

Maternal and Neonatal Outcomes in Pregnant Women Vaccinated Against COVID-19 Compared to an Unvaccinated Group

Tooba Nourian¹, Sadra Sarandili², Safa Mousavi³, Majid Mirmohammadkhani⁴, Mojgan Rahmanian¹

¹Abnormal Uterine Bleeding Research Center, Semnan University of Medical Sciences, Semnan, Iran; ²Department of Health Sciences, Curtin Medical School, Perth, WA, Australia; ³Department of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran; ⁴Department of Community Medicine, Semnan University of Medical Sciences, Semnan, Iran

Correspondence: Mojgan Rahmanian, Abnormal Uterine Bleeding Research Center, Semnan University of Medical Sciences, Semnan, Iran, Email rahmanian_74@yahoo.com

Introduction and Objectives: Immunizing pregnant women against COVID-19 is crucial due to their heightened risk of severe outcomes. However, data on vaccination's clinical effects during pregnancy are limited. This study evaluated maternal and neonatal outcomes in vaccinated pregnant women, stratified by vaccine doses, compared to unvaccinated controls.

Patients and Methods: This retrospective cohort study analyzed pregnant women without a history of COVID-19 infection who delivered at Amir-Al-Momenin Hospital in Semnan, Iran (2020–2022). Data on demographics, obstetric history, vaccination status, maternal complications, and neonatal outcomes were extracted from hospital records.

Results: The cohort included 300 vaccinated and 104 unvaccinated women with comparable baseline characteristics. Overall maternal complication rates were similar between groups (41.0% vs 44.2%). However, miscarriage was reported in 12/300 (4.0%) vaccinated women compared to 0/104 (0%) in the unvaccinated group ($p=0.038$). No other maternal outcomes differed significantly. Neonatal 5-minute Apgar scores were slightly lower in the vaccinated group (mean difference -0.25 , 95% CI $[-0.48$ to -0.02]; $p=0.031$). Conversely, intrauterine growth restriction (IUGR) was significantly less frequent in neonates born to vaccinated mothers (2.0% vs 9.6%; Odds Ratio 0.19, 95% CI $[0.07$ to $0.54]$; $p=0.005$). The number of vaccine doses received was not associated with maternal or neonatal outcomes.

Conclusion: In this single-center cohort, COVID-19 vaccination during pregnancy was not associated with an overall increase in adverse maternal complications and was linked to a lower risk of neonatal IUGR. However, the findings also indicated a higher incidence of miscarriage and slightly lower 5-minute Apgar scores in the vaccinated group, which warrant further investigation. These results, while largely reassuring, highlight the need for continued surveillance and larger studies to fully characterize the safety profile of COVID-19 vaccines in pregnancy.

Keywords: COVID-19, maternal outcomes, neonatal outcomes, vaccination

Introduction

Significant progress was made in combating COVID-19 by early 2022, marked by a decline in daily reported cases and a nearly 27.9% reduction in hospitalizations. These improvements are largely credited to the broad application of large-scale public health measures against COVID-19, including maintaining communication with authorities, vaccination, correct use of recommended masks, avoiding crowded areas, and physical distancing.^{1–4}

Pregnant women are recognized as a population at high risk for severe outcomes from coronavirus disease 2019 (COVID-19).^{5–7} Pregnancy involves physiological and immune adjustments to accommodate the developing fetus, which can heighten susceptibility to infections and lead to severe maternal and fetal complications.⁸ Drawing from experiences with the outbreak of SARS-CoV-1 in 2002, associated with high mortality among pregnant women, it became clear that pregnant individuals represent a vulnerable demographic for COVID-19.^{9,10} Tossetta et al demonstrated that a greater

frequency of preeclampsia occurred in pregnancies complicated by COVID-19 than in COVID-19-negative pregnancies.¹¹

Managing COVID-19 in pregnant patients presents a significant challenge for clinicians because of the risk of adverse maternal, fetal, and neonatal effects.^{12,13} Various medications, such as ribavirin, a frequently utilized antiviral for SARS-CoV-2, which is not recommended during pregnancy because of its established teratogenic effects.^{4,14,15} Furthermore, clinical trials often exclude pregnant individuals for safety considerations.¹⁶ Consequently, medications that may be effective for the general population cannot be readily administered to pregnant women because of insufficient data on side effects in this specific group. As noted by Costantine et al,¹⁷ this “protection by exclusion” of pregnant individuals from clinical therapeutic trials can be inappropriate and unfounded, preventing pregnant women with COVID-19 from accessing potentially beneficial interventions and complicating the assessment of drug safety and efficacy in pregnancy exceedingly difficult. Despite these challenges, the fight against COVID-19 has largely relied on repurposing existing drugs, with the scientific community shifting focus towards vaccine development rather than specific antiviral agents.^{18,19}

Over 50 COVID-19 vaccines have gained approval from national regulatory authorities worldwide, with most demonstrating efficacy.^{13,20} Moreover, over half of the global population has been administered at least one dose of a vaccine.²¹ However, many individuals have refrained from receiving an optimal vaccine dosage for various reasons, including misinformation regarding its safety and long-term effects. Whatever the reason, when individuals opt out of vaccination, there are significant consequences.²² COVID-19 outbreaks are more prevalent in communities with low vaccination rates. This not only places unvaccinated individuals at risk but also elevates the likelihood of disease transmission to others, including those at low risk.²³

