



Increasing autoimmune rheumatic diseases as a consequence of the COVID-19 pandemic: A hypothesis or fact?

The consequences of the Coronavirus Disease 2019 (COVID-19) pandemic, caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), will have a lasting effect on the health of the global population. This disease will most likely be viewed as a plague of the 21st century.

The true toll of the COVID-19 pandemic is difficult to estimate due to its immediate and delayed consequences. Reportedly, about 700 mLn people worldwide have been infected with SARS-CoV-2 and about 7 mLn of them have died due to COVID-19 (<https://www.worldometers.info/coronavirus/>). In the immediate post-pandemic period, the global upsurge of autoimmune rheumatic diseases (ARDs) has been observed among COVID-19 survivors and those exposed to COVID-19 vaccinations. The mainstream rheumatology sources including the International Journal of Rheumatic Diseases (IJRD) have taken the lead in discussing and clarifying plausible associations between COVID-19 and autoimmunity.^{1,2} Importantly, this year's Annual European Congress of Rheumatology arranged a special session titled "Can COVID-19 induce autoimmunity and rheumatic and musculoskeletal diseases?" (EULAR 2023 Debate, June 2023). The latest editorial in IJRD has uncovered the association of COVID-19 with Rheumatoid Arthritis (RA)¹ and referred to our study of definite RA after exposure to SARS-CoV-2.³

RA is the commonest prototype ARD. The disease spreading may reflect the global autoimmunity trends. As such, we aimed to analyze the official RA morbidity records in Kazakhstan, Kyrgyzstan, Uzbekistan, and Tajikistan in the peri-pandemic period (2019–2022), the 2019 year we took as the last year before the pandemic. We formulated our research question to reveal any trend in RA numbers in the last 3 years. We retrieved morbidity records from the official statistical yearbooks of the four Central Asian countries. The analysis of RA morbidity data revealed a substantial increase in the absolute and relative number of RA patients in the four countries. The increase in RA numbers was registered among dispensary follow-up subjects and those with newly diagnosed diseases. The number of registered RA patients in Kazakhstan elevated from 41 044 in 2020 to 66 018 in 2022, accounting for a 61% increase. Such an increase in RA numbers is accompanied by a disproportionately slow increase in the general Kazakhstani population (10.4% in the past 3 years). The increase of newly diagnosed RA patients in Uzbekistan and Kyrgyzstan

accounted for 29% and 31%, respectively, during the same period. In Tajikistan, the number of RA patients increased by 24.4% (from 10 541 in 2020 to 13 112 in 2022) while the general population increased by 5.8%.

Back in 2020, we presented a hypothesis of COVID-19 as a potential trigger of RA at the APLAR congress and published a related abstract in IJRD in October 2020. The same hypothesis, enriched with growing evidence, was discussed in our publication in 2022.⁴ With time passing and accumulating evidence, similar hypotheses of COVID-19-induced RA were tested in large studies with crystallizing a scientific fact of the association. Indeed, cohort studies in Taiwan, Germany, the UK, and South Korea, published in 2023, confirmed that SARS-CoV-2 infection was associated with increased ARD morbidity.^{5–8} Notably, in a German cohort of 641 704 patients with COVID-19, matched with controls, there was a 43% higher likelihood of acquiring a new autoimmune disease within 3–15 months after SARS-CoV-2 infection.⁶

The COVID-19 global vaccination campaign has raised concerns over the scale of adverse outcomes and the likelihood of associated autoimmunity. Importantly, numerous cases of vaccination-associated RA have been described, generating new hypotheses.⁹ COVID-19 vaccinations have saved millions of lives and changed the course of the pandemic. Nonetheless, the same vaccinations coupled with SARS-CoV-2 infections could have a triggering effect among subjects predisposed to autoimmune diseases and those with established ARDs.¹⁰

Osteonecrosis is yet another big issue amid the pandemic.^{11,12} Several factors have been implicated in the pathophysiology of this debilitating complication which is associated with the infection and its irrational corticosteroid therapy. It seems plausible that the developing world, including central Asian countries, encounter an upsurge in osteonecrosis due to unjustified and widespread use of corticosteroids in COVID-19 patients in outpatient and inpatient settings. Rheumatologists like no other specialists are familiar with severe complications of corticosteroid therapies and may take the lead in timely diagnosing and managing patients with osteonecrosis in the aftermath of the pandemic.

Admittedly, the global upsurge of ARDs is not entirely due to the COVID-19 pandemic. A recent article series in *Lancet Rheumatology* has revealed a global increase in musculoskeletal disorders in the last 30 years, unrelated to the pandemic.^{13–15}



Moreover, recent studies have shown that the natural selection of mutations of genes responsible for innate immunity has led to resistance to infections, coming at the cost of a large number of autoimmune inflammatory diseases accumulating in human populations.¹⁶ An increasing number of specialists with an interest in these diseases and continuously advancing diagnostics may also contribute to impressive statistical records of ARDs. For instance, the number of qualified rheumatologists in Kazakhstan has doubled over the past 10 years, partly contributing to the increasing statistics of diseases in the field.

To sum up, the COVID-19 pandemic and its consequences have had a profound effect on the landscape of ARDs. The analysis of increasing statistics of ARDs necessitates more concerted actions of specialists at national and regional levels. The expected global increase of ARDs in the post-pandemic period may lead to the stretching of human and other resources. A concerted action of rheumatologists, including those who member APLAR, is increasingly important to face the growing need of training of new specialists, expanding rheumatology units, and supplying drugs. The time has come to analyze and reach a consensual statement on the consequences of the pandemic and the expected actions by rheumatologists.¹⁷ The IJRD may serve as a platform for initiating the discussion whereas APLAR may help launch a working group for related actions and recommendations.

AUTHOR CONTRIBUTIONS

Chokan Baimukhamedov wrote the manuscript with input from all authors. All authors reviewed the results and approved the final version of the manuscript.

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DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

CONFLICT OF INTEREST STATEMENT

None declared.

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