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The Effects of COVID-19 Vaccination on Neonatal and Pregnancy Outcomes

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ABSTRACT

Background: While general health complications of COVID-19 have been widely studied, the effect of COVID-19 vaccination on pregnant patients is yet to be explored. Vaccination is a highly stigmatized topic in Georgia, which increases reluctance toward COVID-19 immunizations, especially during pregnancy.

Objectives: This study employs a retrospective cohort analysis approach to examine whether there is a statistically significant association between vaccination status and maternal and neonatal health.

Methods: The data was collected from 229 patients who gave birth in Georgia between January and July 2022. Women who were not vaccinated were compared to those who were either vaccinated during pregnancy or six months before conception to explore their pregnancy progression and neonatal outcomes. Patients were divided into two groups: COVID-19-positive and COVID-19-negative.

Results: No statistically significant associations were found between the groups concerning the mode of delivery, hypertensive disorders of pregnancy, pregnancy outcomes, gestational age, neonatal outcomes, newborn respiratory complications, Apgar score, and birth weight, which hints at the general safety of vaccination.

Conclusions: Maternal COVID-19 vaccination has no detrimental impact on neonatal outcomes or the progression/outcomes of pregnancy.

Keywords: COVID-19 vaccination; COVID-19; neonatal outcomes; obstetric outcomes; pregnancy outcomes; pregnancy.

INTRODUCTION

Due to the pandemic in 2019, the COVID-19 virus posed a significant threat to global healthcare and the economy. In particular, older patients, immunocompromised patients, individuals with chronic/systemic disorders, and people with comorbidities are at an increased risk of developing health complications related to COVID-19 infection.[1] Consequently, the administration of vaccines for emergency use has begun in the populations mentioned above. In December 2020, the FDA approved the Pfizer-BioNTech COVID-19 vaccine.[2]

However, there was no substantial evidence available on the safety of administering the COVID-19 vaccine to pregnant patients; thus, pregnant women had not been vaccinated until 2021. A growing body of evidence suggests that pregnant patients with COVID-19 may suffer from aggravated health complications.[3] The changes occurring in the immune system during pregnancy raise a question of the potential health risks to pregnant patients and the fetus.[4] Additionally, it has been established that COVID-19 infection during pregnancy raises the risk of premature delivery, preeclampsia, and stillbirth.[5,6]

The CDC has made recommendations in favor of vaccination during pregnancy.[7] Recent observational studies have shown that mRNA vaccination is safe and effective in the general population and pregnant women.[8,9] Notably, the studies exploring the effects of vaccination on pregnancy outcomes and maternal and neonatal health do not show any significant adversities associated with the treatment.[9] These results provide evidence for the safety of using mRNA vaccines during pregnancy.

Considering the general suspicions concerning the use of vaccines, Georgian healthcare providers are challenged to convince the broader public about the safety of novel vaccines, particularly mRNA vaccines. Moreover, pregnant patients were more reluctant to receive any type of vaccine due to the concerns of potential health complications.

The current study aimed to determine the association between COVID-19 vaccines and obstetric/neonatal outcomes in pregnant COVID-positive and COVID-negative women, respectively, to raise the awareness of immunization in Georgia, which is relatively low compared to other developed countries.

METHODS

Study design and variable definition

The study comprises a retrospective cohort analysis of the data from women who gave birth between January and July 2022. The data was collected from the First University Clinic in Tbilisi, Georgia. Exclusion criteria included patients with unknown vaccination status. Only singleton pregnancies

were chosen for the analysis. Pregnancy and neonatal outcomes were compared between non-vaccinated women and women who received vaccination during pregnancy or six months before conception. Participants were categorized into two groups: COVID-positive and COVID-negative. They were not grouped based on their vaccination type (mRNA/Inactivated vaccines). The following categories of factors were observed: mode of delivery, hypertensive disorders of pregnancy, pregnancy outcomes, gestational age, neonatal outcomes, newborn respiratory complications, Apgar score, and birth weight.

