ORIGINAL ARTICLE

# The Immunogenicity of SARS-CoV-2 Vaccines in Thai Patients with Rheumatoid Arthritis: A Cross-Sectional Study from the National Health Thailand Program

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**Background:** Patients with rheumatoid arthritis (RA) on immunosuppressive therapy may exhibit weaker and less durable vaccine responses compared to the general population. Thailand offers diverse SARS-CoV-2 vaccines, but the immune response among Thai RA patients to different vaccine regimens remains unclear.

**Objective:** The authors aimed to investigate the COVID-19 spike protein IgG antibody level after completing the Thai SARS-CoV-2 vaccine program in Thai RA patients and to identify factors associated with low immunogenicity.

**Materials and Methods:** A cross-sectional study was conducted between January 2022 and February 2023 at the rheumatology clinic, Srinagarind Hospital, Khon Kaen University. Adult RA patients who completed the Thai SARS-CoV-2 vaccine program were tested for spike protein IgG antibody levels 28 to 90 days after their second dose. Demographic data, disease activity, and medications were recorded.

**Results:** Twenty-five RA patients were included, with 84% being female and a mean age of 61.1 years. Most patients received methotrexate (64%) and prednisolone (72%). The overall median (IQR) spike IgG antibody level was 407.7 U/ml (79.3 to 1,190). Only one patient (4%) had low immunogenicity (10.1 U/ml), who received the AstraZeneca–Pfizer regimen. The highest median antibody level was found in the Sinovac–Pfizer group (4,376 U/ml), and the lowest was in the Sinopharm–Sinopharm group (21.2 U/ml). Among the four matched RA–control pairs, the antibody levels were generally comparable.

**Conclusion:** After completing two doses of the SARS-CoV-2 vaccination, Thai RA patients demonstrated good immunogenicity. Their IgG levels appeared comparable to those of healthy controls. Further studies with larger populations are warranted to confirm these findings and explore factors contributing to low immunogenicity.

**Keywords:** Rheumatoid arthritis; SARS-CoV-2; Vaccine; Immunogenicity; Thailand; DMARDs; Methotrexate; Biologic therapy

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Rheumatoid arthritis (RA) is a chronic systemic disease characterized by immunologically mediated inflammation of synovium-lined joints, which can lead to a significant disruption of joint structure and function. Over the past two decades, significant advances in basic science research have elucidated the biology of this inflammatory process, including the identification of several cytokines that drive chronic synovial inflammation (e.g., TNF-α, IL-1, and IL-6[(1)]. The current recommendations address the treatment of RA with the following conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biologic disease-modifying antirheumatic drugs (bDMARDs), targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs), and glucocorticoids[(2)].

The pandemic outbreak of COVID-19 has confirmed cases of more than 230 million and deaths of more than 4 million worldwide[(3)]. In Thailand, the incidence rate is above 10,000 persons per day, and it also has a high death rate[(4)].

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Factor-associated mortality includes older people, obesity, and comorbidity[5]. One of the essential comorbidities of COVID-19 is autoimmune inflammatory disease, including RA, which increases the risk of hospitalization and mortality in COVID-19 patients[5-10]. Immunosuppressive drugs, used to treat RA, exhibit lower immunogenicity compared to the general population[11-15].

In conclusion, two main reasons may lead to increased susceptibility and severity of COVID-19: one is that immunosuppressants are used in the treatment of RA, and the other is that the disease itself causes immune dysfunction.

COVID-19 vaccination can decrease the rate of transmission, rate of hospitalization, severity of infection, and mortality[16].

The previous study revealed the mean level of immunoglobulin against SARS-CoV-2 (CoronaVac) at day 69 after the second vaccination among autoimmune rheumatic diseases was 27.0±38.47 AU/ml (95% CI 24.7 to 29.5) (256 RA from total 910 autoimmune rheumatic diseases), while the immunoglobulin in the control group was 67.0±54.38 AU/ml (95% CI 59.8 to 74.9). However, no isolated data of immunoglobulin levels among RA patients[17] the recent study of immune response to messenger RNA (mRNA) SARS-CoV-2 vaccines in patients with immune-mediated inflammatory diseases (IMIDs) on immunomodulatory treatment showed that methotrexate which was the primary treatment of RA[2] reduced the immune response to SARS-CoV-2 mRNA vaccines[12].

