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Original Article

First Report of the Immunogenicity of an Inactivated SARS-CoV-2 (COVID-19) Vaccine in Iranian Patients with Autoimmune Diseases

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Abstract

Background: Infectious diseases are responsible for considerable morbidity and mortality worldwide, and coronavirus disease 2019 (COVID-19) is one of these infections. Because of the substantial burden on the healthcare system, considerable efforts have been made to immunize the population against severe acute respiratory syndrome coronavirus 2 through vaccination. However, there are considerations regarding the efficacy of vaccines in autoimmune patients. The current study revealed the immunogenicity of inactivated COVID-19 vaccines among the Iranian population with rheumatic diseases.

Methods: As the first report from Iran, in this descriptive cross-sectional study, 196 patients were sampled; 98 of whom had an autoimmune disease and 98 of whom served as controls. Blood samples were collected and tested with IgM and IgG ELISA kits for COVID-19 antibody (Ab) levels. Some demographic characteristics were recorded.

Results: This study revealed an Ab response after inactivated COVID-19 vaccination among 196 participants, including 98 healthy individuals and 98 autoimmune patients. Our analysis revealed that the case group had a profoundly lower percentage of IgG- and IgM-positive individuals, at 37.7% and 13.2%, respectively, than the control group, which had significantly greater percentages of IgG and IgM Abs, at 86.7% and 65.3%, respectively.

Conclusion: Individuals with autoimmune conditions, especially women, presented considerable decreases in IgG levels after vaccination with the inactivated COVID-19 vaccine. It seems that those with autoimmune disorders may experience immune system fatigue, leading to lower Ab levels following COVID-19 vaccination. Several potential factors, such as the use of immunosuppressive medications, could explain the reduced Ab response after COVID-19 vaccination. As a result, individuals with compromised immune systems, including those with autoimmune disorders, should be closely monitored and prioritized for additional COVID-19 vaccine doses to improve protection. Furthermore, the possible effects of repeated vaccinations on immune exhaustion and reduced defense against microbial infections highlight the need for further research in this patient population. It can be concluded that special vaccine protocols for all kinds of vaccinations should be approved for patients with autoimmune diseases.

Keywords: Ab, autoimmune disease, COVID-19 vaccination, ELISA

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Introduction

Infections are still considered a major burden to public health, and they are responsible for numerous disasters worldwide.[1,2] For example, coronavirus disease 2019 (COVID-19) is an infection that has led to a catastrophic pandemic and has caused millions of deaths following its outbreak.[3] Because COVID-19 is responsible for multiple morbidities and mortalities and is an enormous encumbrance to the healthcare system, a reasonable approach to decrease the struggle and adverse effects caused by COVID-19 is to immunize the population against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) through vaccination.[4] Since the beginning of the COVID-19 outbreak, considerable efforts have been made to produce SARS-CoV-2 vaccines, and significant seroconversion has been reported after COVID-19 vaccination regardless of the type of infection in the general population; nevertheless, the results regarding immunocompromised patients have remained controversial.[5,6] Since this group constitutes approximately 3% of the adult population, their immune systems are dysregulated, and they are more susceptible to severe

infections; obtaining data regarding vaccine efficacy in this group is highly important.[5] People with rheumatic diseases and those who are receiving immunosuppressive therapy constitute a part of this immunocompromised population, and as these cases were not included in the vaccine trials, there were concerns about the safety of using the vaccine in this group and the efficacy of the vaccine in patients who were receiving immunosuppressive medications.[4] The fact that some studies have revealed lower antibody (Ab) levels after influenza vaccination in those receiving anti-CD20 medications supports our concern related to the efficacy of COVID-19 vaccination in patients with an impaired immune system.[7,8] Autoimmune diseases produce autoAbs that can activate the complement system and cause systemic inflammation.[9] There are considerations in regard to the influence of COVID-19 on autoimmune patients for 2 reasons: first, the immunosuppressants they use for their illness, and second, the nature of their disease itself, which increases their susceptibility to infection.[9] In this study, we attempted to estimate the immunogenicity of an inactivated COVID-19 vaccine in Iranian patients with autoimmune diseases to improve the effectiveness of vaccination in people with autoimmune diseases to decrease the adverse effects caused by COVID-19 infection. To the best of our knowledge, this is the first study in which the immunogenicity of COVID-19 vaccination in patients with rheumatic diseases has been reported in an Iranian population.