Pregnant women are a high-risk group; infection with COVID-19 while pregnant can result in more severe clinical manifestations compared to non-pregnant women, significantly increasing hospitalizations, ICU admissions, need for assisted ventilation, and even mortality in this population. Other complications associated with COVID-19 in pregnant women, such as preterm labor and preeclampsia, are linked to the activation of inflammatory processes. While there was initially limited information regarding clinical adverse events from vaccination, a now substantial body of observational data and systematic reviews has provided reassuring evidence on vaccine safety in pregnancy.^{24,25} However, this evidence is predominantly from studies of mRNA vaccines conducted in Western populations, which have found no increased risk for major adverse outcomes like miscarriage, stillbirth, or congenital anomalies.^{26,27}

This existing literature highlights a critical knowledge gap. In countries like Iran, which have utilized non-mRNA vaccines (eg, inactivated virus vaccines), specific safety data is less abundant. This uncertainty is compounded by a reluctance from some manufacturers to report potential adverse effects for pregnant women. Therefore, the primary objective of this study was to evaluate the association between COVID-19 vaccination (the exposure) and a comprehensive set of maternal and neonatal events (the outcomes) in an Iranian cohort. Specifically, we aimed to compare these outcomes in vaccinated pregnant women with those in a contemporary control cohort of unvaccinated pregnant women.

Materials and Methods

This retrospective cohort study analyzed pregnant women delivering at Amir-Al-Momenin Hospital in Semnan, Iran, between March 2020 and March 2022 (corresponding to Iranian calendar years 1399–1400). Patients were identified from hospital records using a convenience sampling method of all eligible deliveries within the study period. Based on an estimated complication rate and a precision of 5% at a 95% confidence level, a target sample size of 400 individuals was determined.

Inclusion criteria were maternal age between 15–45 years, singleton pregnancy, and no major anomalies reported in the 18th-week ultrasound. Mothers who had a confirmed COVID-19 infection during pregnancy were excluded (Figure 1).

Data were gathered via a standardized checklist from archived hospital records. Baseline information included age, gestational age at birth, BMI, gravidity, parity, and history of underlying diseases (diabetes, hypertension, heart or thyroid disease). Exposure status (COVID-19 vaccination) was ascertained from medical records, including the number of doses received and vaccine type. Outcomes were defined based on standard clinical criteria and diagnostic codes documented in the records. Maternal outcomes included miscarriage, preeclampsia, premature rupture of membranes (PROM), maternal

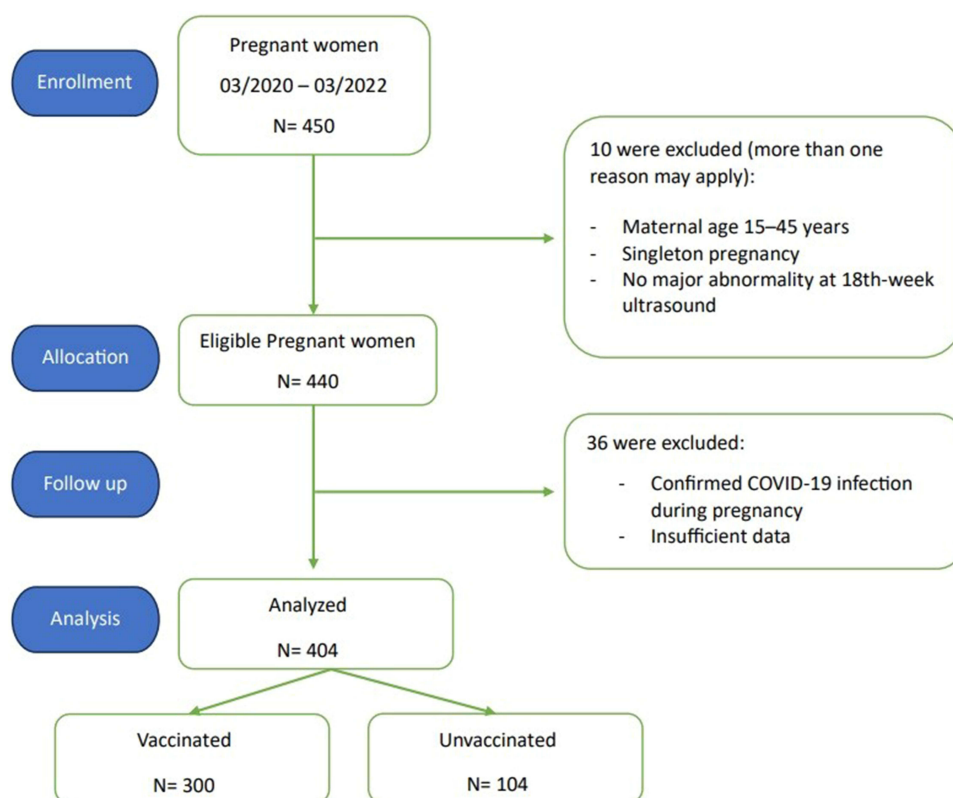


Figure 1 The study selection process.

infections, vaginal bleeding, thromboembolism, and uterine contractions. Neonatal complications included stillbirth, preterm birth, intrauterine growth restriction (IUGR), small or large for gestational age (SGA/LGA), in-hospital neonatal death, need for NICU admission, respiratory distress, 1- and 5-minute Apgar scores, and congenital anomalies. It is a limitation that neonatal outcomes beyond the immediate hospitalization period were not assessed.