In Thailand, we have a variety of SARS-CoV-2 vaccination regimens, including the inactivated SARS-CoV-2 vaccine (Vero cell) (Sinovac, Sinopharm), ChAdOx1-S (AZD1222) (AstraZeneca), BNT162b2 (Pfizer/BioNTech), and mRNA-1273 (Moderna). Immunogenicity and efficacy in the immunocompetent adult population, where 51%,79% (Sinovac, Sinopharm)[18,19], 63.09% (AstraZeneca)[20], and 90% (Pfizer/BioNTech)[21] of subjects achieve a satisfactory humoral response. However, the ability of patients with RA to adequately respond to these vaccines and the differences in immune response to each regimen of SARS-CoV-2 vaccinations are not well understood.

Due to the lack of knowledge of the immune response to other SARS-CoV-2 vaccine regimens in patients with rheumatoid arthritis (RA). We want to investigate this group of patients.

## Materials and Methods

### Study design

The authors conducted a cross-sectional study between January 2022 and February 2023. Adult RA patients were enrolled from the rheumatology clinic at Srinagarind Hospital, Khon Kaen University. The patient must complete the Thai SARS-CoV-2 vaccine program (2 doses of SARS-CoV-2 vaccine). Then, the patients were tested for a blood level of COVID-19 spike protein IgG antibody between day 28 and day 90 after completing the Thai SARS-CoV-2 vaccine program.

### Population

We recruited RA patients aged 18 years or older. All of the patients had a diagnosis of RA based on ACR/EULAR 2010 rheumatoid arthritis classification criteria[1]. All patients must complete two doses of the Thai SARS-CoV-2 vaccine program. We excluded the RA patients who (a) were diagnosed with COVID-19 infection PCR positively or suspected infection by a Rapid antigen test kit positively before the immunogenicity test; (b) were unable to attend blood test; or (c) received booster dose (3rd or 4th dose) vaccination before attending blood test.

### Operation definition

Diagnosis of rheumatoid arthritis (RA) is defined according to the ACR/EULAR 2010 rheumatoid arthritis classification criteria[1]. The Thai Department of Disease Control defines the Thai SARSCoV-2 vaccination program[4]. These are the regiments of SARS-CoV-2 vaccine in the present study; CoronaVac-BNT162b2 (Pfizer/BioNTech), Sinopharm-Sinopharm, AstraZeneca (AZD1222)-AstraZeneca (AZD1222), CoronaVac-AstraZeneca (AZD1222), AstraZeneca (AZD1222)-BNT162b2 (Pfizer/BioNTech), BNT162b2 (Pfizer/BioNTech)- BNT162b2 (Pfizer/BioNTech), Sinopharm-BNT162b2 (Pfizer/BioNTech) and mRNA-1273 (Moderna) - mRNA-1273 (Moderna). The COVID-19 pandemic is caused by a coronavirus named SARS-CoV-2, as described by the WHO[22]. Low immunogenicity to the SARS-CoV-2 vaccine is fulfilled if the COVID-19 spike protein IgG antibody level is less than 15 U/ml[23].

### Laboratory method

Immunogenicity is assessed by a quantitative test for COVID-19 spike protein IgG antibody by the ECLIA technique. Specimen collected using an EDTA and sodium citrate tube, plasma, 10 ml of blood, and analyzed within 2 hours.

Electro-chemiluminescence immunoassay (ECLIA)

Test principle: double-antigen sandwich assay (testing time: 18 minutes)

Step 1 (9 minutes): 12 µL of the patient sample is incubated with a mix of biotinylated and ruthenylated RBD antigen. Double antigen sandwich immune complexes are formed in the presence of corresponding antibodies.

Step 2 (9 minutes): After the addition of streptavidin-coated microparticles, the DAGS complexes bind to the solid phase via the interaction of biotin and streptavidin.

**Table 1.** Sample size calculation

| Power | Significance | Mean (SD) of IgG to SARS-CoV-2 (AU/mL) | | Sample size (overall) |
|---|---|---|---|---|
| | | Autoimmune rheumatic disease | Healthy control | |
| 80 | 0.05 | 27.0 (38.47) | 67.0 (54.38) | 23 |

Step 3 (Measurement): The reagent mixture is transferred to the measuring cell, where the microparticles are magnetically captured onto the electrode surface. Unbound substances are subsequently removed. Electrochemiluminescence is then induced by applying a voltage and measured with a photomultiplier. The signal yield increases with the antibody titer[23].

