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The COVID-19 Global Rheumatology Alliance: collecting data in a pandemic

Philip C. Robinson [1] ✉ *and Jinoos Yazdany* [2]

The global COVID-19 pandemic has the potential to severely affect those with rheumatic diseases or who are taking immunosuppressive therapies. Information is lacking as to how these groups will fare if they become infected. A global alliance has rapidly formed to try to address this information deficit.

The global health emergency resulting from the COVID-19 pandemic is a special concern to rheumatologists and their patients, as most patients seen by rheumatologists have underlying immune dysfunction and are commonly treated with immunosuppressive therapies. Such therapies are often highly effective for rheumatic disease treatment but can increase the risk of serious infections[1], which has raised concern that these individuals might be more vulnerable to severe COVID-19 than the general population.

SARS-CoV-2 is a highly pathogenic virus that causes COVID-19 and is overwhelming the health systems of well-resourced developed countries. According to the Johns Hopkins Coronavirus Resource Center, as of the 27th of March 2020, in Italy alone 80,589 patients had been diagnosed with COVID-19, and 8,215 fatalities had occurred. Doctors in Italy have been forced to face excruciating decisions about which patients should receive access to limited resources such as mechanical ventilation[2]. The severe nature of the SARS-CoV-2 infection also exacerbates resource limitations, as patients often need 15–20 days of ventilation[2]. Many patients are severely or critically ill, and fatality rates have been higher than for viruses such as influenza[3]. Within this context, rheumatologists are understandably worried that COVID-19 could pose a considerable risk to their patients.

At present, there is insufficient data as to whether patients with rheumatic diseases or those using immunosuppressive therapy who contract COVID-19 are at increased risk of worse outcomes, although researchers are beginning to report COVID-19 in patients with rheumatic diseases[4]. Existing literature suggests that there is a substantial increase in serious infections in those treated with commonly used anti-rheumatic agents such as biologic drugs, Janus kinase (JAK) inhibitors and glucocorticoids[1], and there is a particular risk of Herpes zoster infection in those patients receiving JAK inhibitors[5]. However, extrapolation of this data to SARS-CoV-2 infection is problematic given the heterogeneity in specific drug-associated adverse events and the potentially protective role of immunosuppressive drugs in abating a severe inflammatory response to infection. During previous coronavirus epidemics, such as the 2002–2003 SARS-CoV epidemic and the MERS-CoV that has caused sporadic infections globally since 2012, comorbid disease or diabetes portended a worse outcome in some reports[6,7], but not in others[8]. However, only limited data on the disease course of those taking immunosuppressive therapies and who contracted SARS or MERS have been published to date, restricting inferences from these previous coronavirus outbreaks[9].

Although the adverse effects of drugs used to treat rheumatic diseases is a major concern, discussions are also taking place about the potential positive effects of some common rheumatic disease treatments. Antimalarials, JAK inhibitors, IL-1 inhibitors, IL-6 inhibitors, intravenous immunoglobulin and leflunomide have all been put forward as potential treatments for COVID-19. Appropriate trials of these agents are a pre-requisite to their widespread use in treating COVID-19 and are progressing; a phase III trial of tocilizumab for COVID-19 is currently ongoing[10].

In the midst of the pandemic, the need for accurate information is urgent. The rheumatology community has responded rapidly, with a group of over 300 rheumatologists, scientists and patients from around the world forming The COVID-19 Global Rheumatology Alliance over the course of a few days. Remarkably, the idea for the alliance was initially formed through conversations on social media, with Twitter facilitating a rapid information exchange between researchers and clinicians. International collaborators from across six continents were recruited from personal and professional networks to provide complementary areas of expertise. Over a period of days, alliance members swiftly began work on four distinct projects that would address the overall goal of efficiently gathering data regarding patients with rheumatic diseases and immunosuppressive medications during the rapidly evolving pandemic: a registry for physicians around the world to report cases of COVID-19;

[1]*University of Queensland Faculty of Medicine, Royal Brisbane Clinical Unit, Royal Brisbane Hospital, Brisbane, Australia.*

[2]*Division of Rheumatology, University of California San Francisco, San Francisco, CA, USA.*

✉*e-mail: philip.robinson@ uq.edu.au*

analyses of insurer health claims data; systematic literature reviews; and partnerships with researchers who were conducting patient-facing research. Over 100 professional societies, institutions and organizations from around the world have joined the alliance and are supporting its mission, including this journal.

The rheumatology COVID-19 registry will enable the rapid collection of case information from physicians who treat those with rheumatic diseases and is designed to answer two questions: what are the COVID-19 outcomes among patients with rheumatic diseases, particularly those treated with immunosuppressive therapies; and can we make any inferences regarding the potential harms or benefits of particular immunosuppressive and immunomodulatory therapies in COVID-19 infection? Given the need for global collaboration, data is being collected for the registry through a survey that is accessible to clinicians on the registry website. Data on patient demographics, rheumatic disease phenotypes, comorbidities, immunosuppressive and other drug therapies and COVID-19 outcomes will be collected. The registry has been determined 'not human subjects research' under US Federal Guidelines by the University of California, San Francisco Institutional Review Board (IRB): a category that covers activities such as quality improvement and surveillance. No patient identifiers such as name or date of birth will be collected. International partners in Europe and elsewhere are working to address issues related to regional IRBs. Collected data will be rapidly analysed and shared with the rheumatology community.

Physician-derived data from the rheumatology COVID-19 registry will enable rheumatologists to accumulate a rapid, worldwide case series with which to compare trends in COVID-19 outcomes across diseases, therapies and geographical areas. Such data will help the rheumatology community to generate hypotheses regarding risk and therapy and to provide information to physicians and patients in the short-term. Longer term, the data might serve as preliminary information for the design of larger, systematic studies that address outcomes in specific sub-groups of patients or on the management of immunosuppressive therapies during infection. Although the rapid accumulation and dissemination of information is critically important during this pandemic, the alliance also recognizes that the initial data will have limitations and will need to be interpreted conservatively. Issues such as the lack of a control group and a probable reporting bias of more severe cases will limit conclusions about epidemiology and causal inference. The registry will hopefully enable the rapid global exchange of case information to inform the design of studies that can address these important issues in the future.

Although physician-derived data is important, the alliance is also partnering with a number of patient support groups that are administering questionnaires to patients with rheumatic diseases. Understanding the community burden of COVID-19 in those with rheumatic diseases, as well as the patient experience of both the pandemic itself and of infections in general, will be important and complementary to the data collected from physicians.

Of equal importance will be the analysis of rapidly emerging data from existing data sources and from the scientific literature. To this end, alliance members are working with health-care payers to analyse administrative data regarding COVID-19 in patients with rheumatic diseases. This type of data, although not as clinically detailed as physician-derived registry data, provides a population-level view of how people using immunosuppressive medications fare clinically with COVID-19. Similarly, rapidly and rigorously performed systematic literature reviews will enable the analysis of the risks and benefits of immunosuppressive medications. Such reviews will have an important role in the interpretation of research that is being performed at an unprecedented pace in the current environment.

In summary, the rheumatology community has created a global, coordinated and timely response to the COVID-19 pandemic. The alliance aims to harness the breadth of expertise and knowledge in the rheumatology physician and patient communities to advance knowledge about COVID-19 for the benefit of all patients with rheumatic diseases.

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Competing interests
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