Statistical Analysis

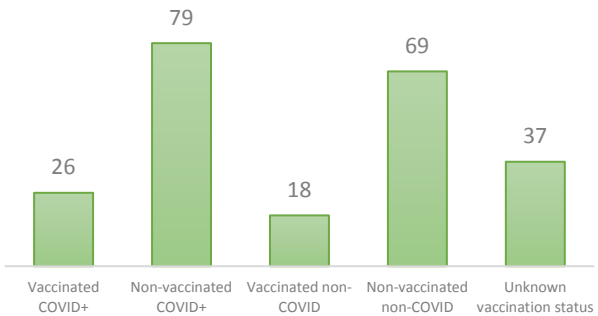
The statistical analysis was performed using Chi-square/Fisher's exact test for categorical variables (mode of delivery, hypertensive disorders of pregnancy, pregnancy outcomes, gestational age, neonatal outcomes, newborn respiratory complications, Apgar score at 1 minute) and t-test/Mann-Whitney U test for continuous variables (birth weight). Statistical analysis was done via R programming.

RESULTS

The data was gathered from 229 women, of whom 192 had complete information regarding vaccination status. The remaining 37 patients had no a complete history and were excluded from the study (Fig.1).

The final study population consisted of 192 individuals, of whom 148 were not vaccinated during or before pregnancy, 33 had received two doses of Pfizer-BioNTech vaccination, and 11 had received two doses of Sinopharm/Sinovac vaccinations (for a total of 44 vaccinations).

FIGURE 1. A histogram representation of the number of patients and groupings according to COVID-19 and vaccination status (Total number of patients: 229)



Tables 1-4 present a comparison of main pregnancy, delivery, and newborn characteristics between vaccinated and unvaccinated pregnant women. These two groups are further divided into COVID-positive and COVID-negative patients. All of the observed parameters are listed. P-value was higher than 0.05 in all examined factors, indicating that there was no statistically significant difference between vaccinated and non-vaccinated patients.

Obstetric outcomes in COVID-positive group

Table 1 describes obstetric outcomes in COVID-positive patients, including preeclampsia (vaccinated: 0 vs. non-vaccinated: 5), eclampsia (0 vs. 1), gestational hypertension (2 vs. 3), postpartum hemorrhage (2 vs. 2), premature rupture of membranes (5 vs. 23), gestational diabetes (0 vs. 3), placental abruption (0 vs. 0), placenta accreta/increta/percreta (0 vs. 1); gestational age: term (25 vs 66) and preterm (1 vs. 13). Mode of delivery: non-urgent C-section (6 vs. 11), urgent C-section (5 vs. 18), non-urgent vaginal delivery (14 vs. 48), and urgent vaginal delivery (1 vs. 2). No statistically significant differences were found between vaccinated and non-vaccinated patients.

TABLE 1. Obstetric outcomes in COVID-positive pregnant women

COVID+	Total n=105	Vaccinated n=26	Non-vaccinated n=79	P-value
Mode of delivery				
Urgent C-section	23	5	18	0.7909
Non-urgent C-section	17	6	11	0.3564
Urgent vaginal delivery	3	1	2	1
Non-urgent vaginal delivery	63	14	48	0.6951
Hypertensive disorders				
Preeclampsia	5	0	5	0.3293
Eclampsia	1	0	1	1
Gestational hypertension	5	2	3	0.5954
Pregnancy outcomes				
Postpartum hemorrhage	4	2	2	0.2556
Premature rupture of membranes	28	5	23	0.4448
Gestational diabetes	3	0	3	0.5727
Placental abruption	0	0	0	NA
Placenta accerta/increta/percreta	1	0	1	1
Gestational age				
Term	91	25	66	0.1802
Preterm	14	1	13	0.1802

Abbreviations: NA: not applicable.

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Obstetric outcomes in COVID-negative group

No statistical differences were found between the groups concerning the mode of delivery: non-urgent C-section (3 vs. 14), urgent C-section (3 vs. 18), non-urgent vaginal delivery (10 vs. 35), and urgent vaginal delivery (2 vs. 2). Table 2 describes obstetric outcomes in COVID-negative patients, including preeclampsia (0 vs. 4), eclampsia (0 vs. 0), gestational hypertension (0 vs. 6), postpartum hemorrhage (1 vs. 4), premature rupture of membranes (4 vs. 12), gestational diabetes (0 vs 1), placental abruption (0 vs. 1), placenta accreta/increta/percreta (1 vs. 2); gestational age: term (18 vs. 62) and preterm (1 vs. 7).

