



Comparison of pregnancy outcomes and neonatal complications between COVID-19-vaccinated and unvaccinated pregnant women in Tabriz, Iran

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Abstract

Introduction: Insufficient information exists regarding the coronavirus disease 2019 (COVID-19) vaccination safety in pregnant women.

Objectives: The present study compared the pregnancy and fetal outcomes among COVID-19-vaccinated and unvaccinated pregnant women.

Patients and Methods: This cross-sectional study was conducted at Tabriz University of Medical Sciences (Tabriz, Iran) on 117 pregnant women (55 vaccinated women as the case group and 62 unvaccinated women as the control group) using census sampling in 2022. The maternal outcomes (death, admission to intensive care unit [ICU], premature birth, gestational hypertension, preeclampsia, oligohydramnios, and polyhydramnios) and neonatal outcomes (neonatal death, congenital disabilities, neonatal weight loss, admission to ICU, neonatal infection, neonatal fever, need for mechanical ventilation of the newborn, and one- and five-minute Apgar scores) were recorded. Then the two groups were compared using independent t-test, along with ANOVA and chi-square tests.

Results: The number of women without pregnancy outcomes was marginally lower in the case group than in the control group ($P=0.099$). Gestational hypertension ($P=0.312$) and preterm birth were lower among unvaccinated women than among vaccinated women but this difference was not significant ($P=0.089$). Hospitalization in the neonatal intensive care unit ($P=0.361$), neonatal fever ($P=0.259$), and neonatal infection ($P=0.079$) were more common in infants born to vaccinated mothers than in infants born to unvaccinated women, although the difference not significant.

Conclusion: Vaccination against COVID-19 appears to not be associated with an increased probability of maternal and neonatal complications.

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Introduction

Since the onset of the coronavirus disease 2019 (COVID-19) pandemic, significant efforts have been made to combat this global phenomenon (1). One of the most effective measures against severe acute respiratory syndrome (SARS) is vaccination. The efficacy and safety of COVID-19 vaccines in adults have been demonstrated in various demographic groups; however, their impact on pregnant women remains unclear due to insufficient data (2,3).

According to the unique physiological changes in the immune, cardiac, and pulmonary systems of pregnant women (4), they are at an increased risk of viral and bacterial respiratory infections (5) and also intensive care unit (ICU) admission (6). Infection with COVID-19 during pregnancy is also associated with increased rates of preterm birth and preeclampsia due to inflammatory

Key point

Insufficient information exists regarding the coronavirus disease 2019 (COVID-19) vaccination safety in pregnant women. This cross-sectional study was conducted on 117 pregnant women (55 vaccinated women as the case group and 62 unvaccinated women as the control group). All participants' maternal and neonatal outcomes were recorded; the results indicated that vaccination against COVID-19 is not associated with an increased probability of maternal and neonatal complications.

mechanisms (7). However, a previous study reported that most hospitalized pregnant women with COVID-19 were asymptomatic, resulting in the possible transmission of infection to others (8). Findings indicate the importance of preventative modalities, such as vaccination in this population (9).

Despite the high risk of COVID-19 infection, pregnant and lactating women have not participated in any early COVID-19

vaccine trials, resulting in insufficient data on vaccination decision for this population (10). There are still insufficient data for decision-making regarding COVID-19 vaccination during pregnancy. However, after assessing the risks, benefits, and lack of hazards on vaccination in pregnant women, most protocols recommend vaccination of pregnant women (11).

Objectives

The present study aimed to compare the pregnancy, and fetal outcomes of pregnant women vaccinated versus unvaccinated against COVID-19.