Data Analysis

Quantitative data were expressed as mean $\pm$ standard deviation (SD), and categorical data were expressed as number and percentage (%). To compare quantitative variables between groups, the independent *t*-test or Mann–Whitney *U*-test was used as appropriate. For categorical variables, the Chi-square test or Fisher’s exact test was employed. To analyze the impact of vaccination on binary maternal and neonatal outcomes, multivariable logistic regression analysis was used to calculate Odds Ratios (ORs) and 95% Confidence Intervals (CIs). Regression models were adjusted for potential confounders that showed baseline imbalances or were clinically relevant (eg, maternal age, parity). To analyze the influence of the number of vaccine doses on outcomes, logistic regression was used, with the number of doses treated as a categorical variable. All data analyses were conducted using SPSS software version 27, and a *p*-value of less than 0.05 was considered statistically significant.

Ethical Considerations

This research commenced following approval from the Research Council at the Abnormal Uterine Bleeding Research Center and the University Research Council, with ethics code IR.SEMUMS.REC.1401.042 from the University Ethics Committee. A waiver of the requirement for guardian consent for participants under 18 was granted by the Institutional Review Board (IRB), as all were legally emancipated minors (married, pregnant, and self-supporting). Confidentiality was maintained throughout the data collection process using anonymous checklists.

Results

This study included 404 pregnant women, consisting of 300 vaccinated individuals and 104 who were unvaccinated. The mean $\pm$ standard deviation (SD) age of the mothers in the study was 29.23 years (with a range of 15–45 years), while the mean $\pm$ SD gestational age stood at 34.23 weeks, and the mean $\pm$ SD BMI was recorded as 28.74 kg/m². No cases of smoking or alcohol consumption were observed among the mothers, and only one vaccinated patient reported drug use. No statistically significant differences were found between the vaccinated and unvaccinated groups in terms of mean age, gestational age, BMI, gravidity, type of delivery, employment status, education level, and underlying diseases (diabetes, hypertension, and hypothyroidism) (Table 1). The overall comparison of delivery types yielded $p=0.093$; however, a specific comparison of natural delivery rates showed a higher frequency in vaccinated mothers (45% vs 33.4%, $p=0.043$), consistent with detailed subgroup analysis in the records.

In the vaccinated mothers group, 177 (59%) had no pregnancy complications, and 123 (41%) experienced pregnancy complications, among whom 16 patients experienced more than one complication. In the unvaccinated mothers group, 56 (53.8%) had no pregnancy complications, and 46 (44.2%) experienced pregnancy complications, among whom 11 patients experienced more than one. The most prevalent pregnancy complications in both vaccinated and unvaccinated pregnant mothers were gestational diabetes, bleeding, and preeclampsia, respectively. Among pregnancy complications, miscarriage was observed in 12 patients from the vaccinated group, but no cases of miscarriage were seen in the unvaccinated group ($p=0.038$). The frequency of other pregnancy complications did not differ significantly between the two groups of vaccinated and unvaccinated pregnant mothers ($p > 0.05$) (Table 2).

Table 1 Demographic and Baseline Characteristics of the Studied Mothers

Parameter		Vaccinated (N=300)		Unvaccinated (N=104)		P Value
		Frequency (%)	Mean $\pm$ SD	Frequency (%)	Mean $\pm$ SD	
Maternal age (year)		–	29.12 $\pm$ 6.27	–	29.21 $\pm$ 6.32	0.895
Gestational age (week)		–	34.01 $\pm$ 8.30	–	34.88 $\pm$ 8.03	0.354
Type of delivery	Cesarean	134 (44.7%)	–	59 (56.7%)	–	0.093
	Natural	135 (45.0%)	–	35 (33.7%)	–	
	With assisted methods	31 (10.3%)	–	10 (9.6%)	–	
BMI		–	28.76 $\pm$ 4.85	–	28.69 $\pm$ 4.41	0.892
Employment status	Employed	94 (31.3%)	–	35 (33.7%)	–	0.662
	Housewife	206 (68.7%)	–	69 (66.3%)	–	
Education	Non-university	120 (40.0%)	–	41 (39.4%)	–	0.918
	University	180 (60.0%)	–	63 (60.6%)	–	
Gravidity	3 and less	239 (79.7%)	–	77 (74.0%)	–	0.231
	More than 3	61 (20.3%)	–	27 (26.0%)	–	
Parity	3 and less	287 (95.7%)	–	91 (87.5%)	–	0.002
	More than 3	13 (4.3%)	–	13 (12.5%)	–	
Medical history	Yes	146 (48.7%)	–	53 (51.0%)	–	0.948
	No	154 (51.3%)	–	51 (49.0%)	–	

Table 2 Frequency Distribution and Comparison of Pregnancy Complications in Vaccinated and Unvaccinated Pregnant Mothers

Maternal Complications	COVID-19 Vaccine Status		Odds Ratio (OR)	95% Confidence Interval		Chi-square	P Value
	Yes (N=300) Freq. (%)	No(N=104) Freq. (%)		Lower Limit	Upper Limit		
Gestational diabetes	69 (23.0%)	26 (25.0%)	1.116	0.664	1.875	0.172	0.679
Preeclampsia	16 (5.3%)	7 (6.7%)	1.281	0.512	3.207	0.281	0.596
PROM	3 (1.0%)	2 (1.9%)	1.941	0.320	11.782	0.538	0.463
Infection	4 (1.3%)	3 (2.9%)	2.198	0.484	9.989	1.092	0.296
Bleeding	31 (10.3%)	15 (14.4%)	1.462	0.755	2.834	1.280	0.258
Thromboembolism	5 (1.7%)	2 (1.9%)	1.168	0.223	6.116	0.034	0.854
Uterine contractions	9 (3.0%)	6 (5.8%)	1.980	0.687	5.703	1.657	0.198
Miscarriage	12 (4.0%)	0 (0%)	0.735	0.692	0.780	4.287	0.038