TABLE 2. Obstetric outcomes in COVID-negative pregnant women

COVID+	Total n=87	Vaccinated n=18	Non-vaccinated n=69	P-value
Mode of delivery				
Urgent C-section	21	3	18	0.7137
Non-urgent C-section	17	3	14	1
Urgent vaginal delivery	4	2	2	0.1917
Non-urgent vaginal delivery	45	10	35	0.9655
Hypertensive disorders				
Preeclampsia	4	0	4	0.5752
Eclampsia	0	0	0	NA
Gestational hypertension	6	0	6	0.6633
Pregnancy outcomes				
Postpartum hemorrhage	5	1	4	1
Premature rupture of membranes	16	4	12	0.7352
Gestational diabetes	1	0	1	1
Placental abruption	1	0	1	1
Placenta accerta/increta/percreta	3	1	2	0.3767
Gestational age				
Term	80	18	62	0.3359
Preterm	8	1	7	0.3359

Abbreviations. NA: not applicable.

Neonatal outcomes in COVID-positive group

Table 3 presents neonatal outcomes in COVID-positive patients, including stillbirth (1 vs. 2), meconium-stained amniotic fluid (0 vs. 2), newborn hypothermia (0 vs. 0), hypoglycemia (0 vs. 1); an Apgar score of 8-10 points at 1 min after birth (23 vs. 66), 6-7 points (2 vs 10), < 5 points (0 vs. 2). Newborn respiratory complications included: normopnea (23 vs. 70), dyspnea (1 vs. 2), transient tachypnea of the newborn (0 vs. 0), acute respiratory distress syndrome (1 vs. 5); Birthweight (3262,5 +/- 391,2 vs. 3128,6 +/- 592,7). No statistically significant differences were found between the two groups.

TABLE 3. Neonatal outcomes in COVID-positive pregnant women

COVID+	Total n=105	Vaccinated n=26	Non-vaccinated n=79	P-value
Neonatal outcomes				
Stillbirth	3	1	2	1
Meconium-stained amniotic fluid	2	0	2	1
Newborn hypothermia	0	0	0	NA
Hypoglycemia	1	0	1	1
Newborn respiratory complications				1
Normopnea	93	23	70	
Dyspnea	3	1	2	
Transient tachypnea of newborn	0	0	0	
Acute respiratory distress syndrome	6	1	5	
Apgar score (1')				0.8429
8-10	89	23	66	
6-7	12	2	10	
<5	2	0	2	
Birth weight (g, mean±SD)	105	3262.5 ± 391.2	3128.6 ± 592.7	0.1367

Abbreviations. NA: not applicable.

Neonatal outcomes in COVID-negative group

Table 4 presents neonatal outcomes in COVID-negative patients, including stillbirth (1 vs. 1), meconium-stained amniotic fluid (0 vs. 3), newborn hypothermia (0 vs. 0), hypoglycemia (0 vs. 1); an Apgar score of 8-10 points at 1 min after birth (17 vs. 59), 6-7 points (0 vs 7), < 5 points (0 vs. 2). Newborn respiratory complications included: normopnea (17 vs. 59), dyspnea (0 vs. 4), transient tachypnea of the newborn (0 vs. 2), acute respiratory distress syndrome (0 vs. 2); Birthweight (3323,8 +/- 357,9 vs. 3164,9 +/- 540,7).

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TABLE 4. Neonatal outcomes in COVID-negative pregnant women

COVID+	Total n=87	Vaccinated n=18	Non-vaccinated n=69	P-value
Neonatal outcomes				
Stillbirth	2	1	1	0.2093
Meconium-stained amniotic fluid	3	0	3	1
Newborn hypothermia	0	0	0	NA
Hypoglycemia	1	0	1	1
Newborn respiratory complications				1
Normopnea	76	17	59	
Dyspnea	3	1	2	
Transient tachypnea of newborn	4	0	4	
Acute respiratory distress syndrome	2	0	2	
Apgar score (1')				0.4513
8-10	76	17	59	
6-7	7	0	7	
<5	2	0	0	
Birth weight (g, mean±SD)	84	3323.8 ± 357.9	3164.9 ± 540.7	0.8265

Abbreviations. NA: not applicable.

DISCUSSION

In this retrospective cohort study, the implications of the COVID-19 vaccination on obstetric and neonatal outcomes for singleton pregnancies have been studied. No discernible differences were discovered for any of the negative outcomes examined between the vaccinated and unvaccinated groups, thus reaffirming the initial assumption of administering the COVID-19 vaccine. At the same time, pregnancy is safe and does not raise the danger of unfavorable perinatal or neonatal outcomes.

