ACCEPTANCE, TOLERABILITY, AND EFFECT OF COVID-19 VACCINATION ON DISEASE ACTIVITY IN A COHORT OF EGYPTIAN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: REAL-LIFE EXPERIENCE

M. H. Abu-Zaid, H. M. Aly, A. Moshrif, R. A. Noor, N. El-Ghobashy

Rheumatology and Rehabilitation, Faculty of Medicine, Tanta University – Egypt
Rheumatology and Rehabilitation, Faculty of Medicine, Al-Azhar University – Cairo, Egypt
Rheumatology and Rehabilitation, Faculty of Medicine, Al-Azhar University Assiut Branch, Branch – Assiut, Egypt
Internal Medicine, Faculty of Medicine, Tanta University – Egypt
Rheumatology and Clinical Immunology, Cairo University – Egypt

Abstract. Objective: *To assess the tolerance and effects of COVID-19 vaccination in Egyptian patients with systemic lupus erythematosus (SLE), such as incident flare risk, based on the patient's perspective.* ***Methods:*** *SLE patients were included in this multicenter cross-sectional questionnaire-based analysis. Data included demographic and clinical features, prior COVID-19 infection, vaccine acceptability, type of vaccination, disease status before and after vaccination, and related side effects.* ***Results:*** *The total number of patients included was 230. Ages ranged from 18 to 64 years, disease duration from 1 to 15 years, and females were 92.6%. Only 31.7% of the study population were COVID-infected; the majority (70.7%) were treated at home, while 1.2% needed ICU. In contrast, 53% of our patients were vaccinated, and 47% were not vaccinated, primarily due to fear of side effects or disease flare. After the first dose of vaccination, 44.1% reported vaccine-related side effects, of which fatigue, fever, myalgia, as well as injection site reaction were the prevalent complications. The highest incidence of side effects was in AstraZeneca (78%), while the least was in Sinopharm (29.6%). 16.3% of vaccinated patients were COVID infected after vaccination, and 88.2% were treated at home. Only 14.6% of the vaccinated population experienced a lupus flare, primarily after the first dose, with no significant difference between the type of vaccine and lupus flares.* ***Conclusion:*** *The acceptance of COVID-19 vaccination among our lupus patients was neutral. The observed adverse effects were comparable to those reported by healthy individuals. Post-vaccination lupus flares were infrequent and unrelated to the vaccine type but rather to the pre-vaccination disease activity state.*

Key words: *lupus, COVID, vaccine, flare*

Introduction

Autoimmune and inflammatory rheumatic diseases (AIIRD) patients, especially systemic lupus erythematosus (SLE) cases, are at greater risk for adverse outcomes due to Corona virus-19 (COVID-19) [1].

Vaccination is a vital and efficient instrument for preventing infections in both AIIRD patients as well as normal people. In spite of specific recommendations, the rates of pneumococcal and influenza vaccination in the targeted population are below the recommended levels [2]. In order to promote vaccination uptake and improve awareness of patients, new plans and strategies are strongly needed. The aims of these plans are the explanation of the patient's autoimmune status and emphasizing the safety and efficacy of vaccines [3].

COVID-19 vaccinations are safe and effective and were made available for the first time in the USA on December 14 2020 [4]. Nevertheless, surveys on SLE cases as well as other AIIRD, have revealed vaccine hesitancy in up to 50% of patients, which can be attributed to concerns regarding potential disease flares, adverse effects, or shortage of knowledge among SLE patients [5].

In a prior international survey (1266 AIIRD patients) administrated prior to the availability of COVID-19 vaccination, only 54% indicated their willingness to receive the vaccination. Thirty-two percent of the participants were hesitant about receiving the vaccination; however, attitudes may have changed since then [5].

In an Italian survey of rheumatic disease patients administered during the first weeks of vaccine availability, 48% of SLE patients who responded to the survey indicated their willingness to get vaccinated [6]. This finding may be attributable to concerns peculiar to this population, especially rheumatic disease flares or diminished vaccine effectiveness due to concomitant immunosuppressive drugs [2].

There is a scarcity of data concerning COVID-19 vaccine safety in musculoskeletal and rheumatic disease cases [7], such as SLE, as SLE patients were excluded from vaccine trials [8].