Main Points

- There are concerns regarding the immunogenicity of an inactivated coronavirus disease 2019 (COVID-19) vaccine in autoimmune patients because of the nature of their disease and the immunosuppressants they use.
- To evaluate the immunological response after COVID-19 vaccination, the levels of IgM and IgG antibodies (Abs) were estimated after two doses of vaccination in autoimmune patients.
- Our results revealed that individuals with rheumatic disease had a markedly lower percentage of IgG- and IgM-positive individuals than did those in the control group (IgG: 37.7% vs. 86.7% and IgM: 13.2% vs. 65.3%).
- Furthermore, our results revealed that the percentage of participants who tested positive for IgM and IgG Abs varied across different age ranges, and male participants had a greater percentage of positive results for IgG than did their female counterparts (86.9% vs. 67.1%).

Material and Methods

Patient Selection

This cross-sectional research took place at the Asia laboratory in Ilam, Iran, in December 2021. Adults with autoimmune diseases who had been vaccinated with the COVID-19 vaccine and were referred to the laboratory for any reason were included in the study via convenience sampling. All patients had medical records, and their disease status was determined by physicians according to the American College of Rheumatology criteria. A total of 98 individuals with autoimmune diseases were selected as the case group, while 98 healthy adult Iranian blood donors with no clinical evidence or family history of autoimmune diseases served as the control group. The healthy donors were matched for age and sex. All the information was handled, examined, and documented confidentially, and all the COVID-19 Ab tests were conducted at no cost to the participants. The ethics committee of Shiraz University of Medicine, Shiraz, Iran, granted ethical permission for this research with the certificate reference number IR.SUMS.REC.1403.064. All patients provided written informed consent according to the guidelines of the Declaration of Helsinki and its subsequent updates. The local Ethics Committee of Shiraz University of Medical Sciences in Shiraz, Iran, approved the research protocol.

Specimen Collection

Five-milliliter peripheral blood samples were taken in a non-heparin tube and allowed to clot. The serum fraction was separated by spinning the tubes at 3000 rpm for 5 minutes and was kept at −70°C for further analyses. IgG and IgM Abs against COVID-19 were assessed according to the guidance of the manufacturer of a kit (Pishtaz Teb, Iran; SARS-CoV-2 IgG & SARS-CoV-2 IgM, Tehran, Iran) that targets the N antigen. Values above 1.1 and below 0.9 were considered positive and negative, respectively, according to the manufacturer's instructions. A volume of 100 μL for each individual serum sample was aliquoted in antigen-coated 96-well plates specific to the SARS-CoV-2 N antigen. This step was followed by incubation of the plate for 30 minutes at 37°C and washing 5 times with an ELISA washer. Then, 100 μL of conjugated enzyme was added to each well, and the plate was incubated for an additional 30 minutes, after which the liquid was removed, and the wells were washed 3 times. The next step consisted of adding the dye mixture (100 μL) and incubating the plates in the dark for 15 minutes at room temperature (RT). Afterward, 100 μL of stop solution was added to stop the reaction. The absorbance of the plates was thereafter compared to that of the blank by adding 100 μL of the dye solution and incubating the plate in the dark for 15 minutes at RT. Then, 100 μL of stop solution was added to each well, and the absorbance was assessed via an ELISA reader at $\lambda = 450$ nm. Importantly, the sensitivity and specificity of SARS-CoV-2 ELISA kits are 79.4% and 97.3% for IgM and 98.3% and 94.1% for IgG, respectively.[10] After the dye solution was added to the wells, it produced a blue color, the intensity of which was directly proportional to the number of immune complexes formed in the wells. The 450 nm wavelength is the optimum for light absorption, where the yellow color results from the addition of the stop solution to the blue solution. Values above 1.1 are set positive, and values below 0.9 are set negative with the use of this kit.