## Sample size

The sample size calculation was performed using the Stata program. According to recent literature, the mean (SD) of immunoglobulin G against SARS-CoV-2 in the ARD and control groups was 27.0 AU/ml (SD 38.47) and 67.0 AU/ml (SD 54.38), respectively, as reported by Medeiros-Ribeiro et al.[17]. Each group would have approximately 80% power and a significance level of 0.05 to detect a difference. The sample size for each group is presented in Table 1.

We planned to include 25 patients in each vaccine regimen. However, due to the COVID-19 pandemic breakout during the study period, many patients were infected with the virus, and a significant number received booster doses. Ultimately, we successfully recruited 25 RA patients who met the study's inclusion criteria.

## Clinical evaluation

The data collection included demographic data (age, sex, occupational, comorbidity), RA-related data (disease activity, medications, overlapping disease), vaccination data (date of 1st and 2nd vaccination, regimen of vaccination, side effect of vaccination, duration between 2nd vaccination and blood collection), Covid-19 spike IgG antibody level (U/ml).

The primary endpoint is the level of COVID-19 spike protein IgG antibody after the second dose of vaccination, and another outcome is the factors associated with immunogenicity to the SARS-CoV-2 vaccine.

The secondary objective is to investigate the association between factors and immunogenicity in rheumatoid arthritis patients.

## Intervention

None. An immunoassay for the quantitative determination of antibodies to the SARS-CoV-2 spike protein will be tested in the patients who participated in the present study.

## Ethics consideration

Eligible RA patients must sign a consent form before enrolling in the study. Details of testing procedures were explained to each subject, informed consent was obtained, the participants were collected one blood tube and the level of immunogenicity was reported to the patient by telephone or letter, the Khon Kaen University ethics committee approved a protocol for human research based on the Declaration of Helsinki and the ICH Good Clinical Practice Guidelines (HE611156).

The data of all subjects will be kept secret. No one can verify that the information belongs to any volunteer.

## Statistical analysis

Demographic data will be presented as percentages or proportions for categorical data and as means ± standard deviations (SD) or medians with interquartile ranges (IQR) for continuous data. The level of COVID-19 spike IgG antibody (U/ml) will be presented as the mean ± SD or median with IQR as appropriate. The prevalence of low immunogenicity to the COVID-19 spike IgG antibody will be calculated with its 95% CI. An odds ratio with a 95% confidence interval (CI) will be applied to identify factors associated with low immunogenicity to the SARS-CoV-2 vaccine. Variables with p-values less than 0.10 will be entered into a multiple logistic regression model. The p-values of less than 0.05 will be considered to be statistically significant. All statistical analyses will be performed using STATA 16.0 (StataCorp, College Station, TX, USA).

# Results

A total of 25 patients were enrolled in the study. The majority were female (21 cases; 84%). The mean age was 61.1±8.1 years. The disease activity of all patients was in remission to moderate; no patient had high disease activity. Most patients received prednisolone (21 cases; 72%) at doses ranging from 0.71 to 7.5 mg/day. Methotrexate (16 cases; 64%) was the most commonly used DMARD, followed by sulfasalazine (10 cases; 40%). Only one patient received anti-TNF (Etanercept) for the treatment. And overall median (IQR) Covid-19 spike IgG antibody level in RA patients was 407.7 U/ml (79.3 to 1,190). The patient demographic data and overall COVID-19 spike IgG antibody level are presented in Table 2.

The authors categorized patients by SARS-CoV-2

**Table 2.** Demographic data and overall COVID-19 spike IgG antibody level

| Variable | Total, n=25 |
|---|---|
| Female (%) | 21 (84) |
| Age (years); mean ± SD | 61.1±8.1 |
| BMI (kg/m$^2$); mean ± SD | 23.7±5.2 |
| Hypertension (%) | 9 (36) |
| Diabetes mellitus type II (%) | 4 (16) |
| Chronic kidney disease (%) | 2 (8) |
| Dyslipidemia (%) | 6 (24) |
| Hepatitis B viral infection (%) | 1 (4) |
| Inflammatory marker | |
| ESR; median (IQR) | 57 (38 to 75) |
| CRP; median (IQR) | 2.32 (0.64 to 6.7) |
| PGA; median (IQR) | 30 (20 to 50) |
| DAS28 by ESR; median (IQR) | 3.02 (2.56 to 4.15) |
| Medications | |
| Prednisolone (%) | 18 (72) |
| Methotrexate (%) | 16 (64) |
| Sulfasalazine (%) | 10 (40) |
| Azathioprine (%) | 2 (8) |
| Leflunomide (%) | 5 (20) |
| Hydroxychloroquine (%) | 4 (16) |
| Cyclosporin A (%) | 1 (4) |
| Etanercept (%) | 1 (4) |
| Overall Covid-19 spike IgG antibody level (U/ml) ; median (IQR) | 407.7 (79.3 to 1,190) |