Consequently, the primary objective of this study was to determine COVID-19 vaccine tolerance in Egyptian SLE patients, particularly incident flare risk, based on the patient's perspective.

Methods

Participants

Inclusion criteria: Lupus patients aged above 18 years who met any of the SLE classification criteria either the 1997 revised American College of Rheumatology classification criteria for SLE [9], Systemic lupus international collaboration clinic (SLICC) (10), as well as the EULAR-ACR 2019 classification criteria for SLE [11].

Exclusion criteria: Patients diagnosed with any rheumatic disease other than lupus, patients who received other vaccines, e.g., influenza vaccine within one month, and patients who were less than 18 years old.

Sample size: All patients fulfilling the eligibility criteria were enrolled in the study.

Study Design: This study was a multicenter cross-sectional study. An online survey was made utilizing the Google Docs application (available at https://docs.google.com/document/u/0/). It included 37 practice as well as experience questions dealing with the subsequent domains: patients' lupus clinical status and activity, demographics, and whether the patient had prior COVID-19 infection, as well as infection severity, if they get vaccinated or not. If they refused vaccination, they were asked about the cause of the refusal. If they were vaccinated, they were asked about the vaccination (type and the number of received doses), incidence and nature of post-vaccination side effects or incidence of the flare of disease after vaccination, and incidence as well as the course of COVID infection in SLE cases following COVID-19 vaccination.

The survey was administered in the Arabic version (see Supplementary Material) and pretested in five rheumatology centers in Egypt (Rheumatology & Rehabilitation Department Kasr Eleiny University Hospital, Rheumatology & Rehabilitation Department Azhar University Hospital, Rheumatology & Rehabilitation Department Assiut Branch of Azhar University Hospital, Rheumatology & Rehabilitation Department and Internal Medicine Department, Tanta University Hospital). Five consultant rheumatologists evaluated face validity and content. All co-authors accepted the final versions following three evaluations. The questionnaire was designed to be completed in 10 min. All lupus patients were invited to participate by directly contacting physicians or via WhatsApp. The survey was conducted for six months, between May and November of 2022.

Study outcomes

Primary outcome:

– The prevalence of acceptance of lupus patients to get COVID-19 vaccinations

– The prevalence of flare of SLE after COVID-19 vaccinations

Secondary outcomes:

– Incidence as well as the course of COVID infection in SLE patients after vaccination.

– Disease activity status in subjects prior to and following the vaccine.

Ethics approval and participation consent

This study compiles with the Declaration of Helsinki's ethical guidelines and adheres to the local ethical standards (the institution's ethics board approval No: 35766/9/22). All subjects provided informed electrical consent as per the local ethical committee. Patients' data was protected (every participant has a code number).

Statistical analysis

Data were statistically analyzed using SPSS version 20. Descriptive analysis of patients characteristics described numerically and by percentages data, and comparative analysis between groups were done using ANOVA and Student's t-test. The P value was considered significant at the level of ≤ 0.05.

Results

Our study included 230 lupus patients; 76.1% of our patients were between 25-54 years old, 18.3% between 18-24, and 6.4% between 55-64 years old. Disease duration was 6-15 years in 39.6%, 2-5 years in 32.2%, 1-2 years in 18.1%, and less than 1 year in 10.6%, with different periods in the remaining percentage. 92.6% of our patients were females, and 7.4% were males. Most participants (93%) were informed about the questionnaire by their physician. All patient characteristics are shown in Table 1.

The results revealed that 31.7% of the study population were COVID-infected, 61.7% denied having COVID infection, and the remaining population did not confirm their infection. Most COVID-infected patients (70.7%) were treated at home, 15.9% were

