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Antibody Response to a Single Dose of SARS-CoV-2 mRNA Vaccine in Patients with Rheumatic and Musculoskeletal Diseases

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Keywords

COVID-19; SARS-CoV-2; mRNA vaccination; rheumatic disease

The immune response to the SARS-CoV-2 mRNA vaccines in patients with rheumatic and musculoskeletal diseases (RMD) is undefined because these individuals were largely excluded from phase 1–3 studies. To better understand the immune response to vaccination

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CONTRIBUTORSHIP

All authors contributed to the planning, conduct, and reporting of the work described in the article.

COMPETING INTERESTS

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ETHICAL APPROVAL INFORMATION

This study was approved by the Johns Hopkins School of Medicine Institutional Review Board (IRB00248540).

DATA SHARING STATEMENT

All data relevant to the study are included in the article or uploaded as supplementary information.

PATIENT AND PUBLIC INVOLVEMENT

Patients or the public WERE NOT involved in the design, or conduct, or reporting, or dissemination plans of our research

in this patient population, we studied the antibody response in patients with RMD who underwent the first dose of SARS-CoV-2 mRNA vaccination.

Participants with RMD across the US were recruited to participate in this prospective cohort via social media. Those with prior SARS-CoV-2 were excluded. We collected demographics, RMD diagnoses, and immunomodulatory regimens, and tested for SARS-CoV-2 antibodies at baseline and prior to the second vaccine dose. Antibody testing was conducted on the semi-quantitative Roche Elecsys® anti-SARS-CoV-2 S enzyme immunoassay (EIA) which tests for antibodies against the receptor binding domain (RBD) of the SARS-CoV-2 spike protein. [1] We evaluated the association between demographic/clinical characteristics and positive antibody response using Fisher's exact test and Wilcoxon rank sum test.

We studied 123 participants who received their first SARS-CoV-2 vaccination dose between January 8, 2021 and February 12, 2021; 52% underwent BNT162b2, and 48% underwent mRNA-1273 (Table 1). The most common reported RMD diagnoses were inflammatory arthritis (28%), systemic lupus erythematosus (SLE) (20%), Sjogren's syndrome (13%), and overlap conditions (29%). Whereas 28% reported not taking immunomodulatory agents, the remainder reported regimens including non- biologic disease modifying anti-rheumatic drugs (DMARDs) (19%), biologic DMARDs (14%), and combination therapy (37%).

At a median (IQR) of 22 (18–26) days after the first vaccine dose, 74% (binomial exact 95% confidence interval 65–81%) had a detectable anti-RBD antibody response (Supplemental Table 1). Younger participants appeared more likely to develop an antibody response (p=0.06). No differences were detected between disease groups or overall immunomodulatory therapy categories. However, those on regimens including mycophenolate or rituximab were less likely to develop an antibody response (p=0.001 and p=0.04, respectively) (Table 2). Nearly all patients (94%) on anti-tumor necrosis factor inhibitor (TNF) therapy had detectable antibodies.

In this study of the immune response to the first dose of the SARS-CoV-2 mRNA vaccine in patients with RMD, the majority of participants developed detectable anti-SARS-CoV-2 RBD antibodies, however patients on regimens including mycophenolate or rituximab were less likely to develop an antibody response. Overall, there were no major differences by diagnosis or being on immunomodulatory therapy (versus not being on therapy), though consistent with prior studies, younger patients were more likely to develop antibody responses. Nearly all patients on anti-TNF therapy developed detectable antibody. These associations warrant further investigation.

Rituximab and methotrexate have been shown to reduce humoral responses to influenza and pneumococcal vaccines [2, 3]. We found that patients on rituximab were less likely to develop antibody response, yet methotrexate did not negatively impact antibody development. Additionally, we found that patients on mycophenolate were less likely to develop antibody response to mRNA vaccination, consistent with observed experience of influenza vaccination in the renal transplant population and reduced response to HPV vaccination in patients with SLE [4].

Limitations of this study include a small, non-randomized sample, limited information on immunomodulatory dosage and timing, lack of serial measurements, and use of an EIA designed to detect antibody response after natural infection. Furthermore, these are data on the first-dose response to a two-dose series.

