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ORIGINAL ARTICLE

Humoral SARS-CoV-2 immunogenicity wanes 3 months after heterologous inactivated vaccine followed by ChAdOx1 nCoV-19 in autoimmune rheumatic diseases

Parichat Uea-areewongsa,[1] Nawamin Pinpathomrat,[2] Jomkwan Ongarj,[2] Ratchanon Sophonmanee,[2] Purilap Seepathomnarong,[2] Bunya Seeyankem,[2] Smonrapat Surasombatpattana,[3] Porntip Intapiboon[1]

Abstract

Background: Alongside vaccine hesitancy, impaired and waning immunity in autoimmune rheumatic diseases (ARDs) are barriers to immunization. The timeframe of immunity waning in ARD remains unclear.

Objectives: We aimed to examine the waning of humoral immunogenicity in a cohort of ARD patients who received the heterologous inactivated vaccine followed by the adenoviral vector SAR-CoV-2 vaccine at a 3-month follow-up.

Methods: The levels of SARS-CoV-2 anti-RBD IgG were evaluated at 1 and 3 months in adults with ARDs (n = 29) and age- and sex-matched healthy controls (HC) that received the heterologous prime-boost CoronaVac vaccine followed by the ChAdOx1 nCoV-19 vaccine. Seropositivity was defined as anti-receptor binding domain (RBD) IgG levels of ≥ 7.15 binding antibody units (BAU)/mL. The kinetic properties of the vaccines were evaluated based on the ratio of anti-RBD IgG values obtained at each follow-up. Disease activity was evaluated.

Results: The seropositivity rate was lower among patients with ARDs than among HCs (89.7% *vs.* 100%, $p = 0.237$). At 3 months, the median (IQR) anti-RBD IgG level was lower among patients with ARDs than among HCs (122.3 [30.6, 247.8] *vs.* 294.2 [127.4,605.7] BAU/mL, $p = 0.006$). Mean antibody levels in patients with ARDs decreased 3.5 (1.9)-fold within 3 months post-vaccination (122.3 [30.6, 247.8] *vs.* 279.9 [86,1076.5] BAU/mL, $p < 0.001$). Disease flare-ups occurred in three patients.

Conclusion: Our findings included changes to anti-RBD IgG levels and may inform vaccination strategies. SAR-CoV2 vaccine-induced immunity was lower in patients with ARDs than in HCs and decreased within 3 months, suggesting a need for booster vaccinations.

Key words: immunogenicity, waning, SAR-CoV2 vaccine, autoimmune rheumatic diseases, immunosuppressive drugs

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Affiliations:
[1] Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand
[2] Department of Biomedical Sciences and Biomedical Engineering, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand
[3] Department of Pathology, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

Corresponding author:
Porntip Intapiboon
Allergy and Rheumatology Unit, Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla 90110, Thailand
E-mail: iporntip@medicine.psu.ac.th

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern are associated with increased infection transmissibility and severity. Two doses of SAR-CoV2 vaccines may be insufficient to curb infection spread due to waning immunity and immune escape by the variants of concern.[1,2] Booster shots are the current strategy for inducing and maintaining immunity, preventing disease symptoms, and reducing mortality risks.

Patients with autoimmune rheumatic diseases (ARDs) require booster shots due to the increased mortality risk from SAR-CoV2 infection.[3] In addition, immunosuppressive drugs may impair humoral immunogenicity from vaccines,[4-6] while vaccine hesitancy is a barrier to achieving vaccine immunogenicity.

The waning of vaccine immunogenicity has been reported after two doses of the mRNA vaccine in healthy populations.[7-9] Some studies have reported a significant decrease in neutralized activity nearly 3 months post-vaccination.[9] Similar waning patterns have been reported in populations that received the adenoviral vector vaccine.[10] However, to the best of our knowledge, there has been no previous study of vaccine immunogenicity kinetics in a heterologous regimen, and vaccine immunogenicity kinetics data from ARD populations are scarce. This study aimed to evaluate humoral immunogenicity kinetics in patients with ARD and healthy controls (HC) that received the heterologous prime-boost inactivated (CoronaVac) vaccine followed by the ChAdOx1 nCoV-19 (Oxford–AstraZeneca) SARS-CoV-2 vaccine. Disease flare-up rates were evaluated.