Table 1. Demographics and patient characteristics

Findings	N (%)
Age groups:	
18-24 y	42 (18.3%)
25-54 y	175 (76.1%)
55-64 y	13 (5.65%)
Gender:	
F	213 (92.6%)
M	17 (7.4%)
Disease duration:	
< 1 y	24 (10.6%)
1-2 y	41 (18.1%)
2-5 y	74 (32.2%)
> 5 y	91 (39.6%)
Disease manifestations:	
Oral ulcers	162 (70.4%)
Arthritis	205 (89.1%)
Pleurisy/Carditis	70 (30.4%)
Nephritis	119 (51.7%)
Photosensitivity	129 (56%)
CNS Lupus	6 (2.6%)
Malar rash	68 (29.6%)
Cutaneous lupus	21 (9.13%)
Anti-ds DNA positivity	184 (80%)
Hemolytic anemia	39 (17%)
Leucopenia; thrombocytopenia	156 (67.8%)
COVID infection before vaccination	
Infected	76 (31.7%)
Not infected	139 (61.7%)
Suspected	15 (6.6%)
Treatment received:	
steroid	225 (97.8%)
hydroxychloroquine	226 (98.3%)
Mycophenolate mofetil	29 (12.6%)
Azathioprine	199 (86.5%)

hospitalized without oxygen, 12.2% were hospitalized with oxygen need, and the remaining were ICU admitted. Concerning vaccination, 53% of our patients were immunized, while 43% were not, primarily out of fear of side effects or disease activation. In the 12 months prior to vaccination, 37% of the vaccinated population experienced disease activity, compared to 21.7% of the unvaccinated population. At the time of vaccination, disease activity was present in only 8% of patients, while 90.2% were not active. The most frequently administered vaccine was the inactivated COVID-19 vaccine manufactured by Sinopharm. Figure 1 depicts the available vaccines. 44.1% of patients who received the first dose of the vaccine experienced vaccine-related side effects, while 54.1% did not. The most common side effects included fatigue, fever, myalgia, and injection site reaction. 3.2% of patients experiencing side effects required hospitalization. Only 25.6% of the vaccinated population reported side effects after receiving the second dose. The most common side effects included fatigue, fever, myalgia, and injection site reaction. The incidence of side effects was lower than with the first vaccination dose.

Only 9% of the vaccinated population received the third dose of vaccine, which significantly reduced side effects, which occurred in only 5.6% of the population. After vaccination, 16.3% of the vaccinated population were infected with COVID, of which 88.2% were treated at home.

Table 2. Characteristics of lupus patients as regards vaccination

Finding	Number
Vaccination:	
Vaccinated	122 (53%)
Not vaccinated	108 (47%)
Disease activity before vaccination	
Active	25 (21.7%)
Not active	84 (73%)
Suspected	6 (5.3%)
Disease activity at the time of vaccination	
Not active	101 (90.2%)
Active	9 (8%)
Suspected	2 (2%)
Side effects after vaccination	
Fatigue	33
Fever	23
Myalgia arthralgia	22
Site injection reaction	21
Shoulder pain	17
Headache	15
Chills	14
Diarrhea	2
Side effects requiring doctor consultation	
Yes	28 (41.8%)
No	39 (58.2%)
Side effects requiring hospitalization	
Yes	2 (3.2%)
No	60 (96.8)
Vaccine booster doses	
Second dose	88 (83%)
Third dose	8 (9%)
COVID infection after vaccination	
Yes	14 (16.3%)
No	72 (83.7%)

The AstraZeneca vaccine had the highest incidence of vaccination-related side effects after the first and second doses (78% and 57%, respectively). There was a significant difference between vaccine types after the first dose but no significant difference concerning side effects after the second dose. While the incidence of side effects was lowest with the first and second doses of Sinopharm (29.6% and 12.0%, respectively) (Table 3).