Data Analysis

Statistical analysis was performed via SPSS version 26.0. Continuous variables are expressed as means ± standard deviations, and categorical variables are expressed as numbers and percentages. The normality of continuous variables was analyzed by the Shapiro-Wilk test. Differences between groups for normally distributed continuous variables were analyzed by the independent samples *t*-test, whereas the Mann-Whitney *U* test was used for non-normally distributed continuous variables. Associations between categorical variables were examined via Pearson's chi-squared test or Fisher's exact test, as appropriate. Multiple logistic regression analysis was executed to determine the independent factors associated with the outcome, and the results are reported as odds ratios (ORs) with 95% CIs. A 2-tailed *P*-value <.05 was considered to indicate statistical significance.

Results

The current study investigated the immunological response to COVID-19 vaccination in participants with and without autoimmune disease. The study was conducted with 196 participants divided into 2 groups, namely, cases and controls, on the basis of their autoimmune status. The groups were comparable in size, and their demographic characteristics were similar. Females comprised the majority of the participants, accounting for 77.5% of the sample, with a similar distribution across both groups. Most of the participants were under 50 years of age (58.1%), and the greatest

number of participants were between the ages of 30 and 50 years (80.7%) (Table 1). Among the participants in the case group, 51% were diagnosed with Rheumatoid arthritis (RA), whereas other autoimmune diseases were less prevalent. Additional details regarding each autoimmune disease can be found in Table 2.

Following vaccination, we evaluated the amounts of IgM and IgG Abs in the participants. Our results revealed that the case group had significantly lower percentages of IgG- and IgM-positive individuals (37.7% and 13.2%, respectively) than the control group, which had significantly greater percentages of IgG and IgM Abs (86.7% and 65.3%, respectively). The statistical analysis revealed a considerable difference between the 2 groups ($P = .000$), as shown in Figure 1.

Moreover, we examined the correlations between the levels of IgM and IgG Abs and the age and sex of the participants. Our findings indicated that the percentage of participants who tested positive for IgM and IgG Abs varied across different age ranges, with Pearson chi-square values of 0.103 for IgG and 0.001 for IgM. Most of the positive patients were above 50 years of age for both IgG and IgM, whereas most of the negative patients were between 30 and 50 years of age, as shown in Figure 2. In addition, male participants had a greater percentage of positive IgG results (86.9%) than their female counterparts (67.1%), and the Pearson correlation analysis was significant ($P = .014$). Furthermore, sex did not have a notable effect on IgM levels ($P = .241$).

Discussion

In this study, we explored the immunological response to COVID-19 vaccination among 196 participants, which included 98 participants with autoimmune diseases and 98 healthy individuals. The case group included mostly patients with RA (51%), but there were also individuals with other autoimmune conditions, such as Systemic lupus erythematosus (SLE) , ankylosing spondylitis, scleroderma, osteoporosis, dermatomyositis, psoriatic arthritis, uveitis, Sjogren's syndrome, and Wagner vasculitis. To evaluate the immunological response after COVID-19 vaccination, the levels of IgM and IgG Abs were estimated after 2 doses of vaccination. Our results revealed that individuals with rheumatic disease had a markedly lower percentage of IgG- and IgM-positive individuals than did those in the control group (IgG: 37.7% vs. 86.7% and IgM: 13.2% vs. 65.3%).

