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COVID-19 vaccine safety during pregnancy in women with systemic lupus erythematosus

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ABSTRACT

COVID-19 vaccination has been shown to be safe in patients with systemic lupus erythematosus (SLE), but data on vaccine-associated adverse events (AEs) during the antenatal and lactation period are scarce or lacking. We investigated COVID-19 vaccination-related AEs in pregnant SLE patients from the COVAD study, a global esurvey involving 157 collaborators from 106 countries. A total of 9201 complete responses were extracted. Among 6787 (73.8%) women, we identified 70 (1.1%) who were exposed to at least one COVID-19 vaccine dose during pregnancy, 11 with SLE. Delayed onset (>7 days) vaccine-related AEs were triangulated with disease activity, treatment changes due to flare after vaccination, and COVID-19 infections in vaccinated pregnant women. Health-related quality of life and physical function was recorded using PROMIS. Age of patients ranged from 28 to 39 years; 5/11 women were of Asian origin. None of these patients reported major vaccine AEs or change in the status of their autoimmune disease. Although minor AEs were common, they did not impair daily functioning, and the symptoms resolved after a median of 3 (IQR: 2.5–5.0) days. All patients reported good to excellent health status. No adverse pregnancy outcomes were reported. Importantly, none of the patients reported thrombotic events post-vaccination, which provides reassurance in a patient population with a high risk for cardiovascular comorbidity and thrombosis, especially in the presence of antiphospholipid antibodies or the antiphospholipid syndrome, a considerable portion of SLE patients. Our findings provide reassurance and can contribute to informed decisions regarding vaccination in patients with SLE and high-risk pregnancies due to their background autoimmune disease. The risk/benefit ratio of COVID-19 vaccination appears favourable, with vaccines both providing passive immunisation to the fetus and active immunisation to the mother with no signals of exacerbation of the mother's autoimmune disease.

Vaccinations comprise a part of the antenatal care of pregnant women, including patients with systemic lupus erythematosus (SLE) who are at increased risk of adverse pregnancy outcomes (APOs) [1]. While COVID-19 vaccination has been shown to be safe in patients with SLE [2], data on vaccine-associated adverse events (AEs) during the antenatal and lactation period are scarce or lacking [3–5]. We herein investigated the association between COVID-19 vaccination and AEs in pregnant SLE patients from the COVID-19 Vaccination in Autoimmune Diseases (COVAD) 2 study.

The COVAD 2 is a global e-survey involving 157 collaborators from 106 countries [6], that has gathered nearly 20,000 responses. Ethical approval for the COVAD study was obtained from the Institutional Ethics Committee of the Sanjay Gandhi Postgraduate Institute of Medical Sciences, Raebareli Road, Lucknow, 226014. A total of 9201 complete responses were extracted on June 21st, 2022; among respondents, 6787 (73.8%) were women. We identified 70 (1.1%) women who were exposed to at least one COVID-19 vaccine dose during pregnancy, among those 11 with SLE (Supplementary Fig. S1).

Delayed onset (>7 days) vaccine-related AEs were extracted and triangulated with disease activity, treatment changes due to flare after vaccination, and COVID-19 infections in vaccinated pregnant women with SLE. Additionally, information on health-related quality of life and physical function was recorded using PROMIS at the time of survey completion.

Characteristics of the patients are depicted in Table 1. Age ranged from 28 to 39 years; 5/11 women were of Asian origin. None of these patients reported major vaccine AEs, including four patients with self-reported active SLE prior to the vaccination. None of them reported any change in the status of their autoimmune disease, and no hospitalisation or special treatment was recorded. Six women experienced minor vaccine AEs; two of them had active disease prior to vaccination. Four patients reported COVID-19 infection; two of them while they were pregnant and post-vaccination and two prior to pregnancy and vaccination. All four patients experienced symptoms of their disease, but no overt SLE flare was reported. At the time of survey completion, all patients reported their general health as being good to excellent in all aspects evaluated. Importantly, no APOs were reported.

