Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2023i1.191
*Biol. Clin. Sci. Res. J., Volume, **2023**: 191*
Original Research Article

ANTIBODY RESPONSE TO THE COVID-19 VACCINE AMONG PREGNANT WOMEN: A PROSPECTIVE STUDY

ZAHRA SS[1*], DARS S[2], KUMARI S[3], SAHAR B[4], WAHID A[5], EJAZ ST[5]

[1]*Department of Gynecology, Bahawalpur Medical & Dental College & Hospital Bahawalpur, Pakistan*
[2]*Department of Gynecology, Liaquat University of Medical & Health Sciences (LUMHS) Jamshoro, Pakistan.*
[3]*Department of Gynecology Khadmat Khaliq Foundation Medical Complex Hyderabad, Pakistan.*
[4]*Department of Gynecology, Buch International Hospital, Multan, Pakistan.*
[5]*Department of Gynecology, DG Khan Medical College & Hospital, Pakistan*
**Correspondence author email address:* syedasahar108@yahoo.com

(Received, 17th October 2022, Revised 25th January 2023, Published 28th January 2023)

Abstract: *The study's objective was to investigate the antibody responses and fetal and maternal adverse effects of the Sinopharm vaccine. A prospective study was conducted in The Gynaecology Department of LUMHS Hospital Jamshoro, Hyderabad, Multan and DG Khan from January 2021 to January 2022. A total of 90 women were included in the study who were administered Sinopharm. 3/90 (3.3%) women received shots in 1st trimester, 56/90 (62%) in 2nd trimester and 31/90 (34%) in 3rd trimester. ELISA measured SARS-CoV-2 receptor binding domain (RBD) specific total antibodies and ACE2 blocking antibodies. The adverse effects on the mother and fetus were evaluated after the delivery. The vaccine administration showed no harmful effects or pregnancy-related complications like congenital anomalies, miscarriage, preterm delivery, thrombotic events, fetal death, or hypertensive disorders. SARS-CoV-2 specific total antibodies were found in 57/90 (63%) women at the time of recruitment (when receiving 1st dose); thus, they were considered to be previously infected. The whole sample was seroconverted after 2nd dose. Significantly high levels of RBD binding antibodies and ACE2 blocking antibodies were observed in previously infected women after administration of the second dose compared to uninfected individuals. The Sinopharm vaccine showed positive results in pregnant women and induced high seroconversion rates and ACE2-blocking antibodies in 2nd and 3rd trimester.*

Keywords: SARS-CoV-2, Pregnant women, receptor binding antibodies, ACE2 blocking antibodies

Introduction

SARS-CoV-2 infection during pregnancy increases the risk of severe illness and maternal and neonatal complications like low birth weight babies and preterm deliveries.(Villar et al., 2021) The risk of early neonatal deaths, stillbirths and acute care admissions was more in unvaccinated pregnant women than the fully vaccinated ones. (Mahase, 2022) Thus, COVID-19 vaccines and boosters are recommended by all countries for preventing neonatal and maternal complications (Donders et al., 2021; Uk, 2022). The AZD1222 (ChAdOx1 nCoV-19), mRNA-1273 (Moderna) and mRNA vaccines BNT162b2 (Pfizer–BioNTech) are safe in all trimesters (Hillson et al., 2021; Lipkind et al., 2022; Shimabukuro et al., 2021). Strong antibody responses were elicited in pregnant women by BNT162b2 (Pfizer-BioNTech), and significant blood levels of SARS-CoV-2 specific antibodies were discovered.(Kugelman et al., 2022; Trostle et al., 2021). Depending on when the vaccine was administered, the mRNA vaccine in pregnant women reduced the hospitalization of infants less than six months by 32 to 80 percent (Halasa et al., 2022). There is a lack of evidence about the safety and immunogenicity of inactivated COVID-19 vaccines when administered to pregnant women. On the other hand, there have been a few clinical tests that demonstrate the immunogenicity and safety of the adenovirus vector (ChAdOx1 nCoV-19). After the outbreak of COVID-19 in Pakistan, many pregnant women were hospitalized, and morbidity and mortality were high before vaccination. The Sinopharm was administered to pregnant women in Pakistan. It induced ACE2-blocking antibodies and a high seroconversion rate soon after administering the second dose. There is a lack of research on the immunogenicity and safety of the Sinopharm/BBIBP-CorV vaccine during pregnancy, so antibody responses and fetal and maternal adverse effects of this vaccine are investigated in this study.