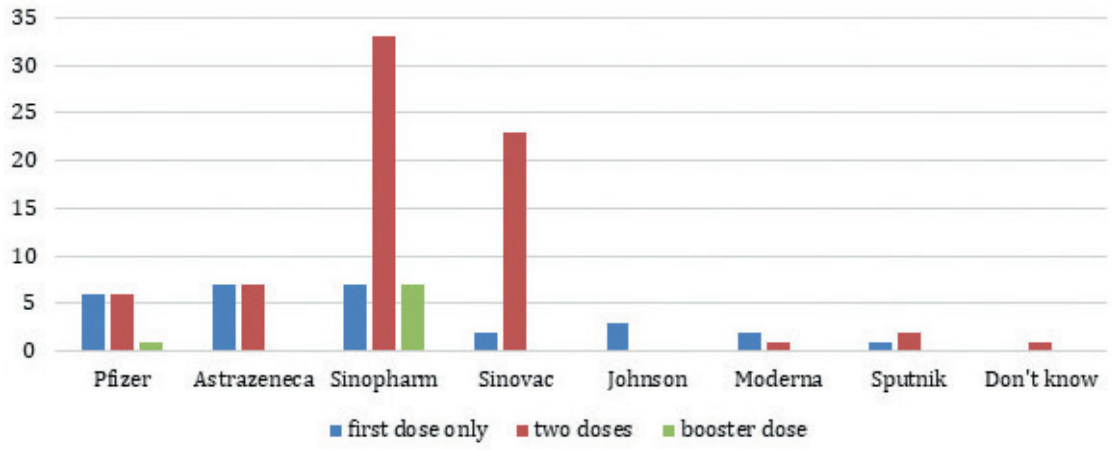


Fig. 1. Types of vaccines received and number of doses

Table 3. Comparison between the type of vaccine and side effects after first and second doses

	Pfizer (n = 10)	AstraZeneca (n = 14)	Sinopharm (n = 44)	Sinovac (n = 27)	Others (n = 7)	P value
	First dose					
Side effect						
No	3 (30.0%)	3 (21.4%)	25 (56.8%)	19 (70.4%)	3 (42.9%)	
Yes	7 (70.0%)	11 (78.6%)	19 (43.2%)	8 (29.6%)	4 (57.1%)	.020
	Second dose					
	(n = 5)	(N = 14)	(n = 37)	(n = 25)	N = 3)	
Yes	4 (80.0%)	3 (42.9%)	26 (70.3%)	22 (88.0%)	2 (66.7%)	
No	1 (20.0%)	4 (57.1%)	11 (29.7%)	3 (12.0%)	1 (33.3%)	.118

Others include Jonson, Moderna, Sputnik

There was no significant difference regarding post-vaccination side effects between patients with previous COVID-19 infection and those without (Table 4).

Table 4. Comparison between patients who had prior COVID-19 infection in side effects post-vaccination

	Prior Covid infection		
Side effects first dose	**No**	**Yes**	**P value**
No	29 (54.7%)	24 (49.0%)	
Yes	24 (45.3%)	25 (51.0%)	.562
Side effects second dose			
No	32 (82.1%)	25 (65.8%)	
Yes	7 (17.9%)	13 (34.2%)	.104

Only 14.6% of the vaccinated population experienced lupus activity, primarily after the first dose Table [6], with variable manifestations of disease activity as shown in Table 5 – 54.2% required consultation with the treating physician, and 46.4% required treatment modification. In addition, there was no significant difference between vaccine types and the incidence of a post-vaccination lupus flare, whereas the incidence of a post-vaccination lupus flare was more significant in those with a pre-vaccination disease flare (Table 6).

Table 5. Lupus Activity after the vaccine

Character	number
Lupus activity after vaccination	
Yes	12 (14.6%)
No	66 (80.5%)
Suspected	4 (4.9%)
Manifestations of lupus activity after vaccine	
Arthritis	9
Fever	8
Leucopenia or thrombocytopenia	8
Nephritis	4
Pleurisy	4
Skin manifestations	4
Cerebritis	1
Manifestations needed doctor consultation	
Yes	13 (54.2%)
No	11 (45.8%)
Activity needed treatment change	
Yes	13 (46.4%)
No	15 (63.6%)

Table 6. Comparison between SLE patients with and without post-vaccination flare as regards the type of vaccine and pre-vaccination flare

	Pfizer (n = 10)	AstraZeneca (n = 14)	Sinopham (n = 44)	Sinovac (n = 27)	Others (n = 7)	P value
	Flare post-vaccine first dose					
Flare post vaccine						
No	9 (90%)	9 (64.3%)	39 (88.6%)	25 (92.6%)	6 (85.7%)	
Yes	1 (10%)	5 (35.7%)	5 (11.4%)	2 (7.4%)	1 (14.3%)	.169
	Flare post-vaccine second dose					
Flare post vaccine						
No	5 (100%)	5 (71.4%)	32 (86.5%)	23 (92.0%)	3 (100%)	
Yes	0 (0%)	2 (28.6%)	5 (13.5%)	2 (8%)	0 (0) %	.319
Comparison between SLE patients with and without flare as regards pre-vaccination flare						
	flare pre-COVID vaccine					
flare post Covid vaccine	No		Yes		P-Value	
No	74 (93.7%)		14 (60.9%)			
	5 (6.3%)		9 (39.1%)		<.001	

