroquine, are being investigated as potential therapies for COVID-19.⁵ Other commonly used therapies, such as biologics targeting interleukin (IL)-6 (eg, tocilizumab, sarilumab) and IL-1 (eg, anakinra), are being assessed in patients with COVID-19 and who have subsequently developed pathological immune responses, including cytokine storm (eg, reactive haemophagocytic lymphohistiocytosis).⁶ Whether background immunosuppressive medications put individuals with rheumatic disease at an increased or decreased risk for severe SARS-CoV-2 infection is unknown,⁷ and evidence is lacking to guide treatment decisions. A general understanding of COVID-19 characteristics in this population is urgently needed to inform management guidelines and identify high-risk individuals during the pandemic.

The need for data to answer these key clinical questions was quickly realised and coordinated on a global scale by rheumatologists, researchers, and patients with rheumatic diseases. Despite the recognised track-record of high-quality observational drug safety research in rheumatology within multiple national biological registries,⁸ immediate data on COVID-19-specific outcomes would need to be collected to address this demand. Therefore, the international rheumatology community mobilised at an unprecedented pace to create the COVID-19 Global Rheumatology Alliance. In less than 1 week, the COVID-19 Global Rheumatology Alliance successfully developed online portals and case report forms to enable health-care providers around the world to enter information on individuals with rheumatic disease who have been diagnosed with COVID-19.

Registry data elements include provider name, city, country, and clinic, and individual patient-level

sociodemographic information, including age, sex, race, and ethnicity. Data regarding rheumatic disease are captured, including medications before COVID-19 diagnosis, disease activity, and comorbidities. Information on COVID-19-related illness includes diagnosis date, symptoms, treatment, and outcomes, such as admission to hospital and maximum level of care (eg, need for supplemental oxygen, invasive ventilation). Laboratory results for other co-infections, IL-6 concentrations, leucopenia, and more are also collected, if available.

Due to international data legislation, in particular, the European General Data Protection Regulations, parallel data entry points (one limited to European League Against Rheumatism [EULAR]-participating countries, the other limited to sites globally) have been launched. Both data entry points link to secure RedCap survey platforms hosted by The University of Manchester (Manchester, UK), and the University of California, San Francisco (UCSF; San Francisco, CA, USA), where providers submit data on individuals with rheumatic disease who have been diagnosed with COVID-19. Individual patient consent is not required for this registry, which was determined “not human subjects research” by the UK Health Research Authority, The University of Manchester, the US Federal Guidelines by UCSF, and several other institutions.

As of April 1, 2020, 110 individuals with rheumatic disease who have been diagnosed with COVID-19 are included from six continents: Europe, North America, South America, Asia, Africa, and Oceania; a summary of data associated with these individuals is shown in the table.

We present proof-of-principle that, with global cooperation, the rapid collection of data during an international crisis is possible. Within 1 week of launching the registry, rheumatology providers from around the world have submitted data on more than 100 cases, allowing very preliminary characterisation and rapid dissemination of information regarding COVID-19 in individuals with rheumatic disease. Over time, the registry aims to examine differences in severity of outcomes by sociodemographic and rheumatic disease characteristics, medications taken before diagnosis of COVID-19, and

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For the European data entry website see eular.org/eular_covid19_database.cfm

