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## SARS-CoV-2 antibody response after COVID-19 in patients with rheumatic disease

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The impacts of rheumatic disease and immunosuppression on the development of antibodies to SARS-CoV-2 are unknown. A study of healthcare workers showed that detectable SARS-CoV-2 antibodies were associated with reduced risk of SARS-CoV-2 reinfection, and the robustness of this neutralising antibody response has implications for seroprevalence studies and vaccine efficacy.<sup>1</sup> While disease-modifying antirheumatic drugs (DMARDs) generally blunt the immune response to pathogens, immunosuppressive medications such as dexamethasone and baricitinib have efficacy in reducing the severity of COVID-19.<sup>2,3</sup> Additionally, tumour necrosis factor inhibition has been proposed as a potential mechanism for enhancing germinal centre formation and antibody production in severe COVID-19.<sup>4</sup> Understanding the SARS-CoV-2 antibody response after COVID-19 among rheumatic disease patients is therefore of particular interest.<sup>5</sup>

We examined the SARS-CoV-2 antibody response among patients with rheumatic diseases and past COVID-19 at the Mass General Brigham (MGB) health system in Boston, Massachusetts, USA. Patients with COVID-19 confirmed by positive PCR testing and rheumatic disease confirmed by electronic health record (EHR) review were identified as previously described.<sup>6</sup> We extracted clinically obtained SARS-CoV-2 antibody results and other relevant variables from the EHR. This study was considered exempt by the MGB Institutional Review Board.

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**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Out of 188 patients with PCR-confirmed COVID-19 and rheumatic disease, 13 patients had subsequent SARS-CoV-2 antibody testing (table 1). Of these, 2 had undetectable antibodies, 1 had variable results and 10 had positive antibodies. Of the two patients with negative antibodies, one patient had psoriatic arthritis treated with leflunomide and prednisone and had an uncomplicated COVID-19 course. The other patient had antineutrophil cytoplasmic antibody-associated vasculitis on rituximab, azathioprine and prednisone. This patient had negative SARS-CoV-2 antibodies between 28 and 216 days after COVID-19 and had a complicated course requiring intensive care unit admission. One patient with antiphospholipid syndrome on prednisone, cyclophosphamide, rituximab and eculizumab had initial positive antibodies 28 to 87 days after COVID-19. However, he had a negative antibody response by 107 days despite persistently positive PCR testing, phylogenetic analysis suggestive of persistent infection and viral evolution, and clinical concern for recurrent COVID-19, and he died from respiratory failure, as reported elsewhere.<sup>5</sup>

The remaining 10 patients had detectable SARS-CoV-2 antibodies despite the presence of rheumatic diseases and/or the use of immunosuppressive medications, including prednisone, methotrexate, azathioprine, etanercept, rituximab and belimumab. The median time between SARS-CoV-2 PCR and antibody testing was 91 days (IQR: 60–146 days). Of these 10 patients, 8 patients had full recovery, 1 patient had persistent fatigue, and 1 patient with systemic lupus erythematosus (without prior haematologic involvement) had a complicated course with recurrent episodes of thrombotic thrombocytopenic purpura.

This case series of rheumatic disease patients with PCR-confirmed COVID-19 and clinically obtained SARS-CoV-2 antibody testing indicates that the majority of patients (10, 77%) developed detectable SARS-CoV-2 antibodies, which is reassuring. Three patients had negative or variable SARS-CoV-2 antibodies, and two of these patients had severe COVID-19. Three patients were on rituximab; two patients on rituximab for many years had undetectable circulating CD19+ B cells and undetectable or variable SARS-CoV-2 antibodies, while one patient who had recently started rituximab (flow cytometry not available) had detectable SARS-CoV-2 antibodies. As tests were obtained as part of routine clinical care at a tertiary care centre, generalisability may be limited, antibody titers and tests for neutralising antibodies are not available, and the timing of antibody testing relative to SARS-CoV-2 infection is variable. Further studies are needed to investigate the effects of specific rheumatic diseases and DMARDs on the efficacy and durability of the antibody response to SARS-CoV-2.