It is worth noting that none of the patients reported thrombotic events post-vaccination, which provides some reassurance regarding COVID-19 vaccination in a patient population with a high risk for cardiovascular comorbidity and thrombosis, especially in the presence of antiphospholipid antibodies or in patients diagnosed with the antiphospholipid syndrome, a considerable portion within SLE populations [7]. Moreover, it was reassuring to note an absence of association between experienced vaccine AEs and active disease prior to vaccination. Although minor AEs were common, they did not impair daily functioning, and the symptoms resolved in all patients after a median of 3 (IQR: 2.5–5.0) days.

Our report adds relevant evidence concerning the sensitive issue of COVID-19 vaccine AEs and flares in SLE patients during the antenatal

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Table 1
Characteristics of 11 patients with SLE who received COVID-19 vaccination during pregnancy.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11
Age (years)	32	33	31	28	30	32	31	33	31	32	39
Country	Costa Rica	Dominican Republic	India	Nigeria	Philippines	Taiwan	Thailand	Thailand	Thailand	United Kingdom	Venezuela
Ethnicity	Hispanic	Hispanic	Indian	African (Black)	Asian	Caucasian (White)	Asian	Asian	Asian	Caucasian (White)	Mixed
Comorbidities	Migraine, HA, ITP	Eosinophilic fasciitis	Tuberculosis	None	None	None	HA, ITP	None	None	None	None
Date of delivery	26 Nov 2021	22 Mar 2022	20 Aug 2022	3 Feb 2022	4 Jan 2022	25 Oct 2021	10 Apr 2022	16 Feb 2022	23 Mar 2022	5 Mar 2022	15 Apr 2022
Vaccine doses, type, timeline (see also Fig. 1)	3 doses 6 Jul 2021: Pf; 27 Jul 2021: Pf; 28 Jan 2022: Pf	3 doses 11 May 2021: Sino; 8 Jun 2021: Sino; 8 Jul 2021: Sino	2 doses 26 May 2021: Covi; 20 Aug 2022: Covi	2 doses 12 Oct 2021: OxAZ; 23 Nov 2021: OxAZ	3 doses 4 Oct 2021: OxAZ; 4 Nov 2021: OxAZ; 11 Mar 2022: Pf	2 doses 1 Aug 2021; 1 Sep 2021; vaccine types not specified	3 doses 2 Jul 2021: OxAZ; 24 Sep 2021: OxAZ; 13 Jan 2022: Pf	3 doses 18 Aug 2021: Pf; 9 Sep 2021: Pf; 22 Apr 2022: Pf	3 doses 4 Aug 2021: Sino; 25 Aug 2021: Sino; 8 Jan 2022: Mo	4 doses 1 Feb 2021: Pf; 1 May 2021: Pf; 1 Nov 2021: Pf; 22 Mar 2022: Mo	2 doses 20 Aug 2021: Sp; 9 Sep 2021: Sp
Minor AE	No	Yes, after the 3rd dose: minor symptoms with no further clarification	No	No	Yes, after all doses: injection site (arm) pain and soreness, fever, chills, headache, fatigue, joint pains	No	Yes, after all doses: minor symptoms with no further clarification	Yes: minor symptoms with no further clarification	Yes: minor symptoms with no further clarification	Yes, after all doses: injection site (arm) pain and soreness, fever	No
Major AE	No	No	No	No	No	No	No	No	No	No	No
Hospitalisation due to AEs	No	No	No	No	No	No	No	No	No	No	No
Disease activity prior to vaccination	Inactive disease	Unable to judge	Stable and manageable disease	Unable to judge	Inactive disease	Inactive disease	Stable and manageable disease	Stable and manageable disease	Inactive disease	Inactive disease	Stable and manageable disease
Treatment until vaccination	HCQ; no GCs	HCQ; AZA; no GCs	HCQ; SSZ; no GCs	HCQ; prednisone eq. <10 mg/day	HCQ; no GCs	HCQ; prednisone eq. <10 mg/day	HCQ; no GCs	HCQ; AZA; prednisone eq. <10 mg/day	HCQ; no GCs	HCQ; CYS-A; no GCs	HCQ; MTX; prednisone eq. <10 mg/day
Disease activity after vaccination	No change in SLE status	No change in SLE status	No change in SLE status	No change in SLE status	No change in SLE status	No change in SLE status	No change in SLE status	No change in SLE status	No change in SLE status	No change in SLE status	No change in SLE status
Treatment changes after vaccination	None	None	None	None	None	None	None	None	None	None	None
COVID positive test (date, symptoms, need for special treatments, days needed to resolve)	No	Yes, once: 4 Jan 2022 (a)	No	No	No	No	Yes, once: 23 Mar 2021 (b)	No	Yes, once: 3 Mar 2022 (c)	No	Yes, once: 5 Apr 2021 (d)
Test for anti-SARS-CoV-2 antibodies	Not done	Yes 2 Feb 2022: (+)	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done

