ORIGINAL ARTICLE

Antibody Responses Following Covid-19 Vaccine in Pregnant Women- A Prospective Study

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ABSTRACT

Objective: To assess the antibody responses and adverse effects of sinopharm vaccine in pregnant women.

Study Design: A prospective cohort study.

Place and Duration of Study: The study was conducted in the Gynaecology Department of Ibn-e-Siena Hospital Multan, Independent Hospital Faisalabad and Mayo Hospital Lahore from January 2021 to January 2022.

Materials and Methods: A total of 90 women were included in the study who were administered Sinopharm. Three out of ninety (3.3%) women received shots in 1st trimester, 56/90 (62%) in 2nd trimester and 31/90 (34%) in third trimester. Enzyme-linked immunosorbent assay (ELISA) was used to measure SARS-CoV-2 receptor binding domain (RBD) specific total antibodies and angiotensin-converting enzyme 2 (ACE2) blocking antibodies. The adverse effects on the mother and fetus were evaluated after the delivery.

Results: The administration of the sinopharm vaccine showed no adverse effects or pregnancy complications such as 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 recruitment (when receiving 1st dose); thus they were considered to be previously infected. After the second dose, all women were seroconverted. 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.

Conclusion: The Sinopharm vaccine showed positive results in pregnant women and induced high seroconversion rates and ACE2 blocking antibodies in second and third trimesters.

Keywords: *ACE2 Blocking Antibodies, Pregnant Women SARS-CoV-2, Receptor Binding Antibodies*.

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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.[1] Risk of early neonatal deaths, stillbirths and critical care admissions was more in more in unvaccinated pregnanten than the fully vaccinated ones.[2] Thus, COVID-19 vaccines and boosters are recommended by all countries for preventing neonatal and maternal complications.[3,4]

The non-human adenovirus-vectored vaccines like AZD1222 (ChAdOx1 nCoV-19) and mRNA vaccines like mRNA-1273 (Moderna) and BNT162b2 (Pfizer–BioNTech) have shown to be safe in all trimesters.[5,7] In pregnant women, strong antibody responses were induced by the BNT162b2 (Pfizer–BioNTech) and SARS-CoV-2 spike protein-specific antibodies were found in large numbers in cord blood.[8,9] The mRNA vaccine in pregnant women resulted in a 32% to 80% reduction in hospitalization of infants below 6 months old, depending upon the

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time of administration of vaccine.[10] Safety and immunogenicity of adenovirus vector (ChAdOx1 nCoV-19) and mRNA in pregnancy has been proven by few studies[5,7]; however there is limited research on safety and immunogenicity of inactivated COVID-19 vaccines in pregnancy.

After the outbreak of COVID-19 in Pakistan many pregnant women were hospitalized, and morbidity and mortality were high before the administration of COVID-19 vaccines.[11] The Sinopharm/BBIBP-CorV (Vero cells) was administered to pregnant women in Pakistan. It induced ACE2 blocking antibodies and high seroconversion rate soon after the second dose was administered.[12] As there is lack of research on immunogenicity and safety of Sinopharm/BBIBP-CorV(Vero cells) vaccine during pregnancy, in this study antibody responses and fetal and maternal adverse effects of this vaccine are investigated.

Materials and Methods

A prospective study was conducted in the Gynecology Department of Ibn-e-Siena Hospital Multan, Independent Hospital Faisalabad and Mayo Hospital Lahore from January 2021 to January 2022. The study included 90 pregnant women > 18 years who gave informed consent and who provided blood sample when the first and second dose was administered and 6-12 weeks after the administration of the second dose. The first dose was administered between January 2021 to February 2021. At the time of administration of the first dose, a first blood sample was collected. The second sample was collected after 4 weeks of the first blood sample (upon receiving the second dose) and a third blood sample was collected 6-12 weeks after the first sample. Data about maternal and fetal outcomes were collected after the delivery. Ethical Review Committee of hospital approved by ref# 12/67 on dated 23-11-2020 for the study.

The SARS-CoV-2 total antibody ELISA was used to determine total antibodies (IgM, IgG or IgA) to the receptor binding domain (RBD) of the virus. Manufacturer's instructions were used for calculating cut off value of ELISA. Absorbance of every sample was divided by cut off value for calculating antibody index (it is indirect indicator of antibody titer).