[Citation: Zahra, S.S, Dars, S., Kumari, S., Sahar, B., Wahid, A., Ejaz, S.T. (2023). Antibody response to the COVID-19 vaccine among pregnant women: a prospective study. *Biol. Clin. Sci. Res. J.*, **2023***: 191*. doi: https://doi.org/10.54112/bcsrj.v2023i1.191]

Methodology

A prospective study was conducted in The Gynaecology Department of LUMHS Jamshoro, Hyderabad, Multan and DG Khan from January 2021 to January 2022. The study included 90 pregnant women > 18 years who gave informed consent and provided blood samples when the first and second dose was administered and six to twelve weeks after issuing the second does. The patients were chosen using a non-probability sampling method from the Gynecology ward. The initial dose was given between January and February of 2021. When the first dose was administered, the first blood sample was taken. Following getting the second dose, the second sample was taken four weeks later, and the third sample was taken six to twelve weeks after the first. The consent was taken by the patients after the approval of ethical review board of the hospital. Total antibodies (IgM, IgG, or IgA) to the receptor binding domain were measured using ELISA (RBD). The cut-off value of ELISA was determined using the manufacturer's instructions. Each sample's absorbance was divided by the cut-off value to determine the antibody index (an indirect antibody titer indicator).

In the vaccinated patients, a surrogate virus neutralization test evaluated neutralizing antibodies; this test looks for antibodies that prevent RBD from binding to ACE2. For these tests, the manufacturer's recommendations were followed, and the amount of ACE2 blocking antibody revealed a percent inhibition of binding. Version 8.3 of GraphPad Prism was used for the statistical analysis. To compare the antibody responses to the first and second dosages, the Wilcoxon matched pairs signed rank test was performed. The difference in the antibody titers of infected and uninfected pregnant women was assessed using the Mann-Whitney test (two-tailed). The correlation between age and antibody response was calculated using Spearman's correlation coefficient.

Results

Of 90 pregnant women, 55(61%) were aged between 18-30 years, and 35 (39 %) were between 31-45 years. 3/90 (3.3%) women received shots in 1st trimester, 56/90 (62%) in 2nd trimester and 31/90 (34%) in 3rd trimester (Table-I).

Table-I: Demographic of patients

Variables	Constructs	No of women (%)
Age	18-30 year	55 (61%)
	31-45 year	35 (39%)
Trimester	1st	3 (3.3%)
	2nd	56 (62%)
	3rd	31(34%)

No adverse pregnancy-related or maternal complications like hypertensive disorders, thrombotic events or miscarriage were reported. No fetal complications like congenital anomalies, preterm delivery or fetal death were reported. SARS-CoV-2 specific total antibodies were found in 57/90 (63%) women at the time of recruitment (when receiving 1st dose); thus, they were considered to be previously infected. Two out of fifty-seven were diagnosed as COVID-19 positive by RT-qPCR, 4-8 weeks before receiving the first dose. Other women were not aware of the infection. Thirty-three women were uninfected at baseline: three developed COVID-19 after 2-4 weeks of obtaining 2nd dose. Thirty-three out of the thirty-three (33) uninfected women received the second dosage (four weeks after the first dose), and six to twelve weeks later, all 33 had seroconverted. Four weeks following the first dose, both infected (p=0.0003) and uninfected (p0.0001) women had considerably increased total antibody indices compared to the baseline. However, the antibody titers in uninfected women weren't significantly different after four weeks or six to twelve weeks following the first dosage. Women with baseline infections had greater antibody titers to RBD than non-infected women (measured four weeks after the first dose, p0.0001, and 6-12 weeks after the first dose, p=0.0002). After the second treatment, there was no correlation between antibody titres and the age of women.

Seropositive women with ACE2-blocking antibodies were not found to be above the positive cut-off criterion in 15 out of 57 (26%) baselines. Angiotensin-converting enzyme-2 blocking antibodies over the positive threshold were generated after the first dose in 2/15 individuals, and after both doses, they were present in all patients. After four weeks, 13/33 (39%) of the uninfected women tested positive for Angiotensin-converting enzyme-2 blocking antibodies, while 20/33 (60%) tested positive after receiving both doses. After the first dose, 54/57 (94%) of the baseline-infected women tested positive, and 55/57 (96%) tested positive after the second dose. After four weeks (p0.0001) and six to twelve weeks (p=0.003) following the initial dose, ACE2-blocking antibodies in those who were not infected significantly increased. Angiotensin-converting enzyme-2 blocking antibodies in baseline infected individuals also increased after 4 weeks (p<0.0001) and 6-12 weeks (p=0.02). In baseline, infected individuals' angiotensin-converting enzyme-2 blocking antibodies were higher after 1st and 2nd doses than uninfected individuals. No association was found between angiotensin-converting enzyme-2 antibody levels in baseline infected and uninfected individuals and age.