Similar to our findings, in a study that analyzed the Ab response after BNT162b2 vaccination among 134 patients (61 with SLE and 73 with RA), detectable Abs were found in 77% of the patients (compared to 100% in healthy individuals).[11] In another prospective phase 4 controlled trial evaluating anti-COVID-19 IgG seroconversion among 910 patients with autoimmune disease and 182 healthy adults as the control group, seroconversion was 70.4% in autoimmune patients (contrary to 95.5% in the control group, $P < .001$) after CoronaVac vaccination.[12] In addition, in an observational survey investigating the immunogenicity of mRNA COVID-19 vaccines in 478 autoimmune patients, the nonresponse rate was significantly greater in the case group than in the control group (13.2% compared with 2.8%; $P < .0001$).[13]

There are reviews that have evaluated vaccine effectiveness for treating COVID-19, severe disease, and COVID-19-related hospital admissions. In a survey evaluating vaccine efficiency against COVID-19 infection, vaccine effectiveness was 52%-90% in immunocompromised populations vs. 90%-95% in the entire study group.[14] Dagan et al[15] and Barda et al reported 100% effectiveness of the BNT162b2 vaccine against severe disease in an immunocompromised group, in contrast to 95% in the general population. In a study guided by Tenforde et al[16] the effectiveness of mRNA vaccines against COVID-19-related hospitalization was 63% in immunocompromised patients versus 87% in the overall study group.

Finally, Furer et al[17] in a survey including 686 participants vaccinated with the Comirnaty Pfizer vaccine, reported a markedly lower immune response in patients treated with rituximab and a moderately lower immune response in patients treated with CCS, abatacept, and mycophenolate mofetil; on the other hand, only slight impairment of the immune response was observed due to methotrexate (MTX). A cohort survey analyzing the immunogenicity of SARS-CoV-2 mRNA vaccines in autoimmune patients and immunocompetent controls revealed that the greatest impact on the Ab response was caused by B-cell depleting therapies and GCs.[18]

According to previous studies, several possible risk factors may be responsible for the decreased Ab response after COVID-19 vaccination. The most important risk factors that have been reported are immunosuppressive medications, especially rituximab.[13] Rituximab has been reported to repress humoral immunity; therefore, adjusting the duration of rituximab use to achieve the best Ab results after COVID-19 vaccination is important.[19,20] With respect to the impact of vaccine type on Ab production, according to an observational study, the Ab response was not strongly affected by vaccine type. In addition, the association between increasing age and a low Ab response was reported only in a monocentric cohort study.[17] There is a settlement among the European League Against Rheumatism and the American College of Rheumatology (ACR) that treatment with corticosteroids (CCSs) and anti-CD20 monoclonal Abs is associated with a noticeably reduced Ab response.[21]

Table 1. Demographic and Clinical Characteristics of the Participants

Characteristics	Autoimmune Group (n = 98)	Healthy Donors (n = 98)	*P*
Mean age (years)	47.5 ± 12.3	45.2 ± 10.8	.15
Sex (female, n [%])	75 (76.5)	72 (73.5)	.62
IgG positive (n [%])	37 (37.7)	85 (86.7)	<.001
IgM ositive (n [%])	13 (13.2)	64 (65.3)	<.001
Autoimmune disease type			
Rheumatoid arthritis	50 (51.0%)	N/A	N/A
Systemic lupus erythematosus	10 (10.2%)	N/A	N/A
Ankylosing spondylitis	10 (10.2%)	N/A	N/A
Others	28 (28.6%)	N/A	N/A
Current/past treatments			
Corticosteroids (n [%])	40 (40.8)	N/A	N/A
Anti-CD20 therapies (n [%])	15 (15.3)	N/A	N/A
Methotrexate (n [%])	25 (25.5)	N/A	N/A
Other immunosuppressants (n [%])	18 (18.4)	N/A	N/A