Neutralizing antibodies in the vaccinated individuals was measured by the surrogate virus neutralization test (sVNT); this test detects antibodies inhibiting RBD binding to ACE2. The manufacturer's instructions were followed for these tests and the level of ACE2 blocking antibody showed % inhibition of binding.

Statistical analysis was done using GraphPad Prism version 8.3. The Wilcoxon matched-pairs signed rank test was used for analyzing antibody responses of the first and second dose. The Mann-Whitney test (two-tailed) was used to determine the difference in antibody titers of uninfected and infected pregnant women. The correlation between age and antibody response was determined by 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 (table 1).

Table 1: Age of women

Age	No of women (n)
18-30 year	55 (61%)
31-45 year	35 (39%)

3/90 (3.3%) of women received shots in 1st trimester, 56/90 (62%) in 2nd trimester and 31/90 (34%) in 3rd trimester (table 2).

Table 2: Time of obtaining vaccine

Trimester	No of Women (n)
1st	3 (3.3%)
2nd	56 (62%)
3rd	31(34%)

No adverse pregnancy-related or maternal complications like hypertensive disorders, thrombotic events or miscarriage was 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 recruitment (when receiving 1st dose); thus they were considered to be previously infected. Two out of fifty seven (2/57) 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 (33) women were uninfected at baseline, 3 developed COVID-19 and tested positive after 2-4 weeks of obtaining 2nd dose.

At the time of receiving the second dose (4 weeks after the first dose), 30/33 (90.9%) women who were uninfected had seroconverted, and 6-12 weeks after

1st dose, all 33 women had seroconverted. The total antibody index in uninfected (p<0.0001) and infected (p=0.0003) women was significantly higher at four weeks after 1st dose as compared to baseline. However, antibody titres in uninfected women were not much different after 4 weeks and 6-12 weeks after 1st dose. The antibody titre to RBD (measured 4 weeks after 1st dose (p<0.0001) and 6-12 weeks after 1st dose (p=0.0002)) was higher in baseline infected women than uninfected. No association was found between antibody titres after the second dose and the age of women.

In 15 out of 57 (26%) baseline seropositive women ACE2 blocking antibodies were not found to be beyond the positive cutoff threshold. In 2/15 patients, ACE2 blocking antibodies above the positive threshold were developed after the first dose, and after both doses, all patients had ACE2 blocking antibodies above the positive threshold. Thirteen out of thirty three (39%) uninfected women were positive for ACE2 blocking antibodies after 4 weeks and 20/33 (60%) were positive after both doses. Fift four out of fifty sevent (94%) of baseline infected women were positive after first dose and 55/57 (96%) were positive after the second dose.

ACE2 blocking antibodies in uninfected individuals increased significantly after four weeks (p<0.0001) and 6-12 weeks (p=0.003) post first dose. The angiotensin-converting enzyme 2 (ACE2) 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, ACE2 blocking antibodies were higher after the first and second dose than in uninfected individuals. No association was found between ACE2 antibody levels in baseline infected and uninfected individuals and age.

Discussion

In this study, immunogenicity, safety and adverse effects of Sinopharm in pregnant women were assessed. It was found that the vaccine was safe, and no fetal and maternal adverse effects occurred in 2nd and 3rd trimesters. A single case of a cardiac anomaly in a neonate was found, the mother had gestational diabetes, and this anomaly was not associated with the use of a vaccine. After two doses, all baseline subjects seroconverted.

ACE2 antibody detection rate and seroconversion rate were same as reported by another study showing rates in non-pregnant women.[13]

The antibody to RBD of COVID-19 was much higher in baseline infected women after first and second dose than base line uninfected women. In both baselines infected or uninfected individuals, RBD binding antibody levels were not significantly raised after the second dose. However, in both baseline infected and uninfected women, ACE2 blocking antibodies significantly increased after the second dose. ACE2 blocking antibodies were found to be a surrogate marker of neutralizing antibodies (Nabs), so inducing a higher Nabs level vaccine is important.[14] However, both ACE2 blocking antibodies and RBD binding antibodies were higher after first and second dose of vaccine in previously infected women then uninfected. It is found that in both infected and uninfected individuals significantly higher neutralizing antibodies and RBD binding antibodies were found after second doses of AZD1222 and mRNA vaccines.[15] However, in previously infected individuals, antibody levels do not rise significantly after the second dose compared to the first.[16] 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 as compared to mRNA vaccines.[17] Though 63% of women were baseline infected, ACE2 blocking antibodies beyond the positive threshold were not found in 26% of patients. It is found that ACE2 blocking antibodies are not detectable in asymptomatic or mild illness, and they may also decline with time in mild illness.[18]