[Citation: Zahra, S.S, Dars, S., Kumari, S., Sahar, B., Wahid, A., Ejaz, S.T. (2023). Antibody response to the COVID-19 vaccine among pregnant women: a prospective study. *Biol. Clin. Sci. Res. J.*, **2023***: 191*. doi: https://doi.org/10.54112/bcsrj.v2023i1.191]

Discussion

The immunogenicity, safety, and side effects of Sinopharm in pregnant women were examined in this study. Because there are few research on the immunogenicity and safety of the Sinopharm/BBIBP-CorV vaccine during pregnancy in Pakistan, this study will add to our understanding of Covid-19. The immunization was declared safe, and in the second and third trimesters there were no adverse effects on the mother or the fetus. There was only one incident of a neonatal cardiac abnormality found, and it had nothing to do with the vaccination given because the mother had gestational diabetes. After receiving two doses, seroconversion occurred in all baseline subjects. In Pakistan, a few studies have been carried out to determine whether the Sinopharm vaccination is beneficial in protecting expectant mothers. In this study, we assessed these effects across all three trimesters. Comparable levels of ACE2 antibody detection and seroconversion were observed in non-pregnant women in other trials.(Jeewandara et al., 2021). After the first and second doses, baseline-infected women had significantly greater antibody levels of COVID-19 RBD than baseline-uninfected women. The RBD binding antibody level was not significantly increased following the second dosage in either of the baseline populations—infected or uninfected people. However, after the second treatment, Angiotensin-converting Enzyme-2 Blocking Antibodies rose dramatically in both baselines infected and uninfected females. Inducing a higher Nabs level vaccination is crucial because it has been discovered that ACE2-blocking antibodies serve as a surrogate marker of neutralizing antibodies. (Tan et al., 2020). However, ACE2 blocking and RBD binding antibodies were higher after the first and second vaccine doses in previously infected women than in uninfected women. In both infected and uninfected individuals, significantly higher neutralizing antibodies and RBD binding antibodies were found after second doses of AZD1222 and mRNA vaccines (Amirthalingam et al., 2021). However, in previously infected individuals, antibody levels do not rise significantly after 2nd dose compared to the first (Moncunill et al., 2022). In this study, ACE2 blocking antibodies and antibodies to the RBD were significantly higher after the second dose than the first in both infected and uninfected women. This may be due to less immunogenicity of inactivated vaccines than mRNA vaccines.16Though 63% of women were baseline infected, Angiotensin-converting enzyme-2 blocking antibodies beyond the positive threshold were not found in 26% of patients. It is found that Angiotensin-converting enzyme-2 blocking antibodies are not detectable in asymptomatic or mild illness, and they may also decline with time in mild illness (Harrington et al., 2021). Our study has some limitations. We had a small sample size and prospective study design. A multi-center study with a large sample size may help yield more helpful results.

Conclusions

Sinopharm was safe and induced ACE2-blocking antibodies and a high seroconversion rate in pregnant women in 2nd and 3rd trimesters. It was found that two doses of vaccine have less immunogenicity in previously uninfected individuals.

Conflict of interest

The authors declared no conflict of interest.

Authors' Contribution

SSZ, SK, AW and BS conceived, designed and did statistical analysis & editing of manuscript.
SK, SSZ, STE, AW, SD did data collection and manuscript writing.
SK, SD, STE did review and final approval of manuscript.
SD the responsible for the accuracy & integrity of the study.

References

Amirthalingam, G., Bernal, J. L., Andrews, N. J., Whitaker, H., Gower, C., Stowe, J., Tessier, E., Subbarao, S., Ireland, G., and Baawuah, F. (2021). Serological responses and vaccine effectiveness for extended COVID-19 vaccine schedules in England. *Nature Communications* **12**, 1-9.

Donders, G. G., Grinceviciene, S., Haldre, K., Lonnee-Hoffmann, R., Donders, F., Tsiakalos, A., Adriaanse, A., Martinez de Oliveira, J., Ault, K., and Mendling, W. (2021). ISIDOG Consensus Guidelines on COVID-19 Vaccination for Women before, during and after Pregnancy. *Journal of clinical medicine* **10**, 2902.