Methods

Study design and population

This prospective cohort study included adult ARD patients from rheumatology clinic, Songklanagarind Hospital, Thailand. All ARD patients who were vaccinated with the heterologous prime-boost CoronaVac vaccine followed by the ChAdOx1 nCoV-19 vaccines over 21–35 days were invited to participate in the study if (i) aged 18-60 year, (ii) had stable disease activity defined by disease activity score 28 (DAS28) ≤ 5.1 points for rheumatoid arthritis (RA), Modified Systemic Lupus Erythematosus Disease Activity Index 2000 (mSLEDAI-2K) ≤ 4 points for SLE, or physician judgment for other ARD types. (iii) received at least one immunosuppressive drug as follows: prednisolone < 20 mg/day, methotrexate ≥ 10 mg/week, azathioprine ≥ 50 mg/day, mycophenolate mofetil ≥ 1,000 mg/day, or leflunomide ≥ 10 mg/day, as a stable dose for a month prior vaccination. (iv) able to temporarily suspended immunosuppressive drugs according to The American College of Rheumatology recommendation.[11] Poster announcements in the vaccine centre were used to invite sex- and age-matched HC without any medical illnesses, who did not take any medication, and had received the same vaccination regimen for the same duration to form control groups. Participants who contacted coronavirus disease 2019 (COVID-19) during the study period were excluded. All participants provided written informed consent. This study was approved by the Human Research Ethics Committee (REC. 64–421–14-1) and adhered to the principles of the Declaration of Helsinki and Good Clinical Practice.

Vaccine humoral immunogenicity

Humoral vaccine immunogenicity was evaluated at 1 and 3 months after the participants received both vaccine doses. Anti-receptor binding domain (RBD) IgG levels were quantified by chemiluminescent assay against a recombinant Spike (S) protein (S1/S2) using the ARCHITECT i System (Abbott, Abbott Park, IL, USA) and chemiluminescent microparticle immunoassay (SARS-CoV-2 IgG II Quant, Abbott Ireland, Sligo, Ireland). The World Health Organization's standardized binding antibody unit (BAU/mL) was used with the SARS-CoV-2 IgG II Quant assay. Values of ≥ 7.15 BAU/mL were considered positive. Changes to antibody levels were evaluated using anti-RBD IgG values expressed as ratios of estimates obtained at 1- and 3-month follow-up.

Disease activity after vaccination

Disease activity was monitored from the date of vaccination completion until 3 months thereafter. DAS28 for rheumatoid arthritis (RA), mSLEDAI-2K for SLE, or physician judgment based on clinical and laboratory assessments for other ARD types. Disease flare-up was defined as an increase in the DAS28 score of > 1.2 points or that of > 0.6 points if current DAS28 scores of ≥ 3.2 points,[12] an increase in the mSLEDAI-2K score by ≥ 4 points,[13] or an increase in corticosteroid and/or immunosuppressive drug doses, as determined by the attending rheumatologist.

Statistical analysis

R version 3.5.1 statistical software (R Foundation for Statistical Computing, Vienna, Austria) was used for data analysis. The variables are presented as mean (SD) or median (interquartile range [IQR]), while categorical variables are presented as counts and percentages. Comparisons between groups were performed using the χ^2 or Wilcoxon rank sum tests, as appropriate. *P*-values of < 0.05 were considered significant.

Results

This study included 29 patients with ARD and HC matched at a 1:1 ratio. All participants received the CoronaVac vaccine followed by the ChAdOx1 nCoV-19 vaccine. The participants' baseline characteristics were similar in both groups and the baseline characteristics of patients with ARD and HC are present in **Table 1**. Most participants were female (86.2%), and the median (IQR) age was 37 (23–49) and 43 (31–52) years in ARD and HC respectively. The median (IQR) number of days between vaccination completion and blood collection at 1 and 3 months in ARD was 33 (29, 34) and 89 (84, 95) days, respectively which was similar to HC. ARDs patients presented with SLE (48.3%) and RA (34.5%), and most (n = 23, 80%) received prednisolone at the mean (SD) dose of 6.8 (3.0) mg/day. The prescribed immunosuppressive drugs and doses as follow; azathioprine (41.4%) at the mean (SD) dose of 70.8 (20.8) mg/day, methotrexate (41.4%) at the mean (SD) dose of 13.3 (2.0) mg/week, mycophenolate mofetil (17.2%) at the mean (SD) dose of 1,500 (353.5) mg/day. Three (10.3%) patients received leflunomide and methotrexate for RA.

