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Comparing the immunogenicity of COVID-19 infection and vaccination in pregnant women as measured by anti-S IgG

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Abstract

Background Pregnancy is a critical time for women, making them more susceptible to infectious diseases like COVID-19. This study aims to determine the immunogenicity of COVID-19 in pregnant women who have been infected compared to those who have received the inactive COVID-19 vaccine.

Materials and methods In this retrospective cohort study, pregnant women who received the inactivated COVID-19 vaccine (Sinopharm) and those with a history of COVID-19 infection during pregnancy were studied. Participants who had experienced stillbirth, received different COVID-19 vaccines, or had intrauterine fetal death were excluded from the study. Overall, the study included 140 participants. The participants were divided into two groups of 70 participants - pregnant women who received the Sinopharm vaccine and pregnant women who had COVID-19 infection during pregnancy. Before delivery, blood samples were collected from all mothers to evaluate the maternal immunoglobulin G (IgG) level. Blood samples were also taken from the baby's umbilical cord during delivery to measure the newborn's IgG level. Additionally, blood samples were collected from babies whose mothers showed signs of acute infection to measure their IgM levels and evaluate vertical transmission.

Findings The study found a significant relationship between the mean level of maternal IgG and umbilical cord IgG within the groups ($P < 0.001$). The highest levels of maternal IgG (2.50 ± 2.17) and umbilical cord IgG (2.43 ± 2.09) were observed in pregnant women with a previous COVID-19 infection and no history of vaccination ($P < 0.001$). Only one baby was born with a positive IgM, and this baby was born to a mother who showed signs of COVID-19 infection in the last five days of pregnancy. The mother was 28 years old, with a BMI of 33; it was her first pregnancy, and she gave birth to a male newborn at term.

Conclusion Administering an inactivated vaccine during pregnancy can generate immunity in both the mother and the child. However, the vaccine's immunity level may not be as potent as that conferred by COVID-19 infection during pregnancy. Nonetheless, the risk of vertical transmission of COVID-19 is considered minimal and can be classified as negligible.

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Keywords COVID-19, Inactivated vaccine, Pregnancy, Vertical transmission, Immunogenicity, IgG, IgM, BBIBP-CorV, Sinopharm

Introduction

The coronavirus disease 2019 (COVID-19) outbreak began in Wuhan, Hubei Province, China, in December 2019 and rapidly spread worldwide. This disease was caused by a novel coronavirus known as acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The SARS-CoV-2 virus is transmitted through airborne particles and can be disseminated from one individual to another via contaminated secretions, including respiratory droplets and saliva. This transmission occurs during sneezing, coughing, speaking, or singing. Upon infiltrating the human body, the virus infiltrates the cells by binding to the angiotensin-converting enzyme type 2 receptor (ACE2) [2, 3]. This receptor is present in various parts of the body, including type II alveolar epithelial cells, vascular endothelial cells, and enterocytes of the small intestine, making them vulnerable to SARS-CoV-2 infection. The preferred method to detect this virus is real-time reverse transcription polymerase chain reaction (RT-PCR). Additionally, antibody-based techniques are used as complementary tools [1].

Universal vaccination is an important strategy to prevent the rapid spread of the pandemic. Due to the high transmission, infection, and mortality rates caused by COVID-19, scientists and pharmaceutical companies around the world developed various types of vaccines in a relatively short period [1, 4].

Two main categories of COVID-19 vaccines were used in this pandemic. The first category, genetic vaccines, includes mRNA, adenoviral vectors (viral vectors), and DNA vaccines. The second category is classified as inactivated vaccines. These vaccines contain killed virus particles, such as protein S and adjuvants that mimic SARS-CoV-2 to trigger an immune response [5]. Inactivated vaccines possess a set of highly desirable features. Firstly, they are based on well-established platforms with a long history of use. Additionally, they can rapidly deploy and produce antibodies with minimal complications. Finally, they can be mass-produced to create large quantities of antibodies [6]. One of the vaccines in this category is the Sinopharm vaccine or BBIBP-CorV, a complete virus vaccine inactivated with aluminum hydroxide. This vaccine was widely distributed globally, with over 400 million doses administered. The SARS-CoV-2 BIBP viral strain used for vaccine production was isolated from clinical samples in China in January 2020. The strain was then inoculated into Vero cells derived from whole African green monkeys [7].