Halasa, N., Olson, S., and Staat, M. (2022). Overcoming COVID-19 Network. Effectiveness of maternal vaccination with mRNA COVID-19 vaccine during pregnancy against COVID-19–associated hospitalization in infants aged< 6 months—17 states, July 2021–January 2022. *MMWR Morb Mortal Wkly Rep* **71**, 264-270.

Harrington, W. E., Trakhimets, O., Andrade, D. V., Dambrauskas, N., Raappana, A., Jiang, Y., Houck, J., Selman, W., Yang, A., and Vigdorovich, V. (2021). Rapid decline of

neutralizing antibodies is associated with decay of IgM in adults recovered from mild COVID-19. *Cell Reports Medicine* **2**, 100253.

Hillson, K., Clemens, S. C., Madhi, S. A., Voysey, M., Pollard, A. J., and Minassian, A. M. (2021). Fertility rates and birth outcomes after ChAdOx1 nCoV-19 (AZD1222) vaccination. *The Lancet* **398**, 1683-1684.

Jeewandara, C., Aberathna, I. S., Pushpakumara, P. D., Kamaladasa, A., Guruge, D., Jayathilaka, D., Gunasekara, B., Tanussiya, S., Kuruppu, H., and Ranasinghe, T. (2021). Antibody and T cell responses to Sinopharm/BBIBP-CorV in naïve and previously infected individuals in Sri Lanka. *MedRxiv*.

Kugelman, N., Nahshon, C., Shaked-Mishan, P., Cohen, N., Sher, M. L., Gruber, M., Marom, I., Zolotarevsky, A., Lavie, O., and Damti, A. (2022). Maternal and neonatal SARS-CoV-2 immunoglobulin G antibody levels at delivery after receipt of the BNT162b2 messenger RNA COVID-19 vaccine during the second trimester of pregnancy. *JAMA pediatrics* **176**, 290-295.

Lipkind, H. S., Vazquez-Benitez, G., DeSilva, M., Vesco, K. K., Ackerman-Banks, C., Zhu, J., Boyce, T. G., Daley, M. F., Fuller, C. C., and Getahun, D. (2022). Receipt of COVID-19 vaccine during pregnancy and preterm or small-for-gestational-age at birth—Eight Integrated Health Care Organizations, United States, December 15, 2020–July 22, 2021. *Morbidity and Mortality Weekly Report* **71**, 26.

Mahase, E. (2022). Covid-19: Severe complications during pregnancy are more common in unvaccinated women, study finds. *BMJ: British Medical Journal (Online)* **376**.

Moncunill, G., Aguilar, R., Ribes, M., Ortega, N., Rubio, R., Salmerón, G., Molina, M. J., Vidal, M., Barrios, D., and Mitchell, R. A. (2022). Determinants of early antibody responses to COVID-19 mRNA vaccines in a cohort of exposed and naïve healthcare workers. *EBioMedicine* **75**, 103805.

Shimabukuro, T. T., Kim, S. Y., Myers, T. R., Moro, P. L., Oduyebo, T., Panagiotakopoulos, L., Marquez, P. L., Olson, C. K., Liu, R., and Chang, K. T. (2021). Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. *New England Journal of Medicine*.

Tan, C. W., Chia, W. N., Qin, X., Liu, P., Chen, M. I.-C., Tiu, C., Hu, Z., Chen, V. C.-W., Young, B. E., and Sia, W. R. (2020). A SARS-CoV-2 surrogate virus neutralization test based on antibody-mediated blockage of ACE2–spike protein–protein interaction. *Nature biotechnology* **38**, 1073-1078.

Trostle, M. E., Aguero-Rosenfeld, M. E., Roman, A. S., and Lighter, J. L. (2021). High antibody levels in cord blood from pregnant women vaccinated against COVID-19. *American journal of obstetrics & gynecology MFM* **3**.

Uk, G. (2022). Covid-19 Vaccination: A Guide on Pregnancy and Breastfeeding. *London: UK G*.

Villar, J., Ariff, S., Gunier, R. B., Thiruvengadam, R., Rauch, S., Kholin, A., Roggero, P., Prefumo, F., Do Vale, M. S., and Cardona-Perez, J. A. (2021). Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID multinational cohort study. *JAMA pediatrics* **175**, 817-826.

[Citation: Zahra, S.S, Dars, S., Kumari, S., Sahar, B., Wahid, A., Ejaz, S.T. (2023). Antibody response to the COVID-19 vaccine among pregnant women: a prospective study. *Biol. Clin. Sci. Res. J.*, **2023***: 191*. doi: https://doi.org/10.54112/bcsrj.v2023i1.191]