Literature dictates that there is a risk of developing severe COVID-19 disease during pregnancy, causing physiological changes that affect obstetric and neonatal outcomes.[6,10,11] However, at least based on the current study, the COVID-19 vaccination looks to be efficient and safe for use during pregnancy. A prior study on a larger cohort of 3,240 vaccinated pregnant women reported no negative effect on pregnancy outcome after receiving the COVID-19 vaccine during pregnancy, which is consistent with the findings of this study.[12-18] Moreover, studies have also shown that vaccination of mothers may provide immunity against COVID-19 in their offspring in addition to the vaccine's protective effects on the mothers.[19-20]

Two retrospective cohorts, including the larger cohort, found that the risk for meconium-stained amniotic fluid was lower in the vaccinated group, suggesting a protective effect against it.[12,18] At the same time, another study, including ours, found no association between the two. Thus, displaying contradicting results.[21] Additionally, it has been observed that mothers who test positive for SARS-CoV-2 infection are more likely to have meconium-stained amniotic fluid than those who test negative. Therefore, in order to confirm whether COVID-19 immunization is effective at preventing this neonatal outcome. More research is needed in this area before any definitive conclusions can be drawn about its effectiveness in preventing this neonatal outcome.[22,23]

In contrast to our findings, Rottenstreich et al. observed that 712 pregnant women who received two doses of the COVID-19 vaccination during the third trimester had an increased rate of elective cesarean birth and a decreased risk of severe newborn outcomes.[21]

The discussion of the findings of this cohort study on maternal COVID-19 vaccination and pregnancy outcomes in Georgia highlights several significant limitations. Firstly, the overall vaccination rate in Georgia for both COVID-19 and seasonal flu is relatively low: only 34.4% of the overall population is fully vaccinated against coronavirus, with many individuals remaining unvaccinated due to the stigmatization of vaccines in the country.[24] The low vaccination rate among the general population may have influenced the results of our study and may not be representative of other areas with higher vaccination rates.

Another limitation of this study is the sample size, which was relatively small, with only 229 participants. While this sample size was sufficient to provide valuable data, similar studies have utilized larger sample sizes, providing a more comprehensive analysis. Furthermore, the participant's medical records did not include information on their vaccination status, which required contacting each participant individually to obtain consent and clarify their immunization status.

Despite these limitations, the findings of this study provide important insights into the potential effects of COVID-19 vaccination on pregnancy outcomes in Georgia. Additionally, in order to increase vaccination rates in Georgia, particularly among pregnant women, there is a need for further exploration of the potential benefits of maternal COVID-19 vaccination.

From a medical standpoint, this research clarifies the safety of administering vaccines to pregnant women since the vaccination was not associated with an increased risk of adverse outcomes. It also increases awareness among women who are either already pregnant or plan to conceive because it increases the perceived reliability of vaccines, as the local community may respond better to the data collected from their immediate environment. Given that

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many pregnant women are hesitant to receive the vaccine due to safety concerns, caregivers must provide accurate information about its safety and efficacy to increase vaccine acceptance rates among pregnant populations. With such awareness, more people may be prone to get vaccinated, which decreases the burden on the economy caused by the pandemic.

From a medical standpoint, this research clarifies the safety of administering vaccines to pregnant women since the vaccination was not associated with an increased risk of adverse outcomes. It also increases the awareness in women who are either already pregnant or plan to conceive because it increases the perceived reliability of vaccines, as the local community may respond better to the data collected from their immediate environment. Given that many pregnant women are hesitant to receive the vaccine due to safety concerns, caregivers must provide accurate information about its safety and efficacy to increase vaccine acceptance rates among pregnant populations. With such awareness, more people may be prone to get vaccinated, which decreases the burden on the economy caused by the pandemic.

Potential confounding factors, such as obesity/high BMI status, smoking, and diabetes, were not considered in the analysis and may have impacted our findings. It has been established that obesity before pregnancy may be associated with an increased risk of hypertensive disorders, for example, preeclampsia.[25] Thus, future studies should include adjusting and eliminating any known clinically relevant confounding variables via multivariable regression analysis.

The scope of the study should be expanded. Namely, bigger population size would increase the statistical power needed to detect clinically relevant and statistically significant differences, thus making the results more reliable. Future studies should focus on larger cohort sizes and longer-term follow-up data to further evaluate the potential benefits and risks of COVID-19 vaccination during pregnancy. Additionally, there is little evidence of innate immunity in a neonate acquired from the mother for COVID-19, making it a significant area for future study.

CONCLUSIONS

Maternal COVID-19 vaccination has no detrimental impact on neonatal outcomes or the progression/outcomes of pregnancy.

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