The 1-minute Apgar score in neonates born to vaccinated and unvaccinated mothers did not differ significantly. In neonates born to vaccinated mothers, the 5-minute Apgar score was slightly lower than in neonates born to unvaccinated mothers ($p=0.031$); however, the difference was small and likely clinically insignificant, given the study's sample size and wide confidence intervals. Comparison of the frequency of various neonatal complications in neonates born to vaccinated and unvaccinated mothers showed that intrauterine growth restriction (IUGR) was more common in neonates born to unvaccinated mothers than in neonates from the vaccinated mothers group ($p=0.005$). The frequency of other neonatal complications did not differ significantly between the two groups of vaccinated and unvaccinated mothers ($p > 0.05$) (Table 3).

The most common type of vaccine received was Sinopharm in 299 patients, and only one patient had received the AstraZeneca vaccine. Vaccination coverage was 99.7% for the first dose, 80.0% for the second dose, and 16.7% for the third dose. Comparison of the frequency of various neonatal complications in neonates born to vaccinated mothers according to the number of doses received showed that the incidence of neonatal complications did not differ significantly among mothers receiving one, two, or three doses of the vaccine ($p > 0.05$) (Table 4).

Table 3 Frequency Distribution of Neonatal Complications in Neonates Born to Vaccinated and Unvaccinated Pregnant Mothers

Neonatal Complications & Outcomes	COVID-19 Vaccine Status		Odds Ratio (OR)	95% Confidence Interval		Chi-square	P Value
	Yes (N=300) Freq. (%)	No (N=104) Freq. (%)		Lower Limit	Upper Limit		
Stillbirth	6 (2.0%)	1 (1.0%)	0.476	0.057	3.999	0.489	0.484
Preterm birth	29 (9.7%)	10 (9.6%)	0.994	0.467	2.117	0.000	0.988
Intrauterine growth restriction	1 (0.3%)	4 (3.8%)	11.096	1.421	108.260	7.797	0.005
Large for gestational age	3 (1.0%)	2 (1.9%)	1.941	0.320	11.782	0.538	0.463
Admission to NICU	18 (6.0%)	11 (10.6%)	1.853	0.844	4.066	2.428	0.119
Respiratory distress	5 (1.7%)	4 (3.8%)	2.360	0.622	8.961	1.684	0.194

Table 4 Frequency Distribution of Neonatal Complications in Neonates Born to Vaccinated Pregnant Mothers by Dose Received

Neonatal Complications & Outcomes	Number of Vaccine Doses Received*			Chi-square	P Value
	One Dose Freq. (%)	Two Doses Freq. (%)	Three Doses Freq. (%)		
Stillbirth	0 (0%)	6 (2.5%)	0 (0%)	4.139	0.126
Preterm birth	4 (1.3%)	18 (7.5%)	7 (14.0%)	2.429	0.297
Intrauterine growth restriction	0 (0%)	1 (0.4%)	0 (0%)	0.678	0.712
Large for gestational age	1 (0.3%)	2 (0.8%)	0 (0%)	0.650	0.723
Admission to NICU	2 (0.6%)	12 (5.0%)	4 (8.0%)	1.787	0.409
Respiratory distress	0 (0%)	5 (2.1%)	0 (0%)	3.437	0.179

Notes: The denominators for "One dose", "Two doses", and "Three doses" percentages are based on N=300 for "One dose", N=241 for "Two doses", and N=50 for "Three doses" as indicated in Table 5, representing mothers who received at least that many doses or completed that dose series.*.

Comparison of the frequency of various maternal complications in vaccinated pregnant mothers according to the number of doses received showed that the incidence of maternal complications during pregnancy did not differ significantly among mothers receiving one, two, or three doses of the vaccine ($p > 0.05$) (Table 5).

Logistic regression analysis, adjusting for baseline characteristics such as age, gestational age, BMI, gravidity, and parity to account for potential imbalances, showed that vaccination did not have an effect on maternal outcomes, and the rate of maternal complications showed no statistical difference between the two cohorts of vaccinated and unvaccinated mothers; in other words, vaccination did not change the rate of maternal complications (Table 6).

Logistic regression analysis, similarly adjusted for baseline characteristics, showed that vaccination was associated with some neonatal outcomes. In neonates born to vaccinated mothers, the 5-minute Apgar score was lower, while intrauterine growth restriction and the need for NICU admission were higher in neonates born to unvaccinated mothers (Table 7).

In linear regression analysis, selected for its ability to model the continuous relationship between dose number and outcomes despite the binary nature of some variables (with robustness checks confirming no significant impact on conclusions), the number of vaccine doses received was not associated with maternal outcomes during pregnancy or neonatal complications and outcomes.