At the 3-month follow-up, the seropositivity rates in the ARD and HC groups were 89.7% and 100% (p = 0.237), respectively. All seronegative patients were found in the SLE group. The median (IQR) anti-RBD IgG level was lower in the ARD group than in the HC group (122.3 [30.6,247.8] *vs.* 294.2 [127.4,605.7] BAU/mL, p = 0.006) (**Table 2** and **Figure 1**). In the SLE group, the median (IQR) anti-RBD IgG level was lower than those in other ARD types; however, this difference was not significant (93.5 [22.4, 205.0] *vs.* 165.6 [69.9, 379.8] BAU/mL, p = 0.156) (**Supplementary Table S1**).

Table 1. Baseline characteristic of participants with autoimmune rheumatic diseases (ARDs) and healthy controls (HC).

Characters	ARDs n = 29 (%)	HC n = 29 (%)	*P*-value
Female sex	25 (86.2)	25 (86.2)	1
Median age, y (IQR)	37 (23, 49)	43 (31, 52)	0.194
Time to blood collection, days (IQR)			
First collection	33 (29, 34)	33 (29, 35)	0.834
Second collection	89 (84, 95)	89 (84, 93)	0.378
ARDs			
SLE	14 (48.3)		
RA	10 (34.5)		
Others[1]	5 (17.2)		
Immunosuppressive dose			
Prednisolone; mg, (mean, (SD))" (n = 23)	6.8 (3.0)		
Azathioprine; mg, (mean, (SD))" (n = 12)	70.8 (20.8)		
Methotrexate; mg, (mean, (SD))" (n = 12)	13.3 (2.2)		
Mycophenolate mofetil; mg, (mean, (SD)) (n = 5)	1,500 (353.5)		
Leflunomide; mg, (mean, (SD)) (n = 3)	20.0 (0.0)		

GC, glucocorticoids; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus
[1]two cases of psoriatic arthritis; one case of systemic vasculitis, one case of systemic sclerosis, and one case of dermatomyositis

Table 2. Third-month humoral immunogenicity of CoronaVac followed by ChAdOx1 nCoV-19 (Oxford-AstraZeneca) vaccine regimen in patients with autoimmune rheumatic diseases (ARDs) compared to healthy controls (HC).

Humoral immunogenicity	Total N = 58 (%)	ARDs N = 29 (%)	HC N = 29 (%)	*P*-value
Seropositivity	55 (94.8)	26 (89.7)	29 (100)	0.237
SARS-CoV-2 anti-RBD Ab (BAU/ml); median (IQR)	183.4 (88.4, 391.3)	122.3 (30.6, 247.8)	294.2 (127.4, 605.7)	0.006
Waning anti-RBD Ab ratio (SD)	3.5 (1.7)	3.5 (1.9)	3.5 (1.5)	0.936

BAU, binding antibody units

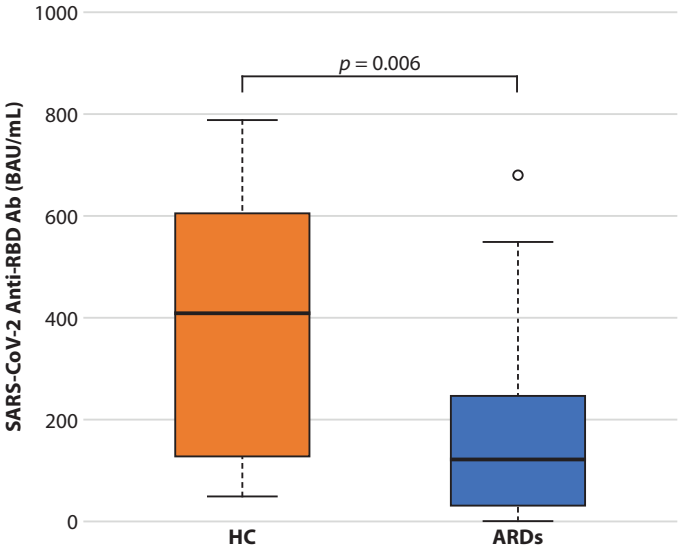

Figure 1. Comparisons of antibody levels at 3 months after SARS-CoV-2 anti-RBD IgG followed by ChAdOx1 nCoV-19 (Oxford-AstraZeneca) vaccination in patients with ARD and healthy controls (HC). Values are presented as medians. *P* < 0.05 indicates statistically significant findings.