Table 2. Information on Each Autoimmune Disease in the Patient Group

Disease	Number of IgG Positive (% of Patients with the Disease)	Number of IgM Positive (% of Patients with the Disease)	Total Number (% of Case Group)
Rheumatoid arthritis	20 (40)	9 (18)	50 (51)
Systemic lupus erythematosus	5 (50)	1 (10)	10 (10.2)
Ankylosing spondylitis	5 (50)	1 (10)	10 (10.2)
Osteoporosis	0 (0)	0 (0)	2 (2)
Scleroderma	2 (50)	0 (0)	4 (4)
Dermatomyositis	1 (50)	0 (0)	2 (2)
Psoriatic arthritis	1 (50)	0 (0)	2 (2)
Uveitis	1 (50)	0 (0)	2 (2)
Sjogren syndrome	0 (0)	0 (0)	2 (2)
Wagner vasculitis	0 (0)	0 (0)	2 (2)
Two of above diseases	2 (16.6)	2 (16.6)	12 (12.6)
Total	37 (37.7)	13 (13.2)	98 (100)

Moreover, patients with autoimmune diseases may experience immune system exhaustion, leading to lower levels of Abs after COVID-19 vaccination, as indicated by a study assessing humoral and cellular responses in autoimmune patients post-booster dose.[22] Therefore, patients with deficient immune responses, including those with autoimmune disease, should be monitored closely and prioritized for additional COVID-19 vaccine doses to enhance protection. Additionally, considerations have been raised with respect to the potential influence of repeated vaccinations on immune exhaustion and reduced protection against microbial infections, emphasizing the need for further research in this area.[23]

In contrast to our results, in an observational survey that determined the immunogenicity of the inactivated COVID-19 vaccine in patients with rheumatic diseases, no statistically significant difference in the seropositivity rate was reported between patients with rheumatic diseases and the control group. However, in this study, as well as in our study, patients who were treated with rituximab had no Ab response, and those who were treated with MTX or iguratimod had a considerably lower Ab response.[24]

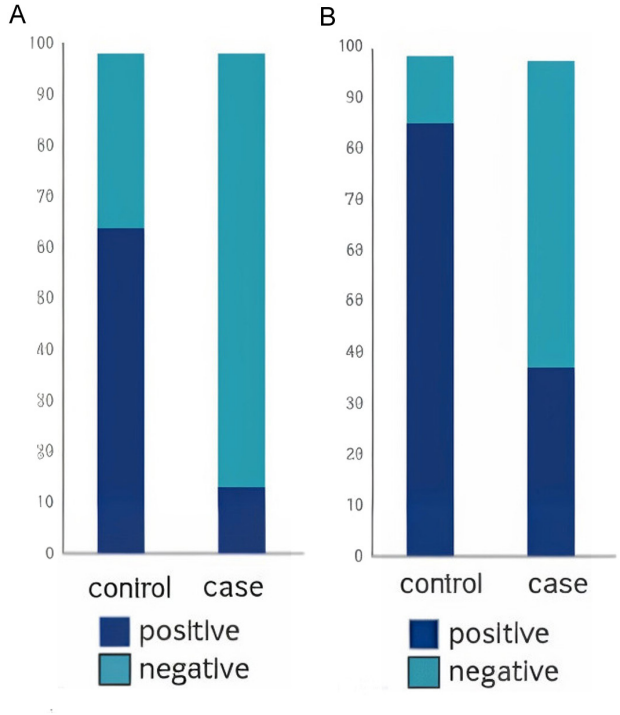

Figure 1. (A) IgM distribution in each group and (B) IgG distribution in each group.

Furthermore, our results revealed that the percentage of participants who tested positive for IgM and IgG Abs varied across different age ranges, and male participants had a greater percentage of positive results for IgG than did their female counterparts (86.9% vs. 67.1%).