Nearly half of patients with RMD have expressed hesitancy or unwillingness to receive a SARS-CoV-2 mRNA vaccine due to a paucity of data [5], however this report can provide reassurance to patients and their providers. We did, however, observe that certain lymphocyte-modulating therapies were associated with poorer humoral vaccine response; potential exploratory strategies to increase immunogenicity in this subgroup may involve adjustment in immunomodulatory therapy, dosage or timing around vaccination.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

RMD	rheumatic and musculoskeletal diseases
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
COVID-19	Coronavirus disease 2019
EIA	enzyme immunoassay
RBD	receptor binding domain
SLE	systemic lupus erythematosus
DMARD	disease modifying anti-rheumatic drug
TNF	tumor necrosis factor

REFERENCES

1. Higgins V, Fabros A, Kulasingam V. Quantitative measurement of anti-SARS-CoV-2 antibodies: Analytical and clinical evaluation. J Clin Microbiol. 2021 Jan 22.
2. Bingham CO 3rd, Looney RJ, Deodhar A, Halsey N, Greenwald M, Codding C, et al. Immunization responses in rheumatoid arthritis patients treated with rituximab: results from a controlled clinical trial. Arthritis Rheum. 2010 Jan; 62(1):64–74. [PubMed: 20039397]

3. Park JK, Lee YJ, Shin K, Ha YJ, Lee EY, Song YW, et al. Impact of temporary methotrexate discontinuation for 2 weeks on immunogenicity of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical trial. Ann Rheum Dis. 2018 Jun; 77(6):898–904. [PubMed: 29572291]

4. McMahan ZH, Bingham CO 3rd., Effects of biological and non-biological immunomodulatory therapies on the immunogenicity of vaccines in patients with rheumatic diseases. Arthritis Res Ther. 2014 Dec 23; 16(6):506.

5. Felten R, Dubois M, Ugarte-Gil MF, Chaudier A, Kawka L, Bergier H, et al. Vaccination against COVID-19: Expectations and concerns of patients with autoimmune and rheumatic diseases. Lancet Rheumatology 2021.

Table 1.

Demographic and Clinical Characteristics of Study Participants, Stratified by Immune Response to the First Dose of SARS-CoV-2 mRNA Vaccine

	Overall (n=123)	Detectable antibody (n=91)	Undetectable antibody (n=32)	p-value[1]
Age, median (IQR)	50 (41, 61)	46 (37, 61)	57 (43, 68)	0.06
Female sex, no. (%)	117 (95)	87 (96)	30 (94)	0.7
Non-white, no. (%)	12 (10)	11 (12)	1 (3)	0.2
Diagnosis, no. (%)				
Inflammatory arthritis[2]	34 (28)	29 (32)	5 (16)	0.5
Systemic lupus erythematous	24 (20)	16 (18)	8 (25)	
Sjogren's syndrome	16 (13)	12 (13)	4 (12)	
Myositis	7 (6)	4 (4)	3 (9)	
Vasculitis	2 (2)	1 (1)	1 (3)	
Overlap[3]	35 (29)	25 (27)	10 (31)	
Other	5 (4)	4 (4)	1 (3)	
Therapy, no. (%)				
None	34 (28)	28 (31)	6 (19)	0.5
Non-biologic DMARD[4]	23 (19)	16 (18)	7 (22)	
Biologic DMARD[5]	17 (14)	11 (12)	6 (19)	
Corticosteroid-monotherapy[6]	4 (3)	4 (4)	0 (0)	
Combination therapy	45 (37)	32 (35)	13 (41)	

[1] Comparing the detectable antibody group to the undetectable antibody group.

[2] Rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, reactive arthritis and inflammatory bowel disease associated arthritis

[3] Overlap denotes a combination of 2 or more of the above conditions, also includes systemic sclerosis

[4] Azathioprine, hydroxychloroquine, leflunomide, methotrexate, mycophenolate, sulfasalazine, tacrolimus

[5] Adalimumab, certolizumab, etanercept, infliximab, tocilizumab, ustekinumab, ixekizumab, belimumab, rituximab, tofacitinib, abatacept

[6] Prednisone and prednisone equivalents

Table 2.

Participant Immunomodulatory Therapy[1], Stratified by Humoral Immune Response to the First Dose of SARS-CoV-2 mRNA Vaccine

	Detectable antibody (n=91)	Undetectable antibody (n=32)	p-value
Medication, no. (%)			
Non-biologic			
Azathioprine	9 (10)	4 (12)	0.7
Hydroxychloroquine	27 (30)	10 (31)	0.9
Mycophenolate[2]	3 (3)	8 (25)	0.001
Sulfasalazine	4 (4)	1 (3)	0.9
Tacrolimus	0 (0)	2 (6)	0.07
Leflunomide	2 (2)	2 (6)	0.3
Methotrexate	10 (11)	3 (9)	0.9
Biologic			
Abatacept	3 (3)	3 (9)	0.5
Belimumab	5 (5)	5 (16)	0.1
Interleukin inhibitor[3]	6 (7)	0 (0)	0.3
Rituximab	2 (2)	4 (12)	0.04
TNF inhibitor[4]	16 (18)	1 (3)	0.07
Tofacitinib	2 (2)	1 (3)	0.9

[1] Since participants could report more than one medication, the total N in this table is greater than the stated cohort size.

[2] Mycophenolic acid or mycophenolate mofetil

[3] Interleukin inhibitors: tocilizumab, ustekinumab, and ixekizumab

[4] TNF inhibitors: Adalimumab certolizumab, etanercept, and infliximab