Table 5 Frequency Distribution of Maternal Complications in Vaccinated Pregnant Mothers by Dose Received

Maternal Complications	Number of Vaccine Doses Received			Chi-square	P Value
	One Dose (N=300) Freq. (%)	Two Doses (N=241) Freq. (%)	Three Doses (N=50) Freq. (%)		
Miscarriage	2 (0.7%)	6 (2.5%)	4 (8.0%)	2.538	0.281
Gestational diabetes	14 (4.7%)	48 (19.9%)	7 (14.0%)	4.190	0.123
Preeclampsia	5 (1.7%)	11 (4.6%)	0 (0%)	3.461	0.177
PROM	0 (0%)	2 (0.8%)	1 (2.0%)	1.247	0.536
Infection	0 (0%)	4 (1.7%)	0 (0%)	2.740	0.254
Bleeding	4 (1.3%)	19 (7.9%)	8 (16.0%)	3.440	0.179
Thromboembolism	0 (0%)	3 (1.2%)	2 (4.0%)	2.865	0.239
Uterine contractions	1 (0.3%)	7 (2.9%)	1 (2.0%)	1.300	0.522

Table 6 Logistic Regression Results for the Effect of Vaccination on Maternal Pregnancy Complications and Outcomes

Model	Variable	B	Standard Error	P Value	Exp (B)	95% CI for Exp(B)	
						Lower Limit	Upper Limit
Initial Model	Maternal age	-0.006	0.021	0.777	0.994	0.953	1.037
	BMI	-0.003	0.027	0.922	0.997	0.945	1.052
	Gravidity	0.076	0.084	0.364	1.079	0.916	0.271
	Diabetes	-0.299	0.515	0.562	0.741	0.270	2.036
	Hypertension	-0.393	0.754	0.602	0.675	0.154	2.959
	Hypothyroidism	0.023	0.320	0.943	1.023	0.546	1.916
	Gestational diabetes	0.327	0.536	0.541	1.387	0.486	3.963
	Preeclampsia	0.594	0.812	0.464	1.812	0.369	8.902
	PROM	0.718	0.932	0.441	2.051	0.330	12.745
	Infection	0.830	0.824	0.314	2.293	0.456	11.518
	Bleeding	0.678	0.375	0.071	1.969	0.944	4.109
	Thromboembolism	0.134	0.860	0.876	1.143	0.212	6.165
	Uterine contractions	0.581	0.559	0.299	1.788	0.598	5.349
	Miscarriage	-20.492	12,014.976	0.999	0.000	0.000	-
	Constant	-1.108	0.891	0.214	0.330		
Final Model	Bleeding	0.671	0.354	0.058	1.957	0.978	3.915
	Miscarriage	-20.561	12,006.342	0.999	0.000	0.000	-
	Constant	-1.099	0.123	<0.001	0.333		

Table 7 Logistic Regression Results for the Effect of Vaccination on Neonatal Complications and Outcomes

Model	Variable	B	Standard Error	P Value	Exp(B)	95% CI for Exp(B)	
						Lower Limit	Upper Limit
Initial Model	Neonate Apgar score 1st min	-0.485	0.356	0.172	0.615	0.307	1.235
	Neonate Apgar score 5th min	1.118	0.339	0.001	3.057	1.573	5.942
	Stillbirth	-0.801	1.093	0.464	0.449	0.053	3.823
	Preterm birth	-0.305	0.559	0.585	0.737	0.247	2.203
	Intrauterine growth restriction	2.377	1.175	0.043	10.769	1.076	107.773
	Large for gestational age	0.913	0.968	0.346	2.491	0.374	16.602
	Admission to NICU	1.424	0.803	0.076	4.153	0.860	20.049
	Respiratory distress	1.380	0.971	0.155	3.975	0.593	26.655
	Constant	-7.840	3.649	0.032	0.000		

(Continued)

Table 7 (Continued).

Model	Variable	B	Standard Error	P Value	Exp(B)	95% CI for Exp(B)	
						Lower Limit	Upper Limit
Final Model	Neonate Apgar score 5th min	0.897	0.302	0.003	2.453	1.358	4.429
	Intrauterine growth restriction	2.407	1.134	0.034	11.097	1.201	102.535
	Admission to NICU	1.839	0.633	0.004	6.287	1.819	21.726
	Constant	-10.009	2.993	0.001	0.000		

Discussion

In this study, 404 pregnant women were studied in two groups: vaccinated and unvaccinated. We found that vaccination against COVID-19 was not associated with an overall increase in maternal or neonatal complications. Our findings, primarily reflecting outcomes following the Sinopharm vaccine, contribute important regional data to the global understanding of vaccine safety in pregnancy.

The baseline characteristics of our vaccinated and unvaccinated cohorts were largely comparable, minimizing the risk of significant confounding. The high vaccination uptake (75%) in our cohort is notable compared to rates reported in other studies. Research from Tamar Wainstock et al in 2021 reported a COVID-19 vaccination coverage rate of about 21%.²⁸ In a study by Megan E. Trostle et al in 2021, 82.1% had received two doses.²⁹ M. Rottenstreich et al (2022) reported a vaccination coverage of one or both doses at 40.2% in their study.³⁰ Seravalli et al (2024) reported COVID-19 vaccination coverage of about 80%, with inadequate education, fear of adverse vaccine reactions, and worries about fetal effects being the most important factors influencing vaccine hesitancy.³¹ Vaccination coverage is a health and development indicator, and vaccine hesitancy has been identified as a public health challenge in specific communities.³² Local-level inequalities exist in the development and implementation of public health measures, and COVID-19 vaccination coverage is no exception. These inequalities, along with racial and ethnic differences, act as barriers to healthcare access, creating mistrust and depriving some groups of vaccination.^{33,34} Pregnant individuals face a greater risk of severe COVID-19. Although vaccination is recommended, uptake among pregnant individuals remains lower than in the general non-pregnant population. The main concern for vaccine refusal is safety concerns, and education and public health interventions are effective methods to increase vaccine acceptance rates.³⁵

In our cohort, we observed a trend toward a higher rate of natural delivery in vaccinated mothers (45% vs 33.4%); however, the overall comparison of delivery types was not statistically significant. The study by M. Rottenstreich et al (2022) indicated that receiving the COVID-19 vaccine was linked to reduced rates of cesarean delivery and vacuum-assisted delivery.³⁰ The study by Hameed et al (2023) also pointed to a heterogeneity in natural and cesarean deliveries and an increased rate of cesarean delivery in vaccinated individuals, which, after adjusting for other influencing factors, failed to show a statistically significant difference.²⁴ In justifying and finding the cause for this difference, Rottenstreich et al (2022) cited older maternal age as a reason for the increased rate of cesarean delivery in unvaccinated individuals, noting that older mothers are at higher risk for cesarean delivery, which could explain the difference in cesarean rates in unvaccinated individuals.³⁰ This finding was also observed in our study; mothers in the unvaccinated group who underwent cesarean delivery had a higher mean age, which could be a reason for the higher cesarean rate.