Patients and Methods

Study design

In this cross-sectional study, 117 pregnant women (55 vaccinated women as the case group and 62 unvaccinated women as the control group) were enrolled. This study was conducted at Al-Zahra hospital of Tabriz University of Medical Sciences Tabriz, Iran. We utilized the census sampling method. All pregnant women presenting to our hospital in 2022 were included in the study based on inclusion and exclusion criteria, as determined by the sampling method.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (a) age between 18 and 45; (b) pregnancy; (c) willingness to participate in the study; (d) vaccination of women in the case group and non-vaccination of women in the control group; and (e) presence of informed consent to participate in the study. Conversely, the exclusion criteria were: (a) COVID-19 vaccination beyond six months in the case group; (b) non-adherence to the prescribed interval between vaccine doses; (c) immunocompromised women; (d) women with a high-risk pregnancy; (e) pulmonary edema; (f) gestational diabetes; (g) a history of infectious diseases; (h) a history of pulmonary diseases; and abnormal pregnancies, including intrauterine insemination (IUI) and in vitro fertilization (IVF) (9).

Data collection

To record maternal and neonatal outcomes, we utilized a data collection form based on findings from studies examining the complications of COVID-19 vaccination during pregnancy. This form included questions on background information (age, blood type, and level of education), pregnancy records (pregnancy age, gravidity, mode of previous deliveries, and surgery history), maternal outcomes (death, ICU hospitalization, premature birth, gestational hypertension, preeclampsia, oligohydramnios, and polyhydramnios), fetal outcomes (miscarriage, intrauterine growth restriction, intrauterine fetal death), and neonatal outcomes (neonatal death, congenital disabilities, neonatal weight loss, ICU hospitalization, neonatal infection, neonatal fever, need for mechanical

ventilation of the newborn, and one- and five-minute Apgar scores).

The created data collection form was presented to five faculty members of the department of gynecology and obstetrics, two epidemiologists, and three pediatricians for their input on the information necessary to meet the research objectives. After considering their revisions and comments regarding eliminating any questions, the form was finally approved and conducted in this study. Using phone calls or in-person visits, one of the researchers evaluated the clinical course of the patients from three months before delivery to two weeks after delivery. All pregnancy-related complications were conducted by a perinatologist, while neonatologists examined neonatal complications. A research team member recorded the information on the data collection form.

Statistical analysis

The data were recorded in the data collection form by a research team member and then entered into SPSS software (version 25). The data were expressed as mean (standard deviation [SD]) and frequency (percentage). Furthermore, independent *t* test, ANOVA, and chi-square tests were employed for data comparisons. A *P* value < 0.05 was considered statistically significant in all tests.

Results

The mean (SD) age of the participants was 28.41 (5.59) years, and the mean (SD) gestational age was 36.14 (4.51) weeks. The comparisons between women's age ($P=0.259$) and gestational age revealed no significant differences between groups ($P=0.419$). A total of 52 women (44.44%) were pregnant for the second time. **Table 1** compares the participants' demographic and midwifery information.

A comparison of maternal outcomes revealed that the proportion of women without pregnancy outcomes was marginally lower in the case group than in the control group ($P=0.099$). In none of the groups, the maternal death was reported. One individual from each group was hospitalized in the ICU. Additionally, gestational hypertension ($P=0.312$) and preterm birth ($P=0.089$) were not significantly reduced in unvaccinated women versus vaccinated women. Other complications were not observed in any participants (**Table 2**).

Moreover, no participants exhibited miscarriage, intrauterine growth restriction, intrauterine fetal death, or fetal abnormalities ($P=0.999$). Regarding neonatal outcomes, none of the infants reported neonatal death, congenital disabilities, neonatal weight loss, or mechanical ventilation ($P=0.999$). Meanwhile, ICU hospitalization ($P=0.361$), neonatal fever ($P=0.259$), and neonatal infection ($P=0.079$) were not significantly more prevalent in the newborns of unvaccinated mothers than in the newborns of vaccinated mothers. Furthermore, the one- and five-minute Apgar scores were the same in the two groups ($P=0.999$; **Table 3**).