(*continued on next page*)

Table 1 (*continued*)

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11
Health status											
General health	Excellent	Good	Very good	Excellent	Excellent	Very good	Very good	Very good	Good	Very good	Good
Quality of life	Excellent	Excellent	Very good	Excellent	Excellent	Good	Very good	Excellent	Very good	Very good	Good
Physical health	Very good	Good	Very good	Very good	Excellent	Very good	Very good	Very good	Good	Very good	Good
Mental health	Excellent	Excellent	Very good	Good	Very good	Good	Very good	Excellent	Very good	Very good	Good
Satisfaction in social activities	Excellent	Excellent	Very good	Very good	Very good	Good	Very good	Excellent	Very good	Excellent	Good
Ability to perform social activities	Excellent	Good	Very good	Good	Excellent	Good	Very good	Excellent	Excellent	Very good	Excellent
During the seven days before the survey											
Emotional problems	Never	Rarely	Rarely	Rarely	Rarely	Sometimes	Rarely	Never	Never	Rarely	Sometimes
Fatigue	Mild	Mild	Mild	Mild	Mild	Mild	None	Mild	None	Mild	Mild
VAS pain	1	1	0	3	1	0	0	0	0	2	0

AZA: azathioprine; Covishield (Serum Institute of India); CYS-A: cyclosporine A; GC: glucocorticoid; HA: haemolytic anaemia; HCQ: hydroxychloroquine; ILD: interstitial lung disease; ITP: idiopathic thrombocytopenic purpura; MTX: methotrexate; Mo: Moderna; OxAZ: Oxford/Astra Zeneca; Pf: Pfizer-BioNTech; Sino: Sinovac-CoronaVac; Sp: Sputnik; SSZ: sulfasalazine; VAS: Visual Analogic Scale (0−10).

(a) Fever, muscles aches, cough, loss of smell, loss of taste, congestion, throat pain/scratchiness. No hospitalisation. No special treatments. Symptoms lasted for 12 days. SLE did not flare up after COVID-19 infection.

(b) Fever, loss of smell, loss of taste, running nose, congestion, throat pain/scratchiness. No hospitalisation. No special treatments. Symptoms lasted for 5 days. SLE did not flare up after COVID-19 infection.

(c) Fever, cough, running nose, congestion. No hospitalisation. No special treatments. Symptoms lasted for 4 days. Reported uncertainty regarding whether SLE flared up after COVID-19 infection.

(d) Fever, cough, fatigue, difficulty in breathing or shortness of breath, loss of smell, loss of taste, diarrhoea. No hospitalisation. No special treatments. SLE did not flare up after COVID-19 infection.