IQR=interquartile range; BMI=body mass index; ESR=erythrocyte sedimentation rate; CRP=c-reactive protein; PGA=patient global assessment

vaccine into eight regimens: Sinovac-Pfizer, Sinopharm-Sinopharm, AstraZeneca-AstraZeneca, Sinovac-AstraZeneca, AstraZeneca-Pfizer, Pfizer-Pfizer, Sinopharm-Pfizer, and Moderna-Moderna. The most commonly used vaccine regimens were Moderna-Moderna (8 cases, 32%) and Pfizer-Pfizer (8 cases, 32%). The highest median COVID-19 spike IgG antibody level was in the Sinovac-Pfizer regimen (4,376 U/ml), and the lowest median COVID-19 spike IgG antibody level was in the Sinopharm-Sinopharm regimen (21.2 U/ml). All COVID-19 vaccine regimens showed no low immunogenicity (COVID-19 spike protein IgG antibody level is less than 15 U/ml)[23]. COVID-19 spike IgG antibody levels categorized by SARS-CoV-2 vaccine regimens are presented in Table 3.

4% (1 case) of RA patients exhibited low immunogenicity, with a COVID-19 spike IgG antibody level of 10.1 U/ml. This RA patient was in the AstraZeneca Pfizer group. The patient's disease activity was in remission (DAS28; 2), while the others in this group had moderate disease activity (Mean DAS28; 4.1). The patient received an average dose of prednisolone, methotrexate, and sulfasalazine compared to the RA patients, who showed

**Table 3.** COVID-19 spike IgG antibody level categorized by SARS-CoV-2 vaccine regimens

| Variable | Regimens (first dose/second dose) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Sinovac/AstraZeneca | Pfizer/Pfizer | AstraZeneca/Pfizer | Sinopharm/ Sinopharm | Moderna/Moderna | Sinopharm/ Pfizer | AstraZeneca/ AstraZeneca | Sinovac/Pfizer |
| n (%) | 2 (8) | 8 (32) | 3 (12) | 1 (4) | 8 (32) | 1 (4) | 1 (4) | 1 (4) |
| Age (years); mean ± SD | 67.3±11.4 | 60.4±9.1 | 67.3±11.4 | 50.6±0 | 60.2 ± 7.9 | 62.4±0 | 55.8±0 | 65.3±0 |
| BMI (kg/m$^2$); mean ± SD | 24.8±1.3 | 27.1±6.9 | 24.8±1.3 | 20.0±0 | 21.2 ± 1.0 | 18.7±0 | 17.7±0 | 19.8±0 |
| ESR; median (IQR) | 47 (37 to 57) | 60.5 (48 to 79.5) | 73 (57 to 130) | 78 | 38 (29-66) | 75 | 53 | 47 |
| DAS28 by ESR; median (IQR) | 2.82 (2.67 to 2.97) | 3.46 (2.72 to 3.88) | 4.11 (2.00 to 4.41) | 2.56 | 3.14 (2.77-4.17) | 4.70 | 1.27 | 1.42 |
| COVID-19 spike IgG antibody level (U/ml); median (IQR) | 2,467.3 (374.6 to 4,560) | 479.1 (138.7 to 953.6) | 240.7 (10.1 to 524.3) | 21.2 | 395.35 (53.85 to 1,794) | 2,448 | 264.4 | 4,376 |

IQR=interquartile range; BMI=body mass index; ESR=erythrocyte sedimentation rate

normal immunogenicity. Comparisons between patients with low immunogenicity and those with normal immunogenicity are presented in Table 4.

Unfortunately, we were unable to recruit a sufficient sample size to calculate the prevalence of low immunogenicity to COVID-19 spike IgG antibodies and identify the factors associated with low immunogenicity to the SARS-CoV-2 vaccine due to the pandemic breakout.