Discussion

Since the announcement of COVID-19 as a pandemic in March 2020, more than 769 million confirmed cases and more than 6,955,141 deaths were reported, according to WHO health emergency dashboard August 2023 [12]. Autoimmune rheumatic diseases (AIRDs), including SLE, are more susceptible to Covid-19 poor outcomes, more hospitalizations, and more deaths due to prolonged steroid and immune-suppressant use, which can also delay viral clearance and increase the incidence of bacterial infections [13-15]. However, some studies showed better AIRDs outcomes due to early cytokine storm suppression by the same drugs [16]. The American College of Rheumatology (ACR) [17] and the European Alliance of Associations for Rheumatology (EULAR) recommend COVID-19 vaccines for people with AIRD, including SLE [18]. Some research has been done to study COVID-19 vaccination in the context of lupus patients, including patients' attitudes towards the vaccine, the efficacy of the vaccine in the prevention of COVID-19 infection, its safety profile and side effects, the effect of the vaccine on lupus activity [14, 19-21]. This study examines the acceptance of COVID-19 vaccination among SLE patients, adverse reactions, as well as its effect on disease activity in a cohort of Egyptian lupus patients due to the paucity of research on lupus and the COVID-19 vaccination in the Middle East.

Our multi-centric cross-sectional investigation was conducted on 230 lupus patients whose disease duration ranged from less than one year to five years. Most of our patients were female; approximately 31% confirmed COVID-19 infection prior to vaccination, 60% [22] were vaccinated, while 47% were apprehensive of the vaccine's adverse effects as well as efficacy and did not receive it. This finding is comparable to other studies conducted in South America and Europe, where 54% of the participants agreed to be vaccinated, and 30% were unsure [22]. In a Chinese study, willingness was 30%, but following physician recommendations, it rose to 90% [23]. In contrast, most other studies demonstrated positive attitudes of lupus patients towards the COVID-19 vaccine, reaching 76-80% [24, 25].

Among the 53% of those who were vaccinated in our study, inactivated COVID-19 vaccines "Sinopharm and Sinovac" were the most received, followed by ChAdOx1 nCoV-19 [Oxford-AstraZeneca], then MRNA vaccines BNT162b2 [Pfizer-BioNTech] and mRNA-1273 [Moderna], small percent received Sputnik vaccine, and some patient did not know the type of vaccine they received. Fatigue was the most frequently reported adverse effect, followed by fever, myalgia, arthralgia, injection site reaction, shoulder pain, headache, cold, and diarrhea. The majority of these adverse effects were self-limiting, and only 2% necessitated hospitalization. 88% of lupus patients who received the vaccine received a second injection, while only 14% received a third dose. The Sinopharm vaccine had the fewest side effects, whereas patients who received the AstraZeneca vaccine reported a significant side effect after the first dose compared to other types of vaccines, but there was no significant difference between the types of vaccines after the

second dose. Regarding post-vaccination adverse effects, there were no substantial differences between patients who had previously contacted COVID-19 and those who had not. Although we did not include normal population in our survey, we compared our findings to those of prior investigations, the majority of studies reported mild side effects regardless of vaccine frequency after the second dose compared to the first [22, 26]. The variation and incidence of adverse effects of the COVID-19 vaccine in the general population are comparable to those observed in SLE patients. Some of them reported adverse effects in 50% to 90% of patients [4] and others in 30% of general populations [27]. Local injection and systemic adverse reactions such as right bundle branch block, fatigue, fever, myalgia, headache, sinus and dyspnea tachycardia, nausea, premature ventricular contractions, and chills may occur [19, 28-30]. Those who received the Sinopharm vaccine demonstrated more side effects following the first dose, and those with prior comorbidities experienced more complications, whereas those who received the Pfizer-BioNTech vaccine demonstrated more side effects following the second dose especially in previously infected persons [31]. The majority of the side effects in general populations were mild. Nevertheless, some severe complications occurred with Oxford-AstraZeneca and BNT162b2 [Pfizer-BioNTech] and mRNA-1273 [Moderna] mRNA vaccination, including cardiovascular effects [28, 32]. Also similar results were reported in some Egyptian studies [33, 34].