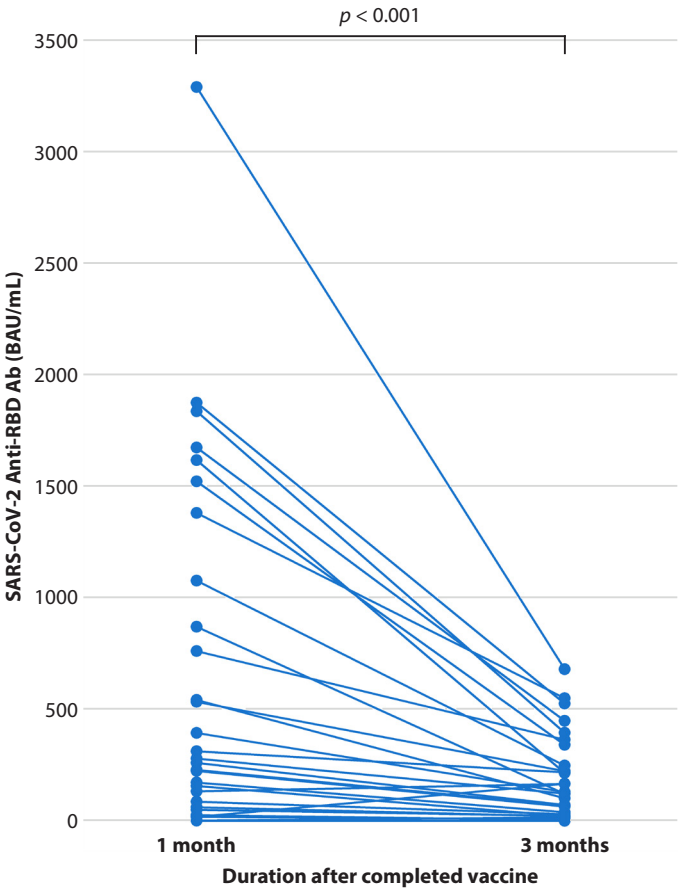

Figure 2. SARS-CoV-2 anti-RBD IgG kinetic findings at 1 and 3 months after completing heterologous prime-boost CoronaVac followed by ChAdOx1 nCoV-19 (Oxford-AstraZeneca) vaccination in patients with autoimmune rheumatic diseases. *P* < 0.05 indicates statistically significant findings.

Humoral immunogenicity was measured using anti-RBD IgG levels at 1- and 3-month follow-up post-vaccination. Values obtained in the ARD group are shown in **Figure 2**. In this group, SARS-CoV-2 anti-RBD antibody levels decreased 3.5 -fold or 56.4% within 3 months post-vaccination (122.3 [30.6, 247.8] *vs.* 279.9 [86.0, 1076.5] BAU/mL, $p < 0.001$).

In this study, three patients experienced disease flare-ups, including increased DAS28 scores in two RA patients and proteinuria in one SLE patient. All patients with disease flare-ups required treatment escalation, including corticosteroids or disease-modifying antirheumatic drugs. No case requiring hospitalization or significant immunomodulatory therapy adjustments was observed.

Discussion

International guidelines recommend that patients with ARD receive a third or further dose of the SARS-CoV-2 vaccine.[14,15] However, vaccine hesitancy and concerns are observed in this population, including worries of adverse events and primary disease flare-ups. As a result, patients tend to delay booster shots, despite emerging variants of concern. This study aimed to examine the waning of vaccine immunogenicity over time. Herein, we demonstrated that anti-RBD IgG levels in ARD patients were lower than those in the healthy population at 3 months post-vaccination. However, the rates of disease flare-ups were relatively low.

The current vaccine could not prevent onward infection by vaccinated people infected by SARS-CoV-2 virus. Vaccine efficacy studies demonstrated that the vaccine prevented severe disease and hospitalization, and decreased the duration of hospital stay and mortality.[16,17] Measures taken by the public for personal protection and social measures implemented by policy-makers are useful methods for preventing infection.[18] Determining the protective activity of antibodies can be done by detecting the neutralizing antibody (Nabs).[19] However, this test is not widely available in laboratories due to the requirement of level 3 biohazard security. Therefore, anti-RBD levels are being used in assessing the humoral immune response and correlation studies of neutralization activity reported an acceptable degree of agreement between IgG titers and neutralizing titers.[20,21] However, Takheaw N et al. showed that anti-RBD IgG levels could not predict the presence of Nabs against the emerging Omicron variant.[22]