Conclusion

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

REFERENCES

1. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID multinational cohort study. JAMA pediatrics. 2021; 175: 817-26.
2. Mahase E. Covid-19: Severe complications during

pregnancy are more common in unvaccinated women, study finds. BMJ: British Medical Journal (Online). 2022; 376: o117.
3. Uk G. Covid-19 Vaccination: A Guide on Pregnancy and Breastfeeding. London: UK G. 2022.
4. Donders GG, Grinceviciene S, Haldre K, Lonnee-Hoffmann R, Donders F, Tsiakalos A, et al. ISIDOG Consensus Guidelines on COVID-19 Vaccination for Women before, during and after Pregnancy. Journal of clinical medicine. 2021; 10: 2902.
5. Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, et al. Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. New England Journal of Medicine. 2021; 385: 15366.
6. Lipkind HS, Vazquez-Benitez G, DeSilva M, Vesco KK, Ackerman-Banks C, Zhu J, et al. 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. 2022; 71: 26.
7. Hillson K, Clemens SC, Madhi SA, Voysey M, Pollard AJ, Minassian AM. Fertility rates and birth outcomes after ChAdOx1 nCoV-19 (AZD1222) vaccination. The Lancet. 2021; 398: 1683-4.
8. Trostle ME, Aguero-Rosenfeld ME, Roman AS, Lighter JL. High antibody levels in cord blood from pregnant women vaccinated against COVID-19. American journal of obstetrics & gynecology MFM. 2021; 3: 100481.
9. Kugelman N, Nahshon C, Shaked-Mishan P, Cohen N, Sher ML, Gruber M, et al. 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. 2022; 176: 290-5.
10. Halasa N, Olson S, Staat M. 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. 2022; 71: 264-70.
11. Begum Z, Sadaf F, Shah H, Amin S, Afridi M, Qureshi R, et al. Fetomaternal Outcome of Pregnancy with COVID-19: An Observational Study in a Tertiary Care Hospital of Pakistan. Pakistan Journal of Medical & Health Sciences. 2021; 18: 13373.
12. Altaf SA, Amer MA, Azhar AA. The safety of verocell covid-19 (sinopharm) vaccination among health care workers in khyber teaching hospital, peshawar. Journal of Medical Sciences. 2021; 29: 99-103.
13. Jeewandara C, Aberathna IS, Pushpakumara PD, Kamaladasa A, Guruge D, Jayathilaka D, et al. Antibody and T cell responses to Sinopharm/BBIBP-CorV in naïve and previously infected individuals in Sri Lanka. MedRxiv. 2021.
14. Tan CW, Chia WN, Qin X, Liu P, Chen MIC, Tiu C, et al. A SARS-CoV-2 surrogate virus neutralization test based on antibody-mediated blockage of ACE2–spike protein–protein interaction. Nature biotechnology. 2020; 38: 1073-8.
15. Amirthalingam G, Bernal JL, Andrews NJ, Whitaker H, Gower C, Stowe J, et al. Serological responses and vaccine effectiveness for extended COVID-19 vaccine schedules in England. Nature Communications. 2021; 12: 1-9.
16. Moncunill G, Aguilar R, Ribes M, Ortega N, Rubio R, Salmerón G, et al. Determinants of early antibody responses to COVID-19 mRNA vaccines in a cohort of exposed and naïve healthcare workers. EBioMedicine. 2022; 75: 103805.
17. Hall V, Foulkes S, Insalata F, Kirwan P, Saei A, Atti A, et al. Protection against SARS-CoV-2 after Covid-19 vaccination and previous infection. New England Journal of Medicine. 2022; 386: 1207-20.
18. Harrington WE, Trakhimets O, Andrade DV, Dambrauskas N, Raappana A, Jiang Y, et al. Rapid decline of neutralizing antibodies is associated with decay of IgM in adults recovered from mild COVID-19. Cell Reports Medicine. 2021; 2: 100253.