Regarding the effectiveness of the vaccine, only 14% of our vaccinated lupus patients were re-infected with the COVID-19 virus. In a large study involving 3245 patients with SLE and 1,755,034 non-SLE individuals, Xiaofeng Jiang and his colleagues found that the risks of COVID-19 infection as well as its severe sequelae, such as hospitalization and death, were considerably greater in lupus than in the general population prior to the administration of the COVID-19 vaccine. Nonetheless, after COVID-19 vaccination, there were no substantial differences in the risk of COVID-19 activation between the two groups, highlighting the significance of vaccination for those with SLE [35]. Other Egyptian study was conducted on different rheumatic diseases including lupus and reported vaccine efficacy [36]. However, a number of studies have shown that lupus patients have a diminished antibody response compared to healthy controls. This finding is typically due to utilizing steroids and immunosuppressive agents in lupus cases, which delay the immune response following vaccination [37, 38].

Regarding lupus disease activity after vaccination, it was subjectively recorded in 12% of our patients, with the following manifestations: arthritis, fever, leucopenia, thrombocytopenia, nephritis, pleurisy, cutaneous manifestations, and cerebritis. Moreover, 13% of them required physician consultations and treatment modifications. There was no significant difference between vaccine types and the incidence of post-vaccination lupus flare; however, the incidence of post-vaccination lupus flare was more significant in those with pre-vaccination disease flare.

A significant VACULOP study [22] was conducted on 696 lupus cases to determine COVID-19 vaccine tolerance in SLE cases, as well as the risk of incident flares from the patients' perspective. Pfizer-BioNTech (57% of participants), Sinovac (22%), AstraZeneca (10% of subjects), and Moderna (8% of subjects) were the most prevalent vaccines in the study. Only 21 (3%) of 696 patients experienced a medically confirmed SLE flare characterized by prevalent fatigue and musculoskeletal symptoms. In 15 (71%) of 21 cases, these flares caused an alteration in SLE treatment, and in four (19%) of these cases, hospitalization was required. Experiencing a flare in the year prior to vaccination has been linked to an elevated SLE flare risk following COVID-19 vaccination, whereas there was no direct connection between obtaining lupus flare and m RNA vaccines, comparable to our findings. In contrast, this contradicts the theory that stimulation of toll-like receptors by nucleic acids could raise lupus flare risks [22]. The primary limitation of both the VACULOP study and our study is the subjective nature of lupus flare reports, which is a result of the difficulty in obtaining medical confirmation during the survey. Other studies, such as those conducted by Ho So et al., measured SLE activity after vaccination and found no significant change in the SLEDAI score, anti-dsDNA titer, or proteinuria following COVID-19 vaccination. In fact, a more significant number of patients experienced numerical improvement than decline [37].

Conclusion

The attitude of our Egyptian lupus patients toward COVID-19 vaccination is neutral, and the most frequently administered vaccines were inactivated vaccines manufactured by "Sinopharm & Sinovac" and Oxford-AstraZeneca. The side effects are typically mild and comparable to those reported in the general population, and they are unrelated to the type of vaccine received or previous COVID-19 in-

fection. Post-vaccination lupus flares are reported infrequently and are not related to the type of vaccine but rather to the pre-vaccination state of lupus disease activity.

Declarations:

Conflict of interest:

Disclosures: None.

All authors have no conflict of interest to declare

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments: We would like to acknowledge Samar Ali Abd Elghany, Ghada Abdelaal Shoaeeb, and Eman Ahmed Basiouny for their great help in data collection.

Contribution: MHA & NE conceived the idea for the study and in conjunction with HMA designed the study and wrote the analysis plan. AM, RAA, & NE undertook data analysis and interpretation, supported MHA. The manuscript was written by HMA and NE, with contribution from RAA. All authors contributed in the study methodology, analysis, and interpretation of the data and outcomes as well as the manuscript writing, reading, and approval of the final version.

Compliance with ethical standards: All steps are performed according to the revised ethical principles of the Declaration of Helsinki in 2000, and local ethical and methodological protocols for approval of the study were followed.