Pregnant women, in general, are more susceptible to pathogenic factors and infections. Recent studies have shown that contracting COVID-19 during pregnancy can result in severe illness and threaten the fetus's health [8, 9]. Reported complications include an increased chance of preterm birth, stillbirth, preeclampsia, intrauterine growth restriction (IUGR), and growth defects in newborns [9–11].

The severity of COVID-19 is primarily influenced by the virus's ability to access host cells by binding to the ACE2 receptor. The placenta expresses high levels of the ACE2 receptor during pregnancy. This high expression of the ACE2 receptor on the placenta, combined with ACE2's important role in regulating maternal hemodynamic adaptations through its effect on the renin-angiotensin system (RAS), is presumed to explain why pregnant women are more susceptible to COVID-19 infection and experience severe symptoms [12, 13].

Vertical transmission is the transfer of an infectious pathogen from the mother to the fetus during pregnancy or to the newborn after birth through the placenta, body fluid contact during childbirth, or breastfeeding [14]. While some studies have indicated limited evidence of vertical transmission, with rates ranging from 1 to 3% or higher, it is challenging to pinpoint the exact route of infection in cases of postpartum neonatal COVID-19 infections. This is due to limitations in data accuracy and the potential for false positive and false negative results in these studies. It remains uncertain whether SARS-CoV-2 was transmitted vertically or during/after delivery [15–20].

Some studies have assessed the immune response of mRNA-based COVID-19 vaccines in pregnant women. The findings indicate that the vaccine-induced immune response in pregnant and lactating women was similar to that of non-pregnant women. Furthermore, the immune response elicited by mRNA vaccines during pregnancy was notably more significant than the response to a COVID-19 infection during pregnancy [21–23].

Few studies have evaluated the immunogenicity of vaccination with inactivated vaccines in pregnant women. This study investigates the levels of humoral immune response produced by COVID-19 vaccination and infection in pregnant participants measured by anti-S IgG and the likelihood of vertical transmission of COVID-19 measured by newborn's anti-S IgM.

Materials and methods

This retrospective cohort study included all pregnant women who received the inactivated COVID-19 vaccine (BBIBP-CorV, Sinopharm, Beijing, China) or had a history of COVID-19 infection without getting vaccinated

during their pregnancy. The study was conducted on pregnant women referred to the Besat Hospital in Sanandaj, Iran, for giving birth from January 2021 to June 2022. women who had a history of vaccination with other types of COVID-19 vaccines, stillbirths, and intrauterine fetal deaths (IUFD) were excluded from the study. The participants were divided into two groups: the first group consisted of pregnant women who received the Sinopharm vaccine (vaccinated), and the second group included pregnant women infected with COVID-19 during pregnancy and who did not receive the COVID-19 vaccine (infected). Initially, the researchers recorded the pregnancy information, such as age, body mass index (BMI), and number of pregnancies. For the vaccinated group, the gestational age at the time of COVID-19 vaccination and vaccination-related data were extracted from the vaccine card or the national vaccination registration system. All participants received two vaccine doses for complete vaccination, given at three to four-week intervals [24]. The study considered the trimester for complete vaccination. To determine whether the mother had contracted COVID-19 during pregnancy, the researchers analyzed the relevant documents, including the positive results of the COVID-19 RT-PCR test. All the collected information was recorded in a questionnaire designed by the researchers. The questionnaire was submitted to the gynecology department of the University of Medical Sciences of Sanandaj and was approved prior to the start of the study. Furthermore, the researcher completed the questionnaire for each participant.