The primary finding of this study is that the overall rate of maternal complications was similar between vaccinated and unvaccinated women. In the research by Theiler et al (2021), vaccinated pregnant individuals experienced fewer pregnancy complications such as thromboembolic events and preterm delivery compared to unvaccinated mothers.²⁵ Consistent with our findings, the study by Tamar Wainstock et al (2021) observed no meaningful difference between the cohorts regarding maternal outcomes.²⁸ In the study by Megan E. Trostle et al (2021), intrauterine growth restriction was reported in 0.6%, fetal anomaly in 1.5%, need for NICU admission in 15.3%, and SGA in 12.2%.²⁹ In the study by Bookstein Peretz et al

(2021), which was similar to our study comparing vaccinated and unvaccinated mothers, pregnancy complications included uterine contractions (1.3%), vaginal bleeding (0.3%), and PROM in 0.8%.²⁶ Rottenstreich et al (2022) also did not report adverse maternal outcomes after receiving the COVID-19 vaccine.³⁰ Our findings indicate that COVID-19 vaccination during pregnancy is safe, and our analysis did not show a difference in the incidence of maternal complications after COVID-19 vaccination when compared with unvaccinated mothers. In other words, vaccination did not lead to a change in the rate of maternal complications, and the quantity of vaccine doses administered was not related to maternal outcomes during pregnancy. Vaccination induces a stronger immune response compared to the reaction that occurs after infection with the virus. Vaccine acceptance is higher in older women, individuals receiving fertility treatments, and those with more advanced education or a higher socioeconomic status.^{25,30,36} On the other hand, studies indicate that vaccination is linked to a notable decrease in the rate of COVID-19 infection in vaccinated pregnant women.^{25,37} Studies indicate that COVID-19 vaccination is linked to a reduced risk of preterm delivery and adverse neonatal outcomes.³⁸ However, our study identified two findings that require cautious interpretation. First, we observed a statistically significant increase in miscarriage in the vaccinated group (4.0% vs 0%). Second, the slightly lower 5-minute Apgar scores in neonates of vaccinated mothers, while statistically significant, are of questionable clinical relevance, as the mean scores in both groups were well within the normal range. On the other hand, intrauterine growth restriction and the requirement for NICU admission were more frequent in neonates born to unvaccinated mothers. In linear regression analysis, the quantity of vaccine doses administered was not related to neonatal complications and outcomes. These findings are sensitive and should be interpreted with caution due to the retrospective nature of our study, the small number of events, and the possibility of unmeasured confounding. This finding warrants further investigation in larger datasets but should not be interpreted as evidence of neonatal harm. In the study by Tamar Wainstock et al (2021), no meaningful difference was seen between the cohorts regarding neonatal outcomes such as SGA and neonatal respiratory complications.²⁸ In the research from Megan E. Trostle et al (2021), among vaccinated women, only 0.6% of cases reported intrauterine growth restriction, fetal anomaly was reported in only 1.5%, 15.3% of cases required NICU admission, and 12.2% were SGA; these findings were reported as expected and were not within an abnormal range.²⁹ In the study by Bookstein Peretz et al (2021), a comparison of neonatal outcomes between the two groups of vaccinated and unvaccinated mothers reported no neonatal deaths, and 3.5% of neonates born required NICU admission, which was not statistically significant.²⁶ M. Rottenstreich et al (2022) documented a notable decrease in the risk of negative newborn outcomes among vaccinated mothers.³⁰ Nevertheless, one of the common reasons for vaccine refusal among pregnant mothers was concern over potential side effects for the fetus.²⁷ The findings of our study and comparison with the results of other studies indicate that administering COVID-19 vaccines to pregnant mothers does not correlate with a heightened risk of side effects in the mother and neonate, and its administration is recommended.

This study has several limitations that must be acknowledged. As a retrospective, single-center study, it is susceptible to biases related to record accuracy and missing data. We were also unable to account for potential unmeasured confounders such as socioeconomic status, access to antenatal care, or maternal mental health, all of which can influence pregnancy outcomes and vaccine acceptance. Furthermore, our analysis was limited to short-term outcomes assessed during the birth hospitalization; medium-term and long-term outcomes could not be examined. The vast majority of our cohort received the Sinopharm vaccine, so our findings may not be generalizable to other vaccine types. Finally, the statistical power was limited for rare outcomes.

Despite these limitations, our findings have important public health implications. By providing data on a non-mRNA vaccine in a Middle Eastern population, this study helps address vaccine hesitancy. However, communicating these results requires a cautious and balanced approach, emphasizing the reassuring aspects while transparently acknowledging the need for further studies to clarify the findings.