Table 1. Comparison of the demographic and midwifery information of the participants

Variables	Study groups (N=117)		P value
	Case group (n=55)	Control group (n=62)	
Maternal age (y)	27.69 (5.03)	30.09 (6.11)	0.259 ^a
Gestational age (wk)	37.55 (4.19)	36.03 (4.85)	0.419 ^a
Previous surgery type	Natural birth	31 (50%)	0.352 ^b
	Cesarean section	17 (27.41%)	
History of previous surgery	Yes	17 (27.41)	0.411 ^b
	No	45 (72.58%)	
Blood type	A	23 (37.09%)	0.559 ^c
	B	10 (16.12%)	
	AB	18 (29.03%)	
	O	11 (17.74%)	
Education level	Illiterate	8 (12.90%)	0.255 ^c
	Non-academic	30 (48.38%)	
Gravidity	Academic	24 (38.70%)	0.637 ^c
	1	11 (20%)	
	2	30 (54.54%)	
	3	10 (18.18%)	
	>3	4 (7.27%)	

^a ANOVA test; ^b Independent t test; ^c Chi-square test.

Table 2. Comparison of the pregnancy outcomes of the participants

Variables	Study groups (n=117)		P value ^a
	Case group (n=55)	Control group (n=62)	
No pregnancy complications	45 (81.81%)	55 (88.70%)	0.099
Hospitalization ICU	1 (1.81%)	1 (1.61%)	0.859
Gestational hypertension	4 (7.27%)	4 (6.45%)	0.312
Preterm birth	5 (9.09%)	2 (3.22%)	0.089
Preeclampsia	0 (0%)	0 (0%)	0.999
Oligohydramnios	0 (0%)	0 (0%)	0.999
Polyhydramnios	0 (0%)	0 (0%)	0.999

^a Chi-square test.

Table 3. Comparison of fetal and neonatal outcomes in the participants

Variables	Study groups (n=117)		P value ^a
	Case group (n=55)	Control group (n=62)	
ICU hospitalization	5 (9.09%)	3 (4.83%)	0.361
Neonatal fever	8 (14.54%)	5 (8.06%)	0.259
Neonatal infection	3 (5.45%)	(1.61%)	0.079

^a Chi-square test.

Fetal information (miscarriage, intrauterine growth restriction, intrauterine fetal death and fetal malformations) and neonatal outcomes (neonatal death, congenital disabilities, low-birth weight, ICU hospitalization, neonatal infection, need for mechanical ventilation of the newborn, and one- and five-minute Apgar scores) are provided in [Table 3](#).

Discussion

Several evidence show the safety and efficacy of vaccines for pregnant women during the COVID-19 pandemic. According to studies, the benefits of vaccination for pregnant women outweigh the known or potential risks. Countries like the United States and Canada and European countries like England and France have

developed strategies to encourage pregnant women to receive the COVID-19 vaccine. According to the recent findings, vaccination against COVID-19 reduces the risk of infection and hospitalization by half. These encouraging statistics can reduce pregnant women's reluctance to vaccinate and encourage relevant departments to develop policies to increase pregnant women's acceptance of these vaccines (13-17).

Findings of the present study can be classified into three main categories. The first category compares pregnancy outcomes among vaccinated and unvaccinated pregnant women. There was no significant difference in maternal complications between the two groups. However, complications such as gestational hypertension and premature birth were marginally more common in the vaccinated group than in the unvaccinated group.

The current findings are consistent with those of several similar studies. Peretz et al, who examined the pregnancy outcomes of 390 women vaccinated with the Pfizer vaccine, found that vaccination against COVID-19 was associated with a non-significant increase in preterm birth and gestational hypertension (16). All participants in the current study were vaccinated with the Sinopharm vaccine, making it difficult to compare our results with those of the study by Peretz et al (16).

Conversely, Rottenstreich et al reported that vaccination of pregnant women against COVID-19 could increase the maternal outcomes (18). Nevertheless, similar to our findings, they observed that vaccination might contribute to the rise in certain maternal outcomes, such as preterm birth. Due to our study's small sample size, it is impossible to conclude with certainty that the increase in these complications results from a vaccination. According to the findings of multiple studies, the incidence of maternal complications following vaccination is extremely low (13-17).

In the present study, there was no significant difference in the incidence of maternal complications among pregnant women vaccinated in the first, second, or third trimester. Notably, the timing of vaccination was not investigated in our study, which represents one of its limitations. Consistent with the current findings, a large-scale study conducted in the United States found no maternal deaths. Vaccination against COVID-19 during pregnancy was associated with an increase in life-threatening pregnancy complications, including thromboembolism, eclampsia, and preeclampsia, stillbirth, and also blood loss (19,20).