To date, there has been no standardized cut-off value of antibody titer that would protect against ARS-CoV-2 infection. Nevertheless, the protective efficacy of a vaccine also depends on cellular immunity and the viral strain. No previous study has defined the levels of protection needed to boost the efficacy of vaccine shots. Meschi S et al. demonstrated that a threshold of 2,000 BAU/mL was strongly correlated with virus neutralization and protective response.[23] A cut-off anti-spike IgG titer against symptomatic infection of ≥ 264 BAU/mL was reported by Feng S et al., but this level only applied to the Alpha (B.1.1.7) variant.[24] The results of our study revealed that the anti-RBD IgG level was 122.3 BAU/mL in ARD patients, which is not enough to prevent severe infection. We aim to highlight the need for booster doses in this vulnerable population.

Previous studies on antibody kinetics were mostly performed in healthy populations and reported inconsistent findings. For example, the humoral response persisted for 3–6 months in the mRNA-1273 or BNT162b2 vaccine recipients.[7-9] Einav et al. reported on decreasing neutralizing antibody titres in the period of 70–80 days after immunization, specifically in patients presenting with an immunosuppressive state.[9] Overall, the humoral immunogenicity kinetic rate declined by approximately 70%–90% within 3–5 months.[25,26] Similar findings were reported in participants that had received two doses of the AZD1222 (ChAdOx1 nCoV-19, AstraZeneca) vaccine; specifically, the anti-spike IgG levels dropped to 52.1 BAU/mL within 3 months in one study.[10] Longitudinal studies are rare on inactivated or adenoviral vector vaccine immunogenicity in patients with ARD. One study reported a decrease in the levels of anti-RBD antibodies at 4–6 weeks after the second dose of either the AZD1222 or BBV152 (Bharat Biotech) vaccine.[27] Little is known about the longitudinal progression of vaccine-induced immunity to COVID-19 in patients with ARD, including post-booster shots. Our study suggested a need for a booster shot at least 3 months after the second primary dose following some evidence of waning immunogenicity.[7-9,25]

The risk of disease flare-up post-vaccination has been reported at a rate of 3–10.5%.[28-30] This risk may be accounted for by the interruption of immunosuppressive drug activity, immune activation triggered by vaccines, and molecular mimicry leading to the aberrant activation of the innate and adaptive immune responses.[31] However, few patients required treatment escalation, and none required hospitalization; similarly, in the present study, three patients experienced disease flare-ups, but none experienced any serious complications. These findings may support vaccination programs and help increase vaccination acceptance. Although disease flare-up risks cannot be eliminated, symptoms can be managed with medication adjustments, increasing patient comfort.

This study had some limitations. First, the sample size was small. Second, antibody levels were not measured before vaccination; however, the enrolled participants did not report any symptoms of COVID-19 infection. Third, only anti-RBD IgG to SAR-CoV2 levels were evaluated; neutralizing antibodies and cellular immunogenicity were not evaluated. Nevertheless, a previous study has demonstrated an association between antibody titres and neutralization.[32] To our knowledge, this is the first study to prospectively evaluate the waning of humoral immunity in patients with ARD that had been vaccinated with the heterologous prime-boost inactivated vaccine followed by ChAdOx1 nCoV-19.

The strength of this study is the use of age- and sex-matched HCs. Future studies should validate these findings using large samples and referring to optimal protective antibody titres. These findings support the use of booster shots for immunocompromised patients that have received the primary series of anti-SAR-CoV2 vaccines as per the current guidelines.[14,15]

Conclusion

The humoral immunity induced by the SAR-CoV2 vaccine in patients with ARD is lower than that in HCs and wanes within 3 months post-vaccination. Booster shots are recommended.

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Conflicts of interests

The authors have no financial or non-financial conflicts of interest to declare.

Author Contributions

- PI and PU enrolled the ARDs and healthy control.
- PI, PU, and NP designed experiments, interpreted the data, and wrote the manuscript with input from NP, JO, RS, PS, BS, and SS.
- All authors had access to the data and approved the manuscript before submitting it.

Data availability

The study data are available from the corresponding author upon reasonable request.