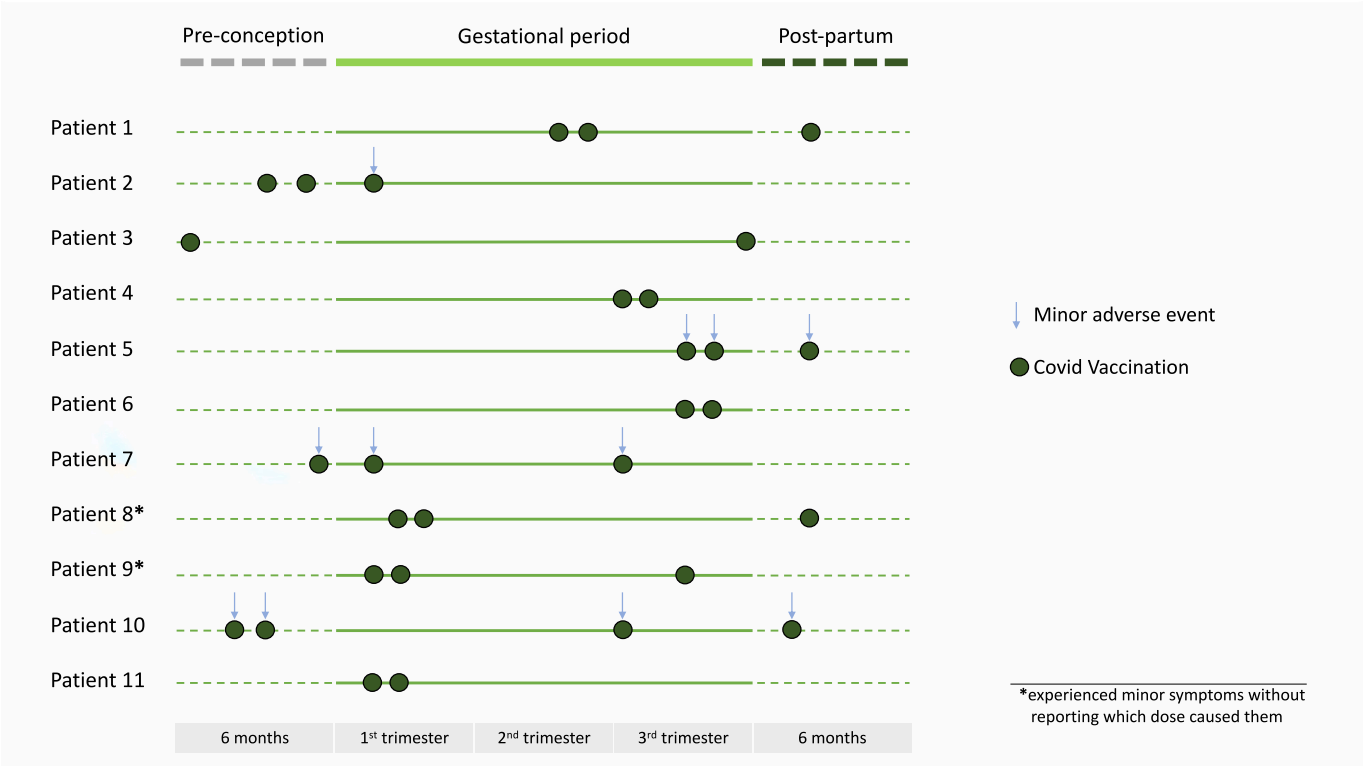

Fig. 1. Timeline showing COVID-19 vaccination and vaccination-related minor adverse events in relation to gestational and post-partum periods in eleven pregnant/lactating women with systemic lupus erythematosus.

and lactation period. Despite the small sample size, the findings provide some reassurance and can contribute to informed decisions regarding vaccination in patients with SLE and high-risk pregnancies due to their background autoimmune disease. Based on the present data, the risk/benefit ratio of COVID-19 vaccination appears favourable, with vaccines both providing passive immunisation to the fetus and active immunisation to the mother with no signals of exacerbation of the mother's autoimmune disease.

This study was not designed to ascertain causality. Further exploration in long-term prospective studies exploring AEs in the gestational and post-partum periods is necessary. Pregnant women with SLE who receive COVID-19 vaccines should be encouraged to report AEs. Alongside, it is crucial to be vigilant to widespread misinformation regarding the safety of COVID-19 vaccination in this group of patients.

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CRediT authorship contribution statement

Nefeli Giannopoulou: Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing. **Latika Gupta:** Conceptualization, Data curation, Investigation, Methodology, Software, Validation, Writing – review & editing. **Laura Andreoli:** Conceptualization, Data curation, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing. **Daniele Lini:** Data curation, Formal analysis, Investigation, Methodology, Validation, Writing – review & editing. **Elena Nikiphorou:** Conceptualization, Data curation, Investigation, Methodology, Validation, Writing – review & editing. **Rohit Aggarwal:** Data curation, Investigation, Methodology, Software, Validation, Writing – review & editing. **Vikas Agarwal:** Data curation, Investigation, Methodology, Software, Validation, Writing – review & editing. **Ioannis Parodis:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Validation, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

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Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.autrev.2023.103292.

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