Vaccination had comparable effects on fetal complications, according to the second category of the present results. In our study, no cases of fetal complications were observed. In accordance with our findings, Gray et al found that messenger RNA vaccines against COVID-19 created robust humoral immunity in pregnancy, with reactogenicity and immunogenicity alike to that observed in non-pregnant women (21).

Pregnant women's immune protection of the fetus along

with the accumulation of B and T cells in the immune system of the fetus has been hypothesized to prevent COVID-19 or weakened COVID-19 from causing fetal complications; however, further clinical and animal experiments are required for validation of this hypothesis (22).

In addition, a previous study demonstrated that vaccination could induce effective IgG transfer from mother to infant. A longer interval between injection and delivery indicated higher antibody levels in the mother and newborn. After receiving a second dose of the vaccine, both the mother and newborn's antibody levels increased. These results indicate that maternal vaccination protects newborns. The importance of informing women about the risks of COVID-19 during pregnancy and the benefits of vaccination, as well as the safety and efficacy of vaccination during pregnancy, is highlighted by these findings (23,24).

The third category of the present results concerned neonatal complications following COVID-19 vaccination during pregnancy. There was no significant correlation between vaccination during pregnancy and the incidence of neonatal complications. Nonetheless, vaccination marginally increased ICU hospitalization, neonatal fever, and neonatal infection rates.

The current findings are consistent with those of Bleicher et al and Theiler et al, who determined that vaccination did not affect the incidence of neonatal complications (25, 26). In their study, the incidence of neonatal infection and fever slightly increased in infants whose mothers had been vaccinated during the third trimester of pregnancy. It is believed that exposure of the fetus to the increased activity of the mother's immune system after vaccination can stimulate the immune system of the newborn. As a result, newborns become more sensitive to pathogenic microorganisms after birth, which can lead to infection and neonatal fever, although further research is required.

Conclusion

According to the findings of this study, vaccination against COVID-19 did not result in high-risk complications. In addition, there were no differences between vaccinated and unvaccinated women regarding maternal outcomes (death, ICU hospitalization, premature birth, gestational hypertension, preeclampsia, oligohydramnios, and polyhydramnios), fetal outcomes (miscarriage, intrauterine growth restriction and intrauterine fetal death), and neonatal outcomes (neonatal death, congenital disabilities, neonatal weight loss, ICU hospitalization, neonatal infection, neonatal fever, need for mechanical ventilation of the newborn, and one- and five-minute Apgar scores). Further investigation is required, but it appears that vaccination against COVID-19 is not associated with an increased risk of maternal and neonatal complications.

Limitations of the study

This study had several limitations. The sample size was the first limitation. The second limitation was that vaccination

times were not accurately recorded. Thirdly, neither the immune nor IgG levels of pregnant women were evaluated. Fourth, the history of COVID-19 could not be assessed because no pregnant women were hospitalized during the study due to COVID-19. However, pregnant women may have had this infection but were not hospitalized due to mild symptoms or the absence of symptoms. This may have contributed to the occurrence of complications observed in our study. It is suggested that future research eliminate the limitations of the current investigation.

Authors' contribution

Conceptualization: ST, MahD.

Methodology: ST, MahD.

Validation: MahD, MarD.

Formal analysis: MahD, MarD.

Investigation: ST, MarD.

Resources: ST, MarD.

Data curation: MahD, MarD.

Writing—original draft: ST, MahD.

Writing—review and editing: ST, MarD.

Visualization: ST, MahD.

Supervision: ST.

Project administration: ST, MahD.

Funding acquisition: ST.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. This study was approved by the Ethics Committee of Tabriz University of Medical Sciences (Ethical code #IR.TBZMED.REC.1401.164). After being briefed on the study's objectives, all participants and their spouses signed a written consent form. Participation, nonparticipation, and withdrawal from the study were free of charge. The authors observed all ethical considerations (including plagiarism, data fabrication, and double publication). Besides, ethical issues (including plagiarism, data fabrication and double publication) have been completely observed by the authors.

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