Ethics approval and consent to participate: This study compiles with the Declaration of Helsinki's ethical guidelines and adheres to the local ethical standards (the institution's ethics board approval No: 35766/9/22). All subjects provided informed electrical consent as per the local ethical committee. Patients' data was protected (every participant has a code number).

Consent for publication: The final manuscript has been seen and approved by all the authors, and they have obtained the required ethical approvals, and they have given the necessary attention to ensure the integrity of the work and agree to publish this work.

Availability of data and materials: Data will be available when reasonable request.

References

1. D'Silva KM, Jorge A, Cohen A et al. COVID-19 outcomes in patients with systemic autoimmune rheumatic diseases compared to the general population: a US multicenter, comparative cohort study. Arthritis & rheumatology. 2021;73(6):914-20.
2. Figueroa-Parra G, Esquivel-Valerio JA, Santoyo-Fexas L et al. Knowledge and attitudes about influenza vaccination in rheumatic diseases patients. Human Vaccines & Immunotherapeutics. 2021;17(5):1420-5.
3. Moraliyska R, Georgiev T, Bogdanova-Petrova S, Shivacheva T. Adoption rates of recommended vaccines and influencing factors among patients with inflammatory arthritis: a patient survey. Rheumatology International. 2023:1-8.
4. Baden LR, El Sahly HM, Essink B et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. New England journal of medicine. 2021;384(5):403-16.
5. Felten R, Dubois M, Ugarte-Gil MF et al. Vaccination against COVID-19: expectations and concerns of patients with autoimmune and rheumatic diseases. The Lancet Rheumatology. 2021;3(4):e243-e5.
6. Priori R, Pellegrino G, Colafrancesco S et al. SARS-CoV-2 vaccine hesitancy among patients with rheumatic and musculoskeletal diseases: a message for rheumatologists. Annals of the rheumatic diseases. 2021;80(7):953-4.
7. Geisen UM, Berner DK, Tran F 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. Annals of the rheumatic diseases. 2021;80(10):1306-11.
8. Ramasamy MN, Minassian AM, Ewer KJ et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. The Lancet. 2020;396(10267):1979-93.
9. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis and rheumatism. 1997;40(9):1725.
10. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis & Rheumatism. 2012;64(8):2677-86.
11. Aringer M, Costenbader K, Daikh D et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Arthritis & rheumatology. 2019;71(9):1400-12.
12. Organization Wh. WHO Corona virus dashboard 2023 [updated 16 Agust 2023. Available from: https://covid19.who.int/.
13. Ahmed S, Zimba O, Gasparyan AY. COVID-19 and the clinical course of rheumatic manifestations. Clinical Rheumatology. 2021:1-9.
14. Mehta P, Gasparyan AY, Zimba O, Kitas GD. Systemic lupus erythematosus in the light of the COVID-19 pandemic: infection, vaccination, and impact on disease management. Clinical Rheumatology. 2022;41(9):2893-910.
15. Gianfrancesco M, Hyrich KL, Al-Adely S 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. Annals of the rheumatic diseases. 2020;79(7):859-66.
16. Tang K-T, Hsu B-C, Chen D-Y. Autoimmune and Rheumatic Manifestations Associated With COVID-19 in Adults: An Updated Systematic Review. Frontiers in immunology. 2021;12:628.
17. Curtis JR, Johnson SR, Anthony DD et al. American College of Rheumatology guidance for COVID-19 vaccination in patients with rheumatic and musculoskeletal diseases: version 3. Arthritis & Rheumatology. 2021;73(10):e60-e75.
18. Landewé RB, Kroon FP, Alunno Aet 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. Annals of the rheumatic diseases. 2022;81(12):1628-39.
19. Dhamanti I, Suwantika AA, Adlia A et al. Adverse Reactions of COVID-19 Vaccines: A Scoping Review of Observational Studies. International Journal of General Medicine. 2023:609-18.
20. Tang W, Gartshteyn Y, Ricker E et al. The use of COVID-19 vaccines in patients with SLE. Current Rheumatology Reports. 2021;23:1-12.
21. González-Meléndez A, Báez-Negrón L, Ríos-Rivera R et al. Short-and mid-term outcomes in systemic lupus erythema-