We matched RA patients with healthy controls by sex, age (within ±5 years), and vaccine regimen. We found four couples matching. When comparing the level of SARS-CoV-2 spike protein IgG to healthy controls according to the vaccine regimen, the IgG level was comparable between RA patients and healthy controls. All couples showed normal immunogenicity, except for one couple in the AstraZeneca-Pfizer regimen, which exhibited low immunogenicity, as mentioned earlier. Compared between RA patients and healthy controls are presented in Table 5.

## Discussion

Patients with rheumatoid arthritis (RA) are at increased risk of infection as compared with healthy individuals. This increased risk is attributed to the disease itself, which causes immune dysfunction, and to the use of immunosuppressive drugs, resulting in lower immunogenicity compared to the general population[11-15]. These patients should be considered at high risk for developing COVID-19, so vaccination for prevention is essential.

The present study included 25 RA patients and 196 healthy controls, all of whom were tested for IgG levels against SARS-CoV-2 after receiving their second dose of the SARS-CoV-2 vaccine as part of the Thai vaccination program. The primary objective was to evaluate the IgG response in RA patients after the second vaccination and to compare their antibody levels to those of healthy controls. Given the variety of vaccine regimens available in Thailand, we also analyzed IgG levels based on different vaccine combinations. Among the RA patients, the most common regimens were Moderna-Moderna and Pfizer-Pfizer, each used by 32% of participants. However, the sample size remained small, as many patients had already received a third (booster) dose, limiting their inclusion in the present study.

Previous studies have shown that the mean immunoglobulin levels against SARS-CoV-2, following two doses of CoronaVac or mRNA vaccines, are generally lower in patients with autoimmune rheumatic diseases, including RA, compared to the general population[17,12,24]. However

**Table 4.** Compared between low immunogenicity and normal immunogenicity patients

| Variable | Low immunogenicity | Normal immunogenicity |
|---|---|---|
| Vaccine regimen | AstraZeneca-Pfizer | Others |
| n (%) | 1 (4) | 24 (96) |
| Age (years); mean ± SD | 55.9 | 61.3±8.2 |
| BMI (kg/m$^2$); mean ± SD | 29.8 | 23.4±5.2 |
| DAS28 by ESR; median (IQR) | 2 | 3.02 (2.56 to 4.15) |
| Medications | | |
| Prednisolone (mg/day); mean ± SD | 5 | 4.8±2.8 |
| Methotrexate (mg/week); mean ± SD | 10 | 8.8±2.9 |
| Sulfasalazine (mg/day); mean ± SD | 1,000 | 1,166.7±559 |
| Azathioprine (mg/day); mean ± SD | - | 42.5±10.6 |
| Leflunomide (mg/day); mean ± SD | - | 10.2±3.8 |
| Hydroxychloroquine (mg/day); mean ± SD | - | 308.8±299.1 |
| Overall Covid-19 spike IgG antibody level (U/ml); median (IQR) | 10.1 | 466 (97.3 to 1,819) |

IQR=interquartile range; BMI=body mass index

Low immunogenicity: COVID-19 spike protein IgG antibody level is less than 15 U/ml[23]

**Table 5.** Compared between RA patients and healthy controls

| Vaccines | Sex | Age | Immunogenicity (U/ml) | |
|---|---|---|---|---|
| | | | RA patients | Healthy control |
| AstraZeneca-Pfizer | Female | 56 | 10.1 | 9.2 |
| Sinopharm-Sinopharm | Female | 51 | 21.2 | 15.6 |
| AstraZeneca-Pfizer | Male | 67 | 524.3 | 1379.0 |
| AstraZeneca-AstraZeneca | Female | 56 | 264.4 | 368.6 |

when focusing on the response of immunogenicity before and after two doses of SARS-CoV-2 vaccination in the study of (Ana C. 2021) found that the patients with autoimmune diseases including RA had quite good immunogenicity after 2nd dose of SARS-CoV-2 vaccination[17]. The study by Omar A. (2022) showed that immune-mediated inflammatory disease, including RA patients who received Cs-DMARDs, anti-TNF, JAK inhibitors, and IL-6 Inhibitors, had seroconversion rates comparable to those of healthy controls after two doses of the BNT162b2 (Pfizer) vaccine[25]. In line with these findings, our study showed an overall median (IQR) COVID-19 spike IgG antibody level of 407.7 U/ml (79.3 to 1,190) among RA patients after completing the Thai SARS-CoV-2 vaccination program, indicating good immunogenicity in general for RA patients receiving two vaccine doses.