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## Competing interests

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**Table 1**  
SARS-CoV-2 antibody test results in rheumatic disease patients with COVID-19 confirmed by PCR

Age, years	Sex	Rheumatic disease diagnosis	Rheumatic disease treatment	Timing of SARS-CoV-2 antibody test(s) relative to first positive COVID-19 PCR	SARS-CoV-2 antibody test result(s)	COVID-19 complications	COVID-19 pharmacologic treatment	COVID-19 clinical outcome
<b>Negative/variable SARS-CoV-2 antibodies</b>								
48	Female	Psoriatic arthritis	Leflunomide 10 mg daily, prednisone 10 mg daily	T+177 days	Negative total antibody*	None	None	Fully recovered
62	Female	ANCA-associated vasculitis	Rituximab 1 g (started T-6 years, most recent dose T-149 days), azathioprine 100 mg daily, prednisone 7.5 mg daily	T+28 days <sup>†</sup> T+71 days T+111 days T+216 days	Negative IgG, negative IgM <sup>‡</sup> Negative total antibody* Negative total antibody* Negative total antibody*	Hospitalisation with ICU admission Respiratory failure requiring oxygen therapy by high flow nasal cannula	Hydroxychloroquine, Remdesivir	Persistent cough (T+238 days). Oxygen requirement resolved by hospital discharge.
45	Male	Antiphospholipid syndrome	Prednisone 15 mg daily, cyclophosphamide 250 mg daily, rituximab 1 g (started T-5 years, most recent dose T-11 days), eculizumab 900 mg (started and most recent dose T-9 days)	T+28 days T+81 days T+87 days T+107 days	Positive IgM, negative IgG <sup>‡</sup> Positive IgM, positive IgG <sup>‡</sup> Positive IgM, positive IgG <sup>‡</sup> Negative total antibody*	Hospitalisation with ICU admission Respiratory failure requiring mechanical ventilation; circulatory shock	Remdesivir, SARS-CoV-2 antibody cocktail (regeneron) (T+145 days)	Death (T+154 days)
<b>Positive SARS-CoV-2 antibodies</b>								
26	Female	Systemic lupus erythematosus	None	T+1 hour T+7 days	Positive total antibody* Positive total antibody*	Hospitalisation with ICU admission TTP requiring plasma exchange and glucocorticoids	None	Recurrent TTP episode (T+58 days)
71	Female	Rheumatoid arthritis	None	T+58 days	Positive total antibody*	None	None	Fully recovered
73	Male	Psoriatic arthritis	Etanercept 50 mg weekly	T+60 days	Positive total antibody*	None	None	Fully recovered
54	Female	Systemic lupus erythematosus	Rituximab 720 mg (started T-86 days, most recent dose T-2 days)	T+60 days	IgG positive, IgM not performed <sup>‡</sup>	None	None	Fully recovered
63	Female	Systemic lupus erythematosus	Azathioprine 100 mg daily, belimumab 720 mg monthly	T+88 days	Positive total antibody*	None	None	Fully recovered

Age, years	Sex	Rheumatic disease diagnosis	Rheumatic disease treatment (started T-336 days, most recent dose T-20 days)	Timing of SARS-CoV-2 antibody test(s) relative to first positive COVID-19 PCR	SARS-CoV-2 antibody test result(s)	COVID-19 complications	COVID-19 pharmacologic treatment	COVID-19 clinical outcome
55	Female	Sarcoidosis	None	T+93 days	Positive total antibody*	None	None	Fully recovered
52	Female	Rheumatoid arthritis	None	T+94 days T+210 days	Positive total antibody* Positive total antibody*	Hospitalisation without ICU admission Supplemental oxygen by nasal cannula	None	Fully recovered
68	Female	Polymyositis	Prednisone 6 mg daily, methotrexate 25 mg weekly	T+129 days	Positive total antibody*	None	None	Fully recovered
51	Female	Neurosarcoidosis	Methotrexate 15 mg weekly	T+155 days	Positive total antibody*	None	None	Fully recovered
72	Female	Psoriatic arthritis	Methotrexate 25 mg weekly	T+203 days	Positive total antibody*	Hospitalisation without ICU admission; no oxygen requirement	None	Prolonged fatigue (T+262 days)

\* Measured with the Roche Elecsys assay, which reports the positivity of total SARS-CoV-2 antibody (IgM and IgG) and has 99.5% sensitivity at 14 days after COVID-19 infection.

† T=time zero, defined as the date of the first positive COVID-19 PCR test.

‡ Measured with the Viracor Eurofins assay, which reports IgM and IgG antibody positivity to SARS-CoV-2. The sensitivity of the assay is unknown.

ANCA, antineutrophil cytoplasmic antibody; ICU, intensive care unit; PCR, polymerase chain reaction; T, time zero; TTP, thrombotic thrombocytopenic purpura.