The study procedure was first presented to the ethical committee of Sanandaj University of Medical Sciences, and it was approved, and the ethical code was obtained. In accordance with the ethical committee's regulations, the participants were fully informed about the study procedures, and their consent was obtained before blood samples were taken. The blood samples were collected separately from routine testing for the study. Before delivery, a maternal blood sample was taken to check each participant's immunoglobulin G (IgG) levels and compare the immune response after vaccination and COVID-19 infection in both groups at the time of delivery. Blood samples were also taken from newborns of mothers with acute COVID-19 to measure IgM and check the possibility of vertical transmission. Acute infection was confirmed when fever, myalgia, cough, shortness of breath, sore throat, lymphopenia, and thrombocytopenia were present, and PCR tests from the oropharynx and nasopharynx were positive for COVID-19 [25]. In addition, blood samples from the baby's umbilical cord were taken during delivery to measure IgG and check the transfer of antibodies from the mother to the fetus during pregnancy. After being collected, the blood sample was centrifuged at room temperature for 10 min. The resulting serum was then transferred separately into cryogenic vials and stored at minus 80 degrees Celsius. ELISA kits manufactured by Pishtaz Teb Zaman Diagnostics in Tehran, Iran, were used to measure the levels of immunoglobulins. The Stat Fax 2100 microplate reader, made by Awareness Technology, Inc. in Palm City, FL, was utilized to obtain an interpretation of the test results, which were recorded in the questionnaire. Based on the manufacturer's guidelines, antibody levels above 0.9 AI (Antibody index) were considered positive, and at or below 0.9 AI were considered negative.

The collected data was coded and entered into SPSS version 24 software for statistical analysis. We used the chi-square and Fisher's exact tests for qualitative analysis purposes. We employed logistic regression to compare the average antibody titer in two groups and to examine their relationship with variables and groups. We used an independent t-test or its parametric equivalent (Mann-Whitney U) to compare the two groups. The significance level was set at $p<0.05$. The study and research method underwent an ethics review by the Sanandaj University of Medical Sciences ethics committee and was assigned a code of ethics IR.MUK.REC.1401.053.

Results

A total of 140 pregnant women participated in the study and were divided into two groups of 70 participants each. The mean age of the participants was 30.89±6.22 years, ranging from 18 to 48 years. The participants' average body mass index (BMI) was 27.80±5.08, ranging from 19.3 to 51.2. Most participants (37.1%) were in their second pregnancy (Gravid 2). 85.7% of mothers gave birth at full term. Out of all the women, 55% gave birth to male babies. 92.85% of participants in the vaccinated group received their second dose during their third trimester. Table 1 presents the frequency distribution of the variables across the studied groups.

The t-test showed a significant difference between the mean maternal and umbilical cord IgG levels in both groups. The mean maternal IgG levels were 1.55±1.23 in vaccinated participants and 2.50±2.17 in infected participants ($P<0.001$). The mean levels of umbilical IgG were 1.42±1.33 in vaccinated participants and 2.43±2.09 in infected participants ($P<0.001$). The infected group had a higher level of IgG than the vaccinated group (Fig. 1).

While both groups showed a significant difference in maternal IgG levels ($P<0.001$), the results for umbilical cord IgG levels were insignificant in both groups ($P=0.33$). The infected group had a higher percentage of people with positive maternal and umbilical cord IgG (72.9% and 70%). Only one baby was born with COVID-19 infection from a mother with an acute COVID-19 infection. Among the 21 participants with acute COVID-19 infection, none of the umbilical cord IgG tests were

Table 1 Frequency distribution of variables in the studied groups

Variables		Groups		*P*-value
		Vaccinated	Infected	
Age		30.60±6.19	31.17±6.28	0.58
Body Mass Index		27.53±5.06	28.07±5.13	0.53
Hospitalization during CCOVID-19 infection	Yes	35 (50%)	0 (0%)	<0.001
	No	35 (50%)	70 (100%)	
Type of delivery	Term	62 (86.6%)	58 (82.9%)	0.33
	Pre-term	8 (11.4%)	12 (17.1%)	
Newborn gender	Girl	33 (47.1%)	30 (42.9%)	0.61
	Boy	37 (52.9%)	40 (57.1%)	
Gravida	1	17 (24.3%)	23 (32.9%)	0.58
	2	30 (42.9%)	22 (31.4%)	
	3	15 (21.4%)	12 (17.1%)	
	4	6 (8.6%)	9 (12.9%)	
	5	1 (1.4%)	2 (2.9%)	
	6	1 (1.4%)	2 (2.9%)	