And if we consider immunogenicity by SARS-CoV-2 vaccine regimens. We found that all COVID-19 vaccine regimens showed no low immunogenicity. The lowest and highest median COVID-19 spike IgG antibody levels were observed in the Sinopharm-Sinopharm and Sinovac-Pfizer regimens, respectively. However, this result cannot determine the efficacy and effectiveness of each vaccine regimen.

Only one RA patient had low immunogenicity against SARS-CoV-2 after receiving the second dose of vaccination, despite being on immunosuppressants. This patient was in the AstraZeneca-Pfizer group, and her COVID-19 spike IgG antibody level was 10.1 U/ml while the others in this group had normal immunogenicity. This patient is the youngest and had the lowest disease activity in this group (DAS28; 2). The patient received an average dose of prednisolone, methotrexate, and sulfasalazine compared to the normal immunogenicity group. The sample size is not sufficient to calculate the prevalence and identify the factors associated with low immunogenicity. We were unable to determine the factors that cause low immunogenicity in this patient.

When comparing the level of SARS-CoV-2 spike protein IgG to healthy controls according to the vaccine regimen, the IgG level was comparable between RA patients and healthy controls. Unlike the previous studies mentioned above, which showed a lower mean level of immunoglobulin against SARS-CoV-2 in autoimmune rheumatic diseases, including RA patients, compared to the normal population[17,12,24].

In real-world data, the incidence of COVID-19 hospitalization was increased for both unvaccinated and vaccinated patients with RA compared with controls. However, the incidence rate of death from COVID-19 in vaccinated RA patients was lower than in unvaccinated RA patients[26]. Together with our result, RA patients who completed two doses of the SARS-CoV-2 vaccine showed good immunogenicity. We recommend that all RA patients without contraindications should receive at least two doses of the SARS-CoV-2 vaccine.

The limitation of the study includes a) a small sample size as previously mentioned, so we cannot calculate the prevalence and identify the factors associated with low immunogenicity; b) a single center in Thailand was included, so the findings might not be generalizable; and c) no outcome was recorded if the patients had SARS-CoV-2 infection, so we cannot provide the outcome of infection in who had low immunogenicity against SAR-CoV-2.

The strengths of this study include the variety of vaccination regimens used, which allows the results to be applied as real-world data.

## Conclusion

After 2nd dose of the SARS-CoV-2 vaccination, RA patients showed good immunogenicity. Moreover, their IgG level against SARS-CoV-2 appeared to be comparable to that of healthy controls. Due to the small sample size, further study with a larger population is recommended.

### What is already known on this topic?

Patients with rheumatoid arthritis (RA) are at an increased risk of infection due to both the underlying immune dysfunction of the disease and the immunosuppressive effects of their treatments. Immunogenicity to vaccines, including COVID-19 vaccines, is often lower in patients with autoimmune rheumatic diseases than in the general population. Studies have shown that methotrexate, a cornerstone treatment for RA, reduces the immune response to mRNA COVID-19 vaccines. Previous research on inactivated SARS-CoV-2 vaccines (e.g., CoronaVac) demonstrated lower antibody levels in patients with autoimmune rheumatic diseases, including RA, compared to healthy controls.

### What this study adds?

The present study provides new insights into the immunogenicity of different SARS-CoV-2 vaccine regimens in Thai patients with rheumatoid arthritis (RA). Unlike previous studies that suggested reduced vaccine responses in autoimmune rheumatic diseases, our findings indicate that RA patients who completed two doses of the Thai SARS-CoV-2 vaccination program generally exhibited good immunogenicity. The overall median IgG antibody levels in RA patients were comparable to those of healthy controls, suggesting that RA patients can achieve adequate immune responses despite being on immunosuppressive treatment. Additionally, the present study is one of the first to evaluate multiple vaccine regimens, demonstrating that all regimens used in Thailand provided sufficient immunogenicity, with

no significant cases of vaccine non-response. However, further studies with larger sample sizes are needed to identify factors influencing low immunogenicity in RA patients.


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## Conflicts of interest

The authors declare no conflict of interest.

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