Conclusion

In this study, COVID-19 vaccination during pregnancy was not associated with an increased risk of overall adverse maternal events and was associated with a lower rate of neonatal intrauterine growth restriction. However, the conclusion must be tempered by the findings of a higher miscarriage rate and slightly lower 5-minute Apgar scores in the vaccinated group, which require cautious interpretation and further investigation in larger, prospective studies. Given the study's limitations, including its retrospective design, single-center nature, and short-term follow-up, these findings should be

considered hypothesis-generating. Future research should focus on long-term neonatal outcomes, investigate the role of psychosocial factors, and include diverse vaccine platforms to provide a more complete picture of vaccine safety in pregnancy.

Data Sharing Statement

The data supporting the conclusions of this study are available from the corresponding author upon reasonable request.

Ethical Approval and Consent to Participate

The Ethics Committee of Semnan University of Medical Sciences approved the study under the reference number IR.SEMUMS.REC.1401.042. The IRB waived the requirement for guardian consent for participants under the age of 18, as all individuals in this category were legally emancipated minors—specifically, married, pregnant, and self-supporting at the time of participation. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Consent for Publication

All procedures were conducted in accordance with relevant ethical guidelines and regulations. Written informed consent was obtained from all participants.

Acknowledgments

The authors thank the patients at Amir-Al-Momenin Hospital for their participation, and acknowledge the hospital staff for their technical support and provision of research facilities.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study did not receive financial support from any funding agency.

Disclosure

The authors declare no competing interests in this work.

References

1. Elmancy L, Alkhatib H, Daou A. SARS-CoV-2: an analysis of the vaccine candidates tested in combatting and eliminating the COVID-19 Virus. *Vaccines*. 2022;10.
2. LaMattina JL. *Pharma and Profits: Balancing Innovation, Medicine, and Drug Prices*. John Wiley & Sons; 2022.
3. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in china: summary of a report of 72 314 cases from the chinese center for disease control and prevention. *JAMA*. 2020;323:1239–1242. doi:10.1001/jama.2020.2648
4. Awasthi S, Dehkharghani MZ, Fudolig M. Emergence to dominance: estimating time to dominance of SARS-CoV-2 variants using nonlinear statistical models. *PLoS One*. 2025;20(4):e0311459. doi:10.1371/journal.pone.0311459
5. Dorjee K, Kim H, Bonomo E, Dolma R. Prevalence and predictors of death and severe disease in patients hospitalized due to COVID-19: a comprehensive systematic review and meta-analysis of 77 studies and 38,000 patients. *PLoS One*. 2020;15:e0243191. doi:10.1371/journal.pone.0243191
6. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020;370:m3320. doi:10.1136/bmj.m3320
7. Tanne JH. Covid-19: US maternal mortality rose during pandemic. *BMJ*. 2023;380:659. doi:10.1136/bmj.p659
8. Sappenfield E, Jamieson DJ, Kourtis AP. Pregnancy and susceptibility to infectious diseases. *Infect Dis Obstet Gynecol*. 2013;2013:752852. doi:10.1155/2013/752852
9. Huntley B, Mulder IA, Di Mascio D, et al. Adverse pregnancy outcomes among individuals with and without severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): a systematic review and meta-analysis. *Obstet Gynecol*. 2021;137:585–596. doi:10.1097/AOG.0000000000004320