Ig: Immunoglobulin

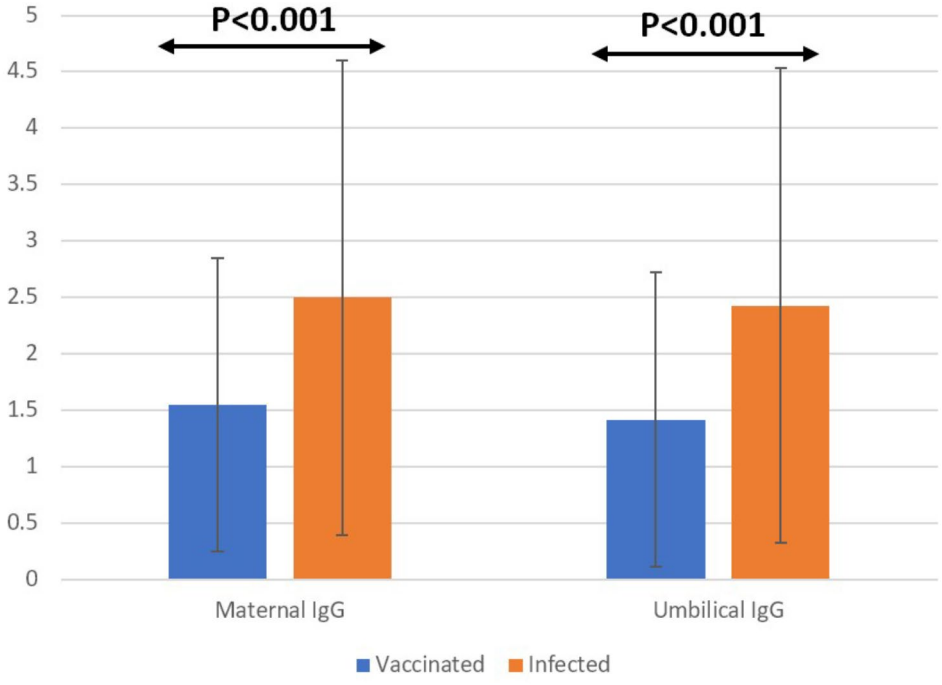

Fig. 1 Comparison of mean maternal and umbilical cord IgG in two groups of infected and vaccinated pregnant women. Ig: Immunoglobulin

positive, and only 2 had positive maternal IgG. Table 2 shows the results of the antibody tests for each group.

The logistic regression analysis investigated the relationship between variables and study groups with maternal and umbilical cord IgG levels. The analysis showed a significant relationship between the study groups with maternal IgG (OR=3.507 with 95% CI=1.422-8-653, P=0.006) and umbilical cord IgG (OR=3.509, 95% CI=1.390–855, P=0.008).

The relationship between variables and maternal and umbilical cord IgG in vaccinated pregnant women was assessed using the Chi-square test, and no significant relationship was observed (Table 3). However, it was found that most mothers with positive maternal IgG were in their third trimester of pregnancy, had a BMI of 25 to 30, delivered at term, and had male newborns (P<0.05).

Analyzing the relationship between variables and the newborn's IgM levels using the Chi-square test indicated no significant relationship was found. However, one newborn with positive IgM (1.02 AI) was born to a mother who showed signs of COVID-19 infection five days before delivery. The mother was pregnant for the first

Table 2 Correlation of antibodies with the studied groups

Antibodies		Groups		P-value
		Vaccinated	Infected (Acute/Non-acute)	
Maternal IgG	Positive	29 (41.4%)	2 (2.9%)/49 (70%)	<0.001
	Negative	54 (58.6%)	19 (27.1%)/ 0 (0%)	
Umbilical cord IgG	Positive	32 (45.7%)	0 (0%)/49 (70%)	0.33
	Negative	38 (54.3%)	21 (30%)/0 (0%)	
Newborn IgM	Positive	0	1 (4.8%)/0 (0%)	0.61
	Negative	0	20 (95.2%)/0 (0%)	

Ig: Immunoglobulin

Table 3 Comparing the relationship between variables and maternal and umbilical cord IgG