References

1. Hu J, Peng P, Cao X, Wu K, Chen J, Wang K, et al. Increased immune escape of the new SARS-CoV-2 variant of concern Omicron. Cell Mol Immunol. 2022;19(2):293-5.
2. Goldberg Y, Mandel M, Bar-On YM, Bodenheimer O, Freedman L, Haas EJ, et al. Waning immunity after the BNT162b2 vaccine in Israel. N Engl J Med. 2021;385(24):e85.
3. Gianfrancesco M, Hyrich KL, Al-Adely S, Carmona L, Danila MI, Gossec L, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis. 2020;79:859-66.
4. Furer V, Eviatar T, Zisman D, Peleg H, Paran D, Levartovsky D, et al. Immunogenicity and safety of the BNT162b2 mRNA COVID-19 vaccine in adult patients with autoimmune inflammatory rheumatic diseases and in the general population: a multicentre study. Ann Rheum Dis. 2021;80(10):1330-8.
5. Geisen UM, Berner DK, Tran F, Sümbül M, Vullriede L, Ciripoi M, et al. Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort. Ann Rheum Dis. 2021;80(10):1306-11.
6. Prendecki M, Clarke C, Edwards H, McIntyre S, Mortimer P, Gleeson S, et al. Humoral and T-cell responses to SARS-CoV-2 vaccination in patients receiving immunosuppression. Ann Rheum Dis. 2021;80(10):1322-9.