In a study that compared vaccine efficacy among immunocompetent and immunocompromised participants, among the immunocompetent group, males had a lower risk of contracting COVID-19; however, among the immunocompromised group, the risk was similar in both sexes.[25] On the other hand, in another study that revealed an Ab response in SLE patients, men had considerably lower Ab levels.[26]

Regardless, in an observational study comparing post-COVID-19 vaccination seroconversion among ASD patients and a control group, no difference in age or sex distribution was reported among ASD responders and nonresponders.[13] Despite the findings of most studies, the impact of increasing age on decreasing Ab response was reported in another cohort study similar to our study.[17]

Some surveys have compared local and systemic adverse effects and the rate of illness flaring after COVID-19 vaccination among patients with autoimmune diseases and healthy individuals. A study that investigated adverse effects post-vaccination among 505 autoimmune cases and 203 healthy participants revealed that adverse reactions to COVID-19 vaccination were comparable among the case and control groups, independent of vaccine type.[27] In another study investigating adverse effects after COVID-19 vaccination, the results demonstrated an increased risk of certain specific minor adverse effects and a greater risk of major adverse effects among participants with autoimmune diseases than among the control group. However, COVID-19 vaccination is relatively safe for these patients.[28]

In this report, individual serology results were reported in positive/negative numbers rather than presenting the data as Ab levels. This approach indeed offers a more granular view of the immunological responses; therefore, the

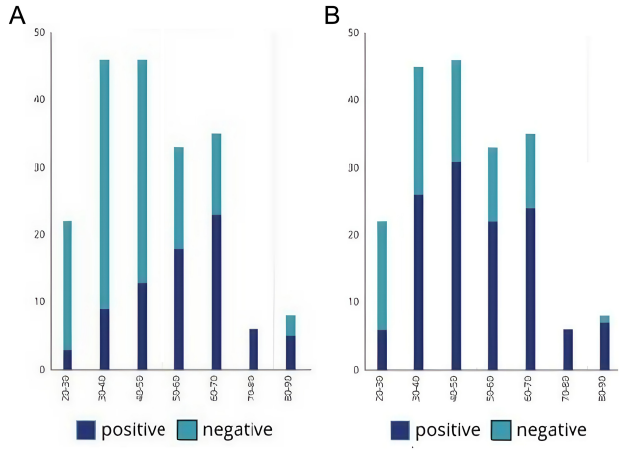

Figure 2. (A) IgM levels in each age range and (B) IgG levels in each age range.

results as positive/negative were based on the following rationale:

Simplified data interpretation: the primary aim of this study was to compare the overall immunogenicity between autoimmune patients and healthy donors. Reporting seropositivity rates (positive/negative) allows readers to easily understand the key differences in the immune response without delving into the variability of individual Ab levels.

Standard reporting in similar studies: comparable studies in the field use positive/negative categorization, as it aligns with the clinical significance of achieving detectable Ab levels, which are directly related to immunity.[29]

Limitations of serology variability: Individual Ab levels may vary owing to numerous factors (e.g., test timing, baseline immune status, and assay sensitivity), which could introduce noise without adding substantial value to the conclusions. By focusing on positivity thresholds, we maintain a clear and actionable narrative.

The discrepancy between our study and others could indeed be linked to various factors, such as the vaccine type, age of the individuals, presence of comorbidities, timing of breakthrough infections post-vaccination, genetic factors, and population dynamics.

Despite some limitations in this study, such as the lack of prior sample size estimation, large sample size, and insufficient demographic and laboratory data, no study has assessed the immunogenicity of the COVID-19 vaccine in patients with autoimmune diseases in Iran. However, there are general restrictions on studies focusing on autoimmune cases. Although COVID-19 vaccines have proven effective at reducing severe outcomes globally, their efficacy among individuals with autoimmune diseases remains less clear due to several limitations, including heterogeneous study designs, underrepresentation in clinical trials, variability in patient characteristics/treatment regimens, lack of long-term data, varying quality of evidence across studies, and challenges posed by emerging variants. Addressing these limitations through well-designed, high-quality randomized controlled trials focusing on this subgroup, along with tailored vaccination strategies, will be essential.