Variables		Umbilical cord IgG		P-value	Maternal IgG		P-value
		Positive	Negative		Positive	Negative	
Trimester of vaccination	First	1 (100%)	0 (0%)	0.25	1 (100%)	0 (0%)	0.39
	Second	3 (75%)	1 (25%)		1 (25%)	3 (75%)	
	Third	28 (43.1%)	37 (56.9%)		27 (41.5%)	38 (58.5%)	
Body Mass Index	Less than 25	21 (51.2%)	20 (48.8%)	0.34	21 (51.2%)	20 (48.8%)	0.31
	25 to 30	32 (56.1%)	25 (43.9%)		31 (54.4%)	26 (45.6%)	
	More than 30	28 (66.7%)	14 (33.3%)		28 (66.7%)	14 (3.33%)	
Type of delivery	Term	73 (60.8%)	47 (39.2%)	0.08	70 (58.3%)	50 (41.7%)	0.48
	Pre-term	8 (40%)	12 (60%)		10 (50%)	10 (50%)	
Newborn gender	Girl	37 (58.7%)	26 (41.3%)	0.85	36 (57.1%)	27 (42.9%)	1.00
	Boy	44 (57.1%)	33 (42.9%)		44 (57.1%)	33 (42.9%)	

Ig: Immunoglobulin

Table 4 Comparing the relationship between variables and newborn IgM

Variables		Newborn IgM		P-value
		Positive	Negative	
Body Mass Index	Less than 25	0 (0%)	2 (%100)	0.62
	25 to 30	0 (0%)	8 (100%)	
	More than 30	1 (9.1%)	10 (90.9%)	
Type of delivery	Term	1 (6.7%)	14 (93.3%)	0.51
	Pre-term	0 (0%)	6 (100%)	
Newborn gender	Girl	0 (0%)	7 (100%)	0.46
	Boy	1 (7.1%)	13 (92.9%)	
Maternal age	30 and less	1 (16.7%)	5 (83.3%)	0.1
	More than 30	0 (0%)	15 (100%)	
Gravida	1	1 (14.3%)	6 (85.7%)	0.55
	2	0 (0%)	5 (100%)	
	3	0 (0%)	4 (100%)	
	More than 3	0 (0%)	5 (100%)	

Ig: Immunoglobulin

time, had a BMI of 33, was 28 years old, and gave birth to a male child at full term ($P>0.05$). The relationship between the variables and the newborn's IgM is shown in Table 4.

Discussion

During pregnancy, high levels of estrogen and progesterone can cause congestion, edema, increased mucus secretion, and fragility in the upper respiratory system. Additionally, as the baby grows, the respiratory surface in the lower respiratory system can be reduced. As a result, pregnant Women are more susceptible to respiratory infectious diseases than the general population [18, 26]. Also, During pregnancy, an increase in diaphragm surface area and edema of the mucous membrane of the respiratory tract lead to intolerance to hypoxia [27].

During the SARS-CoV-1 and Middle East Respiratory Syndrome (MERS) pandemics, which have the same origin as SARS-CoV-2, there were no confirmed cases of vertical transmission [28]. However, the highly contagious nature of COVID-19 raised concerns about possible vertical transmission [29]. In a retrospective cohort study by Dimitri et al., the vertical transmission of COVID-19 infection was investigated. Out of 101 babies born to mothers with COVID-19, no cases of vertical transmission were reported [16]. In our study, only 1 out of 21 babies born to mothers in the acute phase of COVID-19 had a positive IgM (1.02 AI).

Previous research studies have demonstrated the safety of mRNA-based vaccines, including BNT162b2 from Pfizer-BioNTech, mRNA-1273 from Moderna, and AZD1222 (ChAdOx1 nCoV-19), during all trimesters of pregnancy [30, 31]. The research findings indicate that pregnant women who receive the Pfizer-BioNTech vaccine, BNT162b2, develop a robust immune response. Moreover, the vaccine produces high levels of SARS-CoV-2 protein-specific antibodies in the umbilical cord blood [32]. In a retrospective cohort study conducted in

Israel to investigate the effectiveness of the COVID-19 vaccine in pregnant people, 9060 pregnant women were examined. The Pfizer-BioNTech mRNA vaccine significantly reduces COVID-19 infection risk in pregnant women [33]. In another cohort study conducted by Gray et al. with a similar aim, it was also seen that mRNA-based vaccines induced significant humoral immunity and antibody levels in pregnant and lactating women, similar to non-pregnant women. It was also seen that the immunogenicity caused by vaccination was significantly higher than the immune response and antibody levels generated following the COVID-19 infection [21]. The same findings were seen in other studies on COVID-19 mRNA vaccines [21, 30–32]. Our findings showed that the humoral immune response to the inactivated COVID-19 vaccine was weaker than that of infected pregnant women. This suggests that mRNA-based vaccines may be more effective for pregnant women.