7. Tré-Hardy M, Cupaiolo R, Wilmet A, Beukinga I, Blairon L. Waning antibodies in SARS-CoV-2 naïve vaccinees: results of a three-month interim analysis of ongoing immunogenicity and efficacy surveillance of the mRNA-1273 vaccine in healthcare workers. J Infect. 2021;83(3): 381-412.
8. Doria-Rose N, Suthar MS, Makowski M, O'Connell S, McDermott AB, Flach B, et al. Antibody persistence through 6 months after the second dose of mRNA-1273 vaccine for Covid-19. N Engl J Med. 2021;384(23): 2259-61.
9. Levin EG, Lustig Y, Cohen C, Fluss R, Indenbaum V, Amit S, et al. Waning immune humoral response to BNT162b2 Covid-19 vaccine over 6 months. N Engl J Med. 2021;385(24):e84.
10. Cheng S-H, Lin Y-C, Chen C-P, Cheng C-Y. Safety and immunogenicity of a heterologous booster of protein subunit vaccine MVC-COV1901 after two doses of adenoviral vector vaccine AZD1222. medRxiv. 2022; 2021.12.10.21267574.
11. Curtis JR, Johnson SR, Anthony DD, Arasaratnam RJ, Baden LR, Bass AR, et al. American college of rheumatology guidance for COVID-19 vaccination in patients with rheumatic and musculoskeletal diseases: version 2. Arthritis Rheumatol. Version 2. 2021;73(8):e30-45.
12. van der Maas A, Lie E, Christensen R, Choy E, de Man YA, van Riel P, et al. Construct and criterion validity of several proposed DAS28-based rheumatoid arthritis flare criteria: an OMERACT cohort validation study. Ann Rheum Dis. 2013;72(11):1800-5.
13. Mikdashi J, Nived O. Measuring disease activity in adults with systemic lupus erythematosus: the challenges of administrative burden and responsiveness to patient concerns in clinical research. Arthritis Res Ther. 2015;17:183.
14. Curtis JR, Johnson SR, Anthony DD, Arasaratnam RJ, Baden LR, Bass AR, et al. American college of rheumatology guidance for COVID-19 vaccination in patients with rheumatic and musculoskeletal diseases: Version 3. Arthritis Rheumatol; 2021. Vol. 73. p. e60-75.
15. Landewé RBM, Kroon FPB, Alunno A, Najm A, Bijlsma JW, Burmester GR, et al. EULAR recommendations for the management and vaccination of people with rheumatic and musculoskeletal diseases in the context of SARS-CoV-2: the November 2021 update. Ann Rheum Dis. 2022.
16. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, et al. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. Lancet. 2021; 397(10287):1819-29.
17. Madanat L, Sager M, O'Connor D, Thapa B, Aggarwal N, Ghimire B, et al. Prognostic value of SARS-CoV-2 anti-RBD IgG antibody quantitation on clinical outcomes in hospitalized COVID-19 patients. Int J Gen Med. 2022;15:5693-700.
18. Talic S, Shah S, Wild H, Gasevic D, Maharaj A, Ademi Z, et al. Effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and covid-19 mortality: systematic review and meta-analysis. BMJ. 2021;375:e068302
19. Yang Y, Du L. SARS-CoV-2 spike protein: a key target for eliciting persistent neutralizing antibodies. Signal Transduct Target Ther. 2021; 6(1):95
20. Lee B, Ko JH, Park J, Moon HW, Baek JY, Jung S, et al. Estimating the neutralizing effect and titer correlation of semi-quantitative anti-SARS-CoV-2 antibody immunoassays. Front Cell Infect Microbiol. 2022;12:822599.
21. Xue JH, Wang YJ, Li W, Li QL, Xu QY, Niu JJ, et al. Anti-receptor-binding domain immunoglobulin G antibody as a predictor of seropositivity for anti-SARS-CoV-2 neutralizing antibody. Arch Pathol Lab Med. 2022;146(7):814-21.
22. Takheaw N, Liwsrisakun C, Chaiwong W, Laopajon W, Pata S, Inchai J, et al. Correlation analysis of anti-SARS-CoV-2 RBD IgG and neutralizing antibody against SARS-CoV-2 omicron variants after vaccination. Diagnostics (Basel). 2022;12(6).
23. Meschi S, Matusali G, Colavita F, Lapa D, Bordi L, Puro V, et al. Predicting the protective humoral response to a SARS-CoV-2 mRNA vaccine. Clin Chem Lab Med (CCLM). 2021;59(12):2010-8.
24. Feng S, Phillips DJ, White T, Sayal H, Aley PK, Bibi S, et al. Correlates of protection against symptomatic and asymptomatic SARS-CoV-2 infection. Nat Med. 2021;27(11):2032-40.
25. Ibarrondo FJ, Hofmann C, Fulcher JA, Goodman-Meza D, Mu W, Hausner MA, et al. Primary, recall, and decay kinetics of SARS-CoV-2 vaccine antibody responses. ACS Nano. 2021;15:11180-91.
26. Suresh L. Update on COVID-19 vaccines and autoimmune-mediated rheumatic diseases. Reumatologia. 2021;59(4):203-5.
27. Ahmed S, Mehta P, Paul A, Anu S, Cherian S, Shenoy V, et al. Postvaccination antibody titres predict protection against COVID-19 in patients with autoimmune diseases: survival analysis in a prospective cohort. Ann Rheum Dis. 2022;81(6):868-874.
28. Felten R, Kawka L, Dubois M, Ugarte-Gil MF, Fuentes-Silva Y, Piga M, et al. Tolerance of COVID-19 vaccination in patients with systemic lupus erythematosus: the international VACOLUP study. Lancet Rheumatol. 2021;3(9):e613-5.
29. Fan Y, Geng Y, Wang Y, Deng X, Li G, Zhao J, et al. Safety and disease flare of autoimmune inflammatory rheumatic diseases: a large real-world survey on inactivated COVID-19 vaccines. Ann Rheum Dis. 2022;81(3):443-5.
30. Bixio R, Bertelle D, Masia M, Pistillo F, Carletto A, Rossini M. Incidence of disease flare after BNT162b2 coronavirus disease 2019 vaccination in patients with rheumatoid arthritis in remission. ACR Open Rheumatol. 2021;3(12):832-3.
31. Cairoli E, Espinosa G. Autoimmune diseases and vaccines against COVID-19. Decision making in uncertain scenarios. Med Clin (Barc). 2021;157(5):247-52.
32. Shenoy P, Ahmed S, Paul A, Cherian S, Vijayan A, Babu SAS, et al. Inactivated vaccines may not provide adequate protection in immunosuppressed patients with rheumatic diseases. Ann Rheum Dis. 2022;81(2):295-6.

Supplemental Materials

Supplementary Table S1. Third-month humoral immunogenicity of CoronaVac followed by ChAdOx1 nCoV-19 (Oxford-AstraZeneca) vaccine in patients with SLE and non-SLE autoimmune rheumatic diseases

Immunogenicity	Total N = 29 (%)	SLE N = 14 (%)	Non-SLE N = 15 (%)	*P*-value
Seropositivity	26 (89.7)	11 (78.6)	15 (100.0)	0.1
SARS-CoV-2 anti-RBD IgG (BAU/ml) median (IQR)	122.3 (30.6, 247.8)	93.5 (22.4, 205)	165.6 (69.9, 379.8)	0.156

BAU, binding antibody units