For the global data entry point see rheum-covid.org/provider-global/

For the COVID-19 Global Rheumatology Alliance website see rheum-covid.org

Cohort (n=110)	
Sex	
Female	79 (72%)
Male	31 (28%)
Aged >65 years	20 (18%)
Primary rheumatic disease*	
Rheumatoid arthritis	40 (36%)
Psoriatic arthritis	19 (17%)
Systemic lupus erythematosus	19 (17%)
Axial spondyloarthritis	7 (6%)
Vasculitis	7 (6%)
Sjogren's syndrome	5 (5%)
Other	17 (15%)
Medications before diagnosis of COVID-19	
Conventional synthetic DMARDs†	69 (63%)
Biological DMARDs‡	49 (45%)
JAK inhibitor	5 (5%)
NSAIDs†	28 (25%)
Glucocorticoids	27 (25%)
Other§	5 (5%)
Five most common COVID-19 symptoms at onset	
Fever	87 (79%)
Cough	85 (77%)
Shortness of breath	55 (50%)
Myalgia	49 (45%)
Sore throat	41 (37%)
Admitted to hospital	39 (35%)
Died	6 (5%)
Five most common comorbid conditions	
Hypertension	31 (28%)
Lung disease¶	22 (20%)
Cardiovascular disease	12 (11%)
Morbid obesity (BMI ≥40 kg/m ²)	9 (8%)
Diabetes	9 (8%)

Data are n (%). COVID-19=coronavirus disease 2019. DMARD=disease-modifying antirheumatic drug. NSAID=nonsteroidal anti-inflammatory drugs. JAK=Janus kinase. BMI=body-mass index. *Individuals could have more than one rheumatic disease diagnosis; other included (all with n <5): inflammatory myopathy, ocular inflammation, other inflammatory arthritis, polymyalgia rheumatica, sarcoidosis, systemic sclerosis, osteoporosis, psoriasis, isolated pulmonary capillaritis, gout, and autoinflammatory disease. †Conventional synthetic DMARD medications included antimalarials, azathioprine, cyclophosphamide, ciclosporine, leflunomide, methotrexate, mycophenolate mofetil, mycophenolic acid, sulfasalazine, and tacrolimus. ‡Biological DMARDs included abatacept, belimumab, CD20 inhibitors, IL-1 inhibitors, IL-6 inhibitors, IL-12 and IL-23 inhibitors, IL-17 inhibitors, and tumor necrosis factor inhibitors. §Other included antifibrotics, apremilast, intravenous immunoglobulin, thalidomide or lenalidomide, and other not specified. ¶Chronic obstructive pulmonary disease, asthma, interstitial lung disease, or other not specified.

Table: Demographic and disease characteristics of individuals with rheumatic disease diagnosed with COVID-19 in the COVID 19 Global Rheumatology Alliance registry as of April 1, 2020

important risk factors and outcomes. We expect that a major contribution of the COVID-19 Global Rheumatology Alliance will be rapid dissemination of information, since existing national patient registries might be less equipped to capture data on a global scale, given fixed timepoints and restrictions on consent of new individuals.

The registry is not without limitations, including a potential selection bias towards more severe cases, because in many countries only individuals with severe symptoms are being tested for COVID-19. Rheumatologists reporting cases are also under extreme pressure to work outside of rheumatology and provide front-line medical care to all patients with COVID-19 and might be unable to report cases, or reporting might be delayed. Duplicate entries might occur across different providers, although our data analytics teams carefully examine and address data quality on a regular basis. Also, despite including individuals from across the world, specific adjusted analyses might not be possible due to sample size. Finally, as the whole denominator of individuals with rheumatic diseases who acquire COVID-19 is unknown, the database will be unable to provide accurate estimates of the risk of specific outcomes across the entire rheumatic disease population or in association with specific treatments. With time, existing patient registries and administrative databases will provide these data, but likely not until the current pandemic has ended, thus strengthening the current and critical role of this database.

In summary, the COVID-19 Global Rheumatology Alliance represents the commitment of rheumatologists to generate rapid data to help inform the care of individuals with rheumatic disease and those using immunomodulating therapies. Information from this database will provide timely and responsive real-world data where large literature gaps exist, informing providers of treatment patterns for individuals diagnosed with COVID-19, and offering a better understanding of possible risk factors associated with severe outcomes in the rheumatic disease population.

medications administered on diagnosis. These data will serve to inform treatment strategies and better characterise individuals at increased risk of infection.

The strengths of the COVID-19 Global Rheumatology Alliance registry include global representation of individuals with rheumatic disease with COVID-19, which increases the power of the evidence base to examine

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See Online for appendix