The Sinopharm vaccine, despite generating a higher level of humoral immune response compared to the unvaccinated population [34], produced lower antibody levels compared to mRNA vaccines in studies that compared the Sinopharm vaccine, mRNA vaccines, and participants who had recovered from COVID-19 infection. However, the antibody levels were similar to those found in previously infected participants [35].

In Iran, the Sinopharm vaccine was deemed safe for administration in pregnant women. As previous studies indicate better efficacy of COVID-19 vaccination during the third trimester of pregnancy, most of the participants in this study (92.85%) received their second dose of the Sinopharm vaccine during this stage [36]. Despite being of high importance in countries like Iran, where only inactivated vaccines such as the Sinopharm vaccine were used for pregnant women during the COVID-19 pandemic, there have been limited studies on the effectiveness of these vaccines in pregnant women and their babies. In a retrospective study by Jeewandara et al., the humoral immune response to the Sinopharm vaccine in 94 pregnant women was studied. The results revealed no complications for the mother and the newborns, including abortion, thrombotic complications, high blood pressure, newborn mortality, preterm birth, or fetal anomaly. It was also seen that antibody levels in women with a history of COVID-19 infection were higher than those who received vaccination [37]. In our study, similar to the study of Jeewandara et al., all vaccinated mothers had received the Sinopharm vaccine, and the antibody levels obtained in infected mothers were higher than in vaccinated mothers. Our results contradict the findings in the non-pregnant population, which indicated similar immunogenicity between Sinopharm and prior COVID-19 infection [35].

According to research on non-pregnant participants, it has been observed that IgG levels increase seven days after the onset of acute COVID-19 symptoms [38]. Our research evaluated maternal and umbilical cord humoral antibody levels in 21 participants with acute COVID-19 infection. The results revealed that umbilical cord IgG levels in these participants were negative, while two mothers had positive IgG. Our findings align with the referenced study. However, the negative umbilical cord IgG levels suggest that if a mother gives birth while having acute COVID-19 infection seven days prior to delivery, there is a reduced likelihood of passing immunity from mother to fetus. Therefore, it may be suitable to vaccinate these newborns during their early months of life.

One limitation of this study is that a higher number of pregnant women received the vaccine in the third trimester, which prevented determining the effectiveness of the vaccination for those vaccinated in other trimesters. Another limitation is that the study did not consider the time of COVID-19 infection during pregnancy in non-acutely infected participants, which could be an essential factor in determining the level of immunity in mothers and their babies. Also, it would be beneficial to compare the results with those of a non-pregnant population as a control group.

For future studies, it is advisable to conduct a larger statistical population study on the immunogenicity of inactive vaccines during pregnancy. It is also recommended to compare the results of pregnant women with the control population of non-pregnant participants.

Conclusion

The inactivated vaccine administered during pregnancy can provide immunity to both the mother and the fetus. However, COVID-19 infection induces higher immunogenicity compared to inactivated vaccines. In case a woman has a COVID-19 infection within a week of delivery, the chances of the baby receiving congenital immunity may decrease. It's important to note that vertical transmission of COVID-19 from mother to child is rare.

Abbreviations

COVID-19	Coronavirus disease of 2019
BMI	Body mass index
Ig	Immunoglobulin
SARS-CoV-2	Acute respiratory syndrome coronavirus 2
ACE2	Angiotensin-converting enzyme type 2 receptor
IUFD	Intrauterine fetal deaths
MERS	Middle East Respiratory Syndrome
AI	Antibody index

Supplementary Information

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Supplementary Material 1

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Author contributions
ZH Visualized the study, visited the patient and revised the manuscript, SA gathered data, drafted, checked and revised the manuscript, BN, SS, FA, and NS drafted and revised the manuscript, KR analyzed and interpreted the data.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Sanandaj University of Medical Sciences Research Ethics Committee (IR.MUK.REC.1401.053). All methods were performed in accordance with the relevant guidelines and regulations. Informed consent was obtained from all subjects according to the instructions of the Sanandaj University of Medical Sciences Ethics Committee.