10. Wong SF, Chow KM, Leung TN, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am J Obstet Gynecol*. 2004;191:292–297. doi:10.1016/j.ajog.2003.11.019
11. Tossetta G, Fantone S, Delli Muti N, et al. Preeclampsia and severe acute respiratory syndrome coronavirus 2 infection: a systematic review. *J Hypertens*. 2022;40:1629–1638. doi:10.1097/HJH.0000000000003213
12. Vafaiezhad Z, Sarandili S, Mousavi S, Mirmohammadkhani M, Rahmanian M. Assessment of changes in menstrual pattern, menstrual volume, and sex hormones (FSH, LH, TSH, prolactin, and AMH) in women of childbearing age with COVID-19 in Semnan, Iran: a cross-sectional study. *Middle East Fertil. Soc*. 2025;30(1).
13. Silakhori S, Mousavi S, Sarandili S, Rahmanian M. Impact of health literacy and subjective happiness in pregnancy on neonatal anthropometry: a cohort study. *Discover Mental Health*. 2025;5(1):1–15. doi:10.1007/s44192-025-00192-8
14. Rahmani A, Soleymani A, Almukhtar M, et al. Exosomes, and the potential for exosome-based interventions against COVID-19. *Rev. Med. Virol*. 2024;34(4):e2562. doi:10.1002/rmv.2562
15. Zhao X, Jiang Y, Zhao Y, et al. Analysis of the susceptibility to COVID-19 in pregnancy and recommendations on potential drug screening. *Eur J Clin Microbiol Infect Dis*. 2020;39:1209–1220. doi:10.1007/s10096-020-03897-6
16. Mousavi S. Global ethical principles in healthcare networks, including debates on euthanasia and abortion. *Cureus*. 2024;16(4).
17. Costantine MM, Landon MB, Saade GR. Protection by exclusion: another missed opportunity to include pregnant women in research during the coronavirus disease 2019 (COVID-19) pandemic. *Obstet Gynecol*. 2020;136:26–28. doi:10.1097/AOG.0000000000003924
18. Li CC, Wang XJ, Wang HR. Repurposing host-based therapeutics to control coronavirus and influenza virus. *Drug Discov Today*. 2019;24:726–736. doi:10.1016/j.drudis.2019.01.018
19. Favilli A, Mattei Gentili M, Raspa F, et al. Effectiveness and safety of available treatments for COVID-19 during pregnancy: a critical review. *J Matern Fetal Neonatal Med*. 2022;35:2174–2187. doi:10.1080/14767058.2020.1774875
20. Md Khairi LNH, Fahrni ML, Lazzarino AI, Sah R, Rodriguez-Morales AJ. The race for global equitable access to COVID-19 vaccines. *Vaccines*. 2022;11:10. doi:10.3390/vaccines11010010
21. Lukaszuk K, Podolak A, Malinowska P, Lukaszuk J, Jakiel G. Cross-reactivity between half doses of pfizer and astrazeneca vaccines-a preliminary study. *Vaccines*. 2022;10.
22. Liu X, Zhao N, Li S, Zheng R. Opt-out policy and its improvements promote COVID-19 vaccinations. *Soc Sci Med*. 2022;307:115120. doi:10.1016/j.socscimed.2022.115120
23. Moore S, Hill EM, Dyson L, Tildesley MJ, Keeling MJ. Retrospectively modeling the effects of increased global vaccine sharing on the COVID-19 pandemic. *Nat Med*. 2022;28:2416–2423. doi:10.1038/s41591-022-02064-y
24. Hameed I, Khan MO, Nusrat K, et al. Is it safe and effective to administer COVID-19 vaccines during pregnancy? A systematic review and meta-analysis. *Am J Infect Control*. 2023;51:582–593. doi:10.1016/j.ajic.2022.08.014
25. Theiler RN, Wick M, Mehta R, Weaver AL, Virk A, Swift M. Pregnancy and birth outcomes after SARS-CoV-2 vaccination in pregnancy. *Am J Obstet Gynecol MFM*. 2021;3:100467. doi:10.1016/j.ajogmf.2021.100467
26. Bookstein Peretz S, Regev N, Novick L, et al. Short-term outcome of pregnant women vaccinated with BNT162b2 mRNA COVID-19 vaccine. *Ultrasound Obstet Gynecol*. 2021;58:450–456.
27. Moini A, Rabiei M, Pirjani R, Abiri A, Maleki-Hajiagha A. COVID-19 vaccine hesitancy among pregnant women and their reported reasons for vaccine refusal - A prospective study in Tehran, Iran. *Vaccine*. 2023;41:1490–1495. doi:10.1016/j.vaccine.2023.01.022
28. Wainstock T, Yoles I, Sergienko R, Sheiner E. Prenatal maternal COVID-19 vaccination and pregnancy outcomes. *Vaccine*. 2021;39:6037–6040. doi:10.1016/j.vaccine.2021.09.012
29. Trostle ME, Limaye MA, Avtushka V, Lighter JL, Penfield CA, Roman AS. COVID-19 vaccination in pregnancy: early experience from a single institution. *Am J Obstet Gynecol MFM*. 2021;3:100464. doi:10.1016/j.ajogmf.2021.100464
30. Rottenstreich M, Sela HY, Rotem R, Kadish E, Wiener-Well Y, Grisaru-Granovsky S. Covid-19 vaccination during the third trimester of pregnancy: rate of vaccination and maternal and neonatal outcomes, a multicentre retrospective cohort study. *BJOG*. 2022;129:248–255. doi:10.1111/1471-0528.16941
31. Seravalli V, Romualdi I, Ammar O, et al. Vaccination coverage during pregnancy and factors associated with refusal of recommended vaccinations: an Italian cross sectional study. *Vaccine: X*. 2024;18:100483. doi:10.1016/j.jvax.2024.100483
32. Quint JJ, Van Dyke ME, Maeda H, et al. Disaggregating data to measure racial disparities in COVID-19 outcomes and guide community response - hawaii. *MMWR Morb Mortal Wkly Rep*. 2021;70:1267–1273. doi:10.15585/mmwr.mm7037a1
33. Harron K, Dibben C, Boyd J, et al. Challenges in administrative data linkage for research. *Big Data Soc*. 2017;4:2053951717745678. doi:10.1177/2053951717745678
34. Shephard HM, Manning SE, Nestoridi E, Brown C, Yazdy MM. Characteristics of people with and without laboratory-confirmed SARS-CoV-2 infection during pregnancy, massachusetts. *Public Health Rep*. 2022;137:782–789. doi:10.1177/00333549221084721
35. Regan AK, Kaur R, Nosek M, Swathi PA, Gu NY. COVID-19 vaccine acceptance and coverage among pregnant persons in the United States. *Prev. Med. Rep*. 2022;29:101977. doi:10.1016/j.pmedr.2022.101977
36. Gray KJ, Bordt EA, Atyeo C, et al. Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study. *Am J Obstet Gynecol*. 2021;225:303.e301–303.e317. doi:10.1016/j.ajog.2021.03.023
37. Dagan N, Barda N, Biron-Shental T, et al. Effectiveness of the BNT162b2 mRNA COVID-19 vaccine in pregnancy. *Nat Med*. 2021;27:1693–1695. doi:10.1038/s41591-021-01490-8
38. Barros FC, Gunier RB, Rego A, et al. Maternal vaccination against COVID-19 and neonatal outcomes during Omicron: INTERCOVID-2022 study. *Am J Clin Exp Obstet Gynecol*. 2024;231:460.e1–460.e17. doi:10.1016/j.ajog.2024.02.008

International Journal of Women's Health

Publish your work in this journal

The International Journal of Women's Health is an international, peer-reviewed open-access journal publishing original research, reports, editorials, reviews and commentaries on all aspects of women's healthcare including gynecology, obstetrics, and breast cancer. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/international-journal-of-womens-health-journal>

Dovepress
Taylor & Francis Group