Patients with autoimmune conditions, particularly female individuals, exhibited a notably diminished IgG Ab reaction subsequent to receiving inactivated COVID-19 vaccination. Individuals with autoimmune disorders may experience immune system exhaustion, resulting in decreased Ab levels after COVID-19 vaccination. Various potential risk factors, such as the use of immunosuppressive drugs, could account for the reduced Ab response after COVID-19 vaccination. Consequently, individuals with impaired immune responses, which may include autoimmune conditions, should be closely monitored and given priority for additional COVID-19 vaccine doses to enhance protection. Furthermore, the potential consequences of repeated vaccinations on immune fatigue and decreased defense against microbial infections underscore the necessity for further exploration in this patient population.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the Ethics Committee of Shiraz university of medicine, Shiraz, Iran University (Approval no.: IR.SUMS.REC.1403.064; Date: 8/25/2024).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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Declaration of Interests: The authors have no conflicts of interest to declare.

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References

1. Hashempour T, Dehghani B, Mousavi Z, et al. Evaluating drug resistant mutations to HCV NS3 protease inhibitors in Iranian Naïve patients. *Int J Pept Res Ther.* 2020;26(4):1699-1710. [CrossRef]
2. Dehghani B, Hashempour T, Hasanshahi Z, Moayedi J. Bioinformatics analysis of domain 1 of HCV-core protein: Iran. *Int J Pept Res Ther.* 2020;26(1):303-320. [CrossRef]
3. Negahdaripour M, Shafiekhani M, Moezzi SMI, et al. Administration of COVID-19 vaccines in immunocompromised patients. *Int Immunopharmacol.* 2021;99:108021. [CrossRef]
4. Sen P, Gupta L, Lilleker JB, et al. COVID-19 vaccination in autoimmune disease (COVAD) survey protocol. *Rheumatol Int.* 2022;42(1):23-29. [CrossRef]
5. Lee ARYB, Wong SY, Chai LYA, et al. Efficacy of Covid-19 vaccines in immunocompromised patients: systematic review and meta-analysis. *BMJ.* 2022;376:e068632. [CrossRef]
6. Galmiche S, Luong Nguyen LB, Tartour E, et al. Immunological and clinical efficacy of COVID-19 vaccines in immunocompromised populations: a systematic review. *Clin Microbiol Infect.* 2022;28(2):163-177. [CrossRef]
7. Westra J, van Assen S, Wilting KR, et al. Rituximab impairs immunoglobulin (Ig) M and IgG (subclass) responses after influenza vaccination in rheumatoid arthritis patients. *Clin Exp Immunol.* 2014;178(1):40-47. [CrossRef]
8. Beck CR, McKenzie BC, Hashim AB, Harris RC; University of Nottingham Influenza and the ImmunoCompromised (UNIIC) Study Group, Nguyen-Van-Tam JS. Influenza vaccination for immunocompromised patients: systematic review and meta-analysis by etiology. *J Infect Dis.* 2012;206(8):1250-1259. [CrossRef]
9. Li J, Liu HH, Yin XD, Li CC, Wang J. COVID-19 illness and autoimmune diseases: recent insights. *Inflamm Res.* 2021;70(4):407-428. [CrossRef]
10. Mortezagholi S, Rostamzadeh D, Alinejad M, Younesi V, Tabarsi P, Shabani M. Prevalence of