Consent for publication
not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Ponnampalli S, Venkata Suryanarayana Birudukota N, Kamal A. COVID-19: vaccines and therapeutics. Bioorg Med Chem Lett. 2022;75:128987.
2. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054–62.
3. Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579(7798):270–3.
4. Pollard AJ, Bijker EM. A guide to vaccinology: from basic principles to new developments. Nat Rev Immunol. 2021;21(2):83–100.
5. Heinz FX, Stiasny K. Distinguishing features of current COVID-19 vaccines: knowns and unknowns of antigen presentation and modes of action. npj Vaccines. 2021;6(1):104.
6. Kudlay D, Svistunov A. COVID-19 vaccines: an overview of different platforms. Bioengineering. 2022;9(2):72.
7. Wang C, Chen LY, Lu QB, Cui F. Vaccination with the inactivated vaccine (Sinopharm BBIBP-CorV) ensures Protection against SARS-CoV-2 Related Disease. Vaccines. 2022;10(6).
8. Patberg ET, Adams T, Rekawek P, Vahanian SA, Akerman M, Hernandez A, et al. Coronavirus disease 2019 infection and placental histopathology in women delivering at term. Am J Obstet Gynecol. 2021;224(4):382. e1-. e18.
9. Verma S, Carter EB, Mysorekar IU. SARS-CoV2 and pregnancy: an invisible enemy? Am J Reprod Immunol. 2020;84(5):e13308.
10. Girardelli S, Mullins E, Lees CC. COVID-19 and pregnancy: lessons from 2020. Early Hum Dev. 2021;162:105460.
11. Rasmussen SA, Smulian JC, Lednicky JA, Wen TS, Jamieson DJ. Coronavirus disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. Am J Obstet Gynecol. 2020;222(5):415–26.
12. Azinheira Nobrega Cruz N, Stoll D, Casarini DE, Bertagnolli M. Role of ACE2 in pregnancy and potential implications for COVID-19 susceptibility. Clin Sci. 2021;135(15):1805–24.
13. Shang J, Wan Y, Luo C, Ye G, Geng Q, Auerbach A, et al., et al. Cell entry mechanisms of SARS-CoV-2. Proc Natl Acad Sci. 2020;117(21):11727–34.
14. Kotlyar AM, Grechukhina O, Chen A, Popkhadze S, Grimshaw A, Tal O, et al. Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis. Am J Obstet Gynecol. 2021;224(1):35–e533.
15. Adhikari EH, Moreno W, Zofkie AC, MacDonald L, McIntire DD, Collins RR, et al. Pregnancy outcomes among women with and without severe acute respiratory syndrome coronavirus 2 infection. JAMA Netw open. 2020;3(11):e2029256–e.
16. Dumitriu D, Emeruwa UN, Hanft E, Liao GV, Ludwig E, Walzer L, et al. Outcomes of neonates born to mothers with severe acute respiratory syndrome coronavirus 2 infection at a large medical center in New York City. JAMA Pediatr. 2021;175(2):157–67.
17. Edlow AG, Li JZ, Ai-ris YC, Atyeo C, James KE, Boatin AA, et al. Assessment of maternal and neonatal SARS-CoV-2 viral load, transplacental antibody transfer, and placental pathology in pregnancies during the COVID-19 pandemic. JAMA Netw open. 2020;3(12):e2030455–e.
18. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet. 2020;395(10226):809–15.
19. Kotlyar AM, Grechukhina O, Chen A, Popkhadze S, Grimshaw A, Tal O, et al. Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis. Am J Obstet Gynecol. 2021;224(1):35–53. e3.
20. Kreis N-N, Ritter A, Louwen F, Yuan J. A message from the human placenta: structural and immunomodulatory defense against SARS-CoV-2. Cells. 2020;9(8):1777.
21. Gray KJ, Bordt EA, Atyeo C, Deriso E, Akinwunmi B, Young N, et al. Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study. Am J Obstet Gynecol. 2021;225(3):303. e1-. e17.
22. Paul G, Chad R. Newborn antibodies to SARS-CoV-2 detected in cord blood after maternal vaccination - a case report. BMC Pediatr. 2021;21(1):138.
23. Rottenstreich A, Zarbiv G, Oiknine-Djian E, Zigron R, Wolf DG, Porat S. Efficient Maternofetal Transplacental transfer of Anti- severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) spike antibodies after Antenatal SARS-CoV-2 BNT162b2 Messenger RNA vaccination. Clin Infect Diseases: Official Publication Infect Dis Soc Am. 2021;73(10):1909–12.
24. Zhang Y, Belayachi J, Yang Y, Fu Q, Rodewald L, Li H, et al. Real-world study of the effectiveness of BBIBP-CorV (sinopharm) COVID-19 vaccine in the Kingdom of Morocco. BMC Public Health. 2022;22(1):1584.
25. Baj J, Karakuła-Juchnowicz H, Teresiński G, Buszewicz G, Ciesielka M, Sitarz R et al. COVID-19: specific and non-specific clinical manifestations and symptoms: the current state of knowledge. J Clin Med. 2020;9(6).
26. Lee S-Y, Chien D-K, Huang C-H, Shih S-C, Lee W-C. Chang W-H. Dyspnea in pregnancy. Taiwan J Obstet Gynecol. 2017;56(4):432–6.
27. Chow EP, Danielewski JA, Fehler G, Tabrizi SN, Law MG, Bradshaw CS, et al. Human papillomavirus in young women with Chlamydia trachomatis infection 7 years after the Australian human papillomavirus vaccination programme: a cross-sectional study. Lancet Infect Dis. 2015;15(11):1314–23.
28. Chelsea Elwood M, Isabelle Boucoiran M, Julie VanSchalkwyk M, Deborah Money M, Mark Yudin M. Vanessa Poliquin M. SOGC committee opinion–COVID-19 in pregnancy. J Obstet Gynecol Can. 2020.
29. Qiao J. What are the risks of COVID-19 infection in pregnant women? Lancet. 2020;395(10226):760–2.
30. Hillson K, Clemens SC, Madhi SA, Voysey M, Pollard AJ, Minassian AM. Fertility rates and birth outcomes after ChAdOx1 nCoV-19 (AZD1222) vaccination. Lancet. 2021;398(10312):1683–4.