tosus patients presenting with disease exacerbation after SARS-CoV-2 mRNA vaccination: A cohort study from Puerto Rico. Lupus. 2023:09612033231151898.
22. Felten R, Kawka L, Dubois M et al. Tolerance of COVID-19 vaccination in patients with systemic lupus erythematosus: the international VACOLUP study. The Lancet Rheumatology. 2021;3(9):e613-e5.
23. Chen J, Cai W, Liu Tet al. The COVID-19 vaccine: Attitudes and vaccination in patients with autoimmune inflammatory rheumatic diseases. Rheumatology & Autoimmunity. 2022;2(02):82-91.
24. Rezende RPV, Braz AS, Guimarães MFB et al. Characteristics associated with COVID-19 vaccine hesitancy: a nationwide survey of 1000 patients with immune-mediated inflammatory diseases. Vaccine. 2021;39(44):6454-9.
25. Sattui SE, Liew JW, Kennedy K et al. Early experience of COVID-19 vaccination in adults with systemic rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance Vaccine Survey. RMD open. 2021;7(3):e001814.
26. Bartels LE, Ammitzbøll C, Andersen JB et al. Local and systemic reactogenicity of COVID-19 vaccine BNT162b2 in patients with systemic lupus erythematosus and rheumatoid arthritis. Rheumatology international. 2021;41(11):1925-31.
27. Polack FP, Thomas SJ, Kitchin N et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. New England journal of medicine. 2020;383(27):2603-15.
28. Oh TH, Woo SH, Hong S et al. Clinical features of patients presenting to the emergency department with cardiovascular adverse reactions after COVID-19 mRNA vaccination. Journal of Korean medical science. 2022;37(9).
29. Menni C, Klaser K, May A et al. Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study. The Lancet Infectious Diseases. 2021;21(7):939-49.
30. Bsoul EA, Loomer PM. COVID-19 vaccination experience among United States dental professionals and students: Safety, confidence, concerns, and side effects. PloS one. 2022;17(2):e0264323.
31. Ganesan S, Al Ketbi LMB, Al Kaabi N et al. Vaccine side effects following COVID-19 vaccination among the residents of the UAE – An Observational study. Frontiers in public health. 2022;10.
32. Perrotta A, Biondi-Zoccai G, Saade W et al. A snapshot global survey on side effects of COVID-19 vaccines among healthcare professionals and armed forces with a focus on headache. Panminerva Medica. 2021;63(3):324-31.
33. Orebi HA, Emara HE, Alhindi AA et al. Perceptions and experiences of COVID-19 vaccines' side effects among healthcare workers at an Egyptian University Hospital: a cross-sectional study. Tropical medicine and health. 2022;50(1):37.
34. Elgendy MO, El-Gendy AO, Mahmoud S et al. Side effects and efficacy of COVID-19 vaccines among the Egyptian population. Vaccines. 2022;10(1):109.
35. Jiang X, Sparks J, Wallace Z et al. Risk of COVID-19 among unvaccinated and vaccinated patients with systemic lupus erythematosus: a general population study. RMD open. 2023;9(1):e002839.
36. Aboud FM, Hussein RS, El Bably MM, Hassan RM. COVID-19 Vaccine in egyptian patients with systemic lupus erythematosus, rheumatoid arthritis and other rheumatic diseases. Ain Shams Medical Journal. 2023;74(1):21-32.
37. So H, Li T, Chan V et al. Immunogenicity and safety of inactivated and mRNA COVID-19 vaccines in patients with systemic lupus erythematosus. Therapeutic advances in musculoskeletal disease. 2022;14:1759720X221089586.
38. Pugès M, Biscay P, Barnetche T et al. Immunogenicity and impact on disease activity of influenza and pneumococcal vaccines in systemic lupus erythematosus: a systematic literature review and meta-analysis. Rheumatology. 2016;55(9):1664-72.

Submitted: 30.10.2023

✉ *Correspondence address:*
Assoc. Prof. Hany Mohamed Aly
Rheumatology and Rehabilitation Department
Al-Azhar Faculty of Medicine
El-Mokhaam eldayem St
31527 Nasr City, Cairo, EGYPT
mobile: +201007796825
e-mail: hanyaly79@azhar.edu.eg
ORCID; ORCID; https://orcid.org/0000-00-1-5024-2516