anti-SARS-CoV-2 specific Abs in health-care workers compared to general population during an early phase of the pandemic, Tehran-Iran. *Iran J Immunol*. 2021;18(1):82-92. [CrossRef]
11. Ammitzbøll C, Bartels LE, Bøgh Andersen J. et al. Impaired Ab response to the BNT162b2 messenger RNA coronavirus disease 2019 vaccine in patients with systemic lupus erythematosus and rheumatoid arthritis. *ACR Open Rheumatol*. 2021;3(9):622-628. [CrossRef]
12. Medeiros-Ribeiro AC, Aikawa NE, Saad CGS, et al. Immunogenicity and safety of the CoronaVac inactivated vaccine in patients with autoimmune rheumatic diseases: a phase 4 trial. *Nat Med*. 2021;27(10):1744-1751. [CrossRef]
13. Ferri C, Ursini F, Gragnani L, et al. Impaired immunogenicity to COVID-19 vaccines in autoimmune systemic diseases. High prevalence of non-response in different patients' subgroups. *J Autoimmun*. 2021;125:102744. [CrossRef]
14. Di Fusco M, Lin J, Vaghela S, et al. COVID-19 vaccine effectiveness among immunocompromised populations: a targeted literature review of real-world studies. *Expert Rev Vaccines*. 2022;21(4):435-451. [CrossRef]
15. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. *N Engl J Med*. 2021;384(15):1412-1423. [CrossRef]
16. Tenforde MW, Patel MM, Ginde AA, et al. Effectiveness of severe acute respiratory syndrome coronavirus 2 messenger RNA vaccines for preventing coronavirus disease 2019 hospitalizations in the United States. *Clin Infect Dis*. 2022;74(9):1515-1524. [CrossRef]
17. Furer V, Eviatar T, Zisman 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):1330-1338. [CrossRef]
18. Deepak P, Kim W, Paley MA, et al. Effect of immunosuppression on the immunogenicity of mRNA vaccines to SARS-CoV-2: a prospective cohort study. *Ann Intern Med*. 2021;174(11):1572-1585. [CrossRef]
19. Subesinghe S, Bechman K, Rutherford AI, Goldblatt D, Galloway JB. A systematic review and metaanalysis of antirheumatic drugs and vaccine immunogenicity in rheumatoid arthritis. *J Rheumatol*. 2018;45(6):733-744. [CrossRef]
20. Arad U, Tzadok S, Amir S, et al. The cellular immune response to influenza vaccination is preserved in rheumatoid arthritis patients treated with rituximab. *Vaccine*. 2011;29(8):1643-1648. [CrossRef]
21. D'Amelio R, Asero R, Cassatella MA, et al. Anti-COVID-19 vaccination in patients with autoimmune-autoinflammatory disorders and primary/secondary immunodeficiencies: the position of the task force on behalf of the Italian immunological societies. *Biomedicines*. 2021;9(9):1163. [CrossRef]
22. Munro C. Covid-19: 40% of patients with weakened immune system mount lower response to vaccines. *Br Med J Publ Group*. 2021;374:n2098. [CrossRef]
23. Azim Majumder MA, Razzaque MS. Repeated vaccination and 'vaccine exhaustion': relevance to the COVID-19 crisis. *Expert Rev Vaccines*. 2022;21(8):1011-1014. [CrossRef]
24. Zheng Y-Q, Li H-J, Chen L, Lin S-P. Immunogenicity of inactivated COVID-19 vaccine in patients with autoimmune inflammatory rheumatic diseases. *Sci Rep*. 2022;12(1):17955. [CrossRef]
25. Risk M, Hayek SS, Schiopu E, et al. COVID-19 vaccine effectiveness against omicron (B. 1.1. 529) variant infection and hospitalisation in patients taking immunosuppressive medications: a retrospective cohort study. *Lancet Rheumatol*. 2022;4(11):e775-e784. [CrossRef]
26. Petri M, Joyce D, Haag K, et al. Effect of systemic lupus erythematosus and immunosuppressive agents on COVID-19 vaccination Ab response. *Arthritis Care Res*. 2023;75(9):1878-1885. [CrossRef]
27. Boekel L, Kummer LY, van Dam KPJ, et al. Adverse events after first COVID-19 vaccination in patients with autoimmune diseases. *Lancet Rheumatol*. 2021;3(8):e542-e545. [CrossRef]
28. Sen P, Ravichandran N, Nune A, et al. COVID-19 vaccination-related adverse events among autoimmune disease patients: results from the COVAD study. *Rheumatology (Oxford)*. 2022;62(1):65-76. [CrossRef]
29. Hoffman T, Nissen K, Krambrich J, et al. Evaluation of a COVID-19 IgM and IgG rapid test; an efficient tool for assessment of past exposure to SARS-CoV-2. *Infect Ecol Epidemiol*. 2020;10(1):1754538. [CrossRef]