31. 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. N Engl J Med. 2021;384(24):2273–82.
32. Trostle ME, Aguero-Rosenfeld ME, Roman AS, Lighter JL. High antibody levels in cord blood from pregnant women vaccinated against COVID-19. Am J Obstet Gynecol MFM. 2021;3(6).
33. Goldshtein I, Nevo D, Steinberg DM, Rotem RS, Gorfine M, Chodick G, et al. Association between BNT162b2 vaccination and incidence of SARS-CoV-2 infection in pregnant women. JAMA. 2021;326(8):728–35.
34. Wang Q, Ning J, Chen Y, Li B, Shi L, He T, et al. The BBIBP-CorV inactivated COVID-19 vaccine induces robust and persistent humoral responses to SARS-CoV-2 nucleocapsid, besides spike protein in healthy adults. Front Microbiol. 2022;13:1008420.
35. Petrović V, Vuković V, Patić A, Marković M, Ristić M. Immunogenicity of BNT162b2, BBIBP-CorV and Gam-COVID-Vac vaccines and immunity after natural SARS-CoV-2 infection—A comparative study from novi sad, Serbia. PLoS ONE. 2022;17(2):e0263468.
36. Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, et al. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status—United States, January 22–October 3, 2020. Morb Mortal Wkly Rep. 2020;69(44):1641.
37. Jeewandara C, Jayampathi KCS, Ranasinghe T, Aberathna IS, Gunasekara B, Danasekara S, et al. Antibody responses to Sinopharm/BBIBP-CorV in pregnant mothers in Sri Lanka. PLOS Global Public Health. 2022;2(7):e0000607.
38. Augustine R, Das S, Hasan A, Abdul Salam S, Augustine P, Dalvi YB, et al. Rapid antibody-based COVID-19 mass surveillance: relevance, challenges, and prospects in a pandemic and post-pandemic world. J Clin Med. 2020;9(10):3372.

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