original article

Impact of SARS-CoV-2 infection and vaccination on cesarean section outcomes: a retrospective analysis

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BACKGROUND: Pregnant individuals have faced unique challenges during the COVID-19 pandemic, necessitating a closer examination of maternal and fetal health outcomes.

OBJECTIVES: Investigate the morbidity and mortality associated with SARS-CoV-2 infection among pregnant individuals, considering vaccination status and variant strains.

DESIGN: Retrospective cohort

SETTING: Tertiary state hospital

PATIENTS AND METHODS: Patients who underwent cesarean sections were categorized into three periods: pre-vaccination (before 31 August 2021), early post-vaccination (from September 2021), and late post-vaccination (aligned with 70% immunization coverage by 2 September 2021). Data collected included demographic information (age, gravidity, parity count, gestational age, newborn APGAR scores), cesarean section indications, chronic diseases, vaccination status, vaccine type and doses, SARS-CoV-2 variant status, ICU admission, and mortality due to COVID-19.

MAIN OUTCOME MEASURES: ICU admission and mortality rates, focusing on the impact of SARS-CoV-2 infection and vaccination status.

SAMPLE SIZE: 297 COVID PCR-positive symptomatic patients who underwent cesarean sections.

RESULTS: In the pre-vaccination group, there were 13 mortalities (8.1%) compared to 9 (6.6%) post-vaccination (P=.610). Maternal ARDS was seen in 46.2% of pre-vaccination mortalities versus 11.1% post-vaccination (P=.045). COVID-19 delta variant patients had higher ICU admission (80%) and mortality rates (40%). Rates of COVID-19 PCR-positive cesarean sections, ICU admissions, and mortality declined significantly in early (P=.021, P=.004, P=.009), respectively and late post-vaccination periods (P<.001, P<.001, P=.0019), respectively. Vaccinated patients had no ICU admissions or mortality.

CONCLUSIONS: Vaccination against COVID-19 is crucial for pregnant individuals as it significantly reduces the risk of severe illness. While vaccines offer substantial protection, the pandemic's acute phase might be waning, yet COVID-19 remains a global threat, particularly in regions with limited vaccine access. Continued vigilance and proactive measures are essential to mitigate ongoing risks and the emergence of new variant strains.

LIMITATIONS: Retrospective observational design and the single-center setting, which may affect the generalizability of the findings.

CONFLICT OF INTEREST: None.

The novel coronavirus, the Delta variant (B.1.617.2) of COVID 19. or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in Wuhan, Hubei Province, China, in December 2019, marked the onset of a transformative global health crisis. Originating in a bustling metropolis, this previously unknown virus rapidly traversed borders and continents, igniting a pandemic of unprecedented scale and complexity. The ensuing COVID-19 pandemic reshaped societies, economies, and global governance structures.

SARS-CoV-2, a member of the Coronaviridae family, is characterized by its enveloped, single-stranded RNA genome and distinctive spike proteins facilitating viral entry into host cells.[1] Its remarkable transmissibility, driven by factors such as asymptomatic spread, prolonged viral shedding, and intimate human-to-human contact, posed formidable challenges to containment efforts.[2] Despite unprecedented public health interventions and a multifaceted approach to disease control, the virus continued its relentless march, exacting a profound toll on public health.

Epidemiologically, COVID-19 unfolded in dynamic phases, spanning continents with variable intensity and impact. From its origins in Wuhan, the virus swiftly disseminated globally, assuming pandemic proportions within months. The World Health Organization's (WHO's) declaration of a Public Health Emergency of International Concern (PHEIC) on 30 January 2020 and a pandemic on 11 March 2020 underscored the gravity of the situation, catalyzing a collective global response to curb transmission and mitigate morbidity and mortality.[3,4] Yet, the pandemic's trajectory was marked by regional outbreaks, fluctuating incidence rates, and the emergence of viral variants with divergent transmissibility and antigenic properties, challenging the efficacy of containment strategies and vaccine development efforts.[5]

The virological landscape of SARS-CoV-2 further compounded the challenges posed by the pandemic, with the virus demonstrating a remarkable capacity for genetic evolution. The emergence of variants of concern (VOCs), characterized by mutations in the spike protein, raised concerns regarding altered transmissibility, immune evasion, and potential impacts on diagnostic testing and vaccine efficacy.[5,6] Genomic surveillance efforts underscored the need for agile and adaptive strategies to combat emerging threats.

The historical context of pandemics provides poignant parallels to the COVID-19 crisis, underscoring the enduring threat posed by infectious diseases and the critical importance of preparedness, resilience, and global cooperation. From the devastating influenza pandemic of 1918 to more recent outbreaks of Ebola, Zika, and H1N1 influenza, humanity has grappled with recurrent reminders of its vulnerability to microbial threats.[7] However, the unprecedented scale and societal impact of the COVID-19 pandemic serve as a stark reminder of the evolving nature of infectious disease threats in an interconnected world.

In response to the COVID-19 pandemic, public health authorities deployed a multifaceted arsenal of preventive measures and interventions aimed at interrupting viral transmission, safeguarding vulnerable populations, and mitigating the burden on healthcare systems. Non-pharmaceutical interventions such as physical distancing, mask-wearing, and hand hygiene, alongside targeted quarantine measures and travel restrictions, formed the cornerstone of containment strategies.[8-10] The rapid development and deployment of COVID-19 vaccines represented a watershed moment in pandemic response, offering a beacon of hope amidst uncertainty and despair.[11-15]

Pregnant individuals emerged as a particularly vulnerable subset of the population amidst the COVID-19 pandemic, grappling with unique challenges and uncertainties regarding maternal and fetal health. The physiological changes inherent to pregnancy, coupled with the need to balance optimal obstetric care with infection control measures, underscored the complexity of managing COVID-19 in this population. Prenatal care disruptions, obstetric complications, vertical transmission risks, and implications for perinatal outcomes highlighted the need for tailored approaches to antenatal care, delivery planning, and postpartum support.[16]

This retrospective cohort study aim of this study was to investigate the impact of COVID-19 infection on cesarean section outcomes among pregnant individuals. Clinical data, including vaccination status and variant strains, and maternal and neonatal outcomes are collected. Our primary objective was to retrospectively examine the maternal and fetal morbidity and mortality associated with COVID-19-positive cases identified via polymerase-chain reaction (PCR) testing undergoing cesarean sections. Additionally, we endeavor to explore the influence of vaccination status and variant strains on clinical outcomes within this cohort.

PATIENTS AND METHODS

Study design

This retrospective cohort study investigates the impact of COVID-19 infection on cesarean section outcomes among pregnant individuals. Demographic data,

including age, gravidity, parity count, gestational age, 1st and 5th-minute APGAR scores of the newborn, indications for cesarean section, presence of additional chronic diseases, vaccination status, type of vaccine received, repetition doses, if applicable, variant status of SARS-CoV-2, need for intensive care unit (ICU) admission, and mortality due to SARS-CoV-2, were collected (**Table 1**). Patients operated on before 31 August 2021, are categorized as the 'pre-vaccination period,' and patients operated on September 2021 are categorized as the 'early post-vaccination period,' marking the beginning of nationwide vaccination of pregnant individuals on 1 September 2021.[17] Additionally, the 'late post-vaccination period' specifically refers to the timeframe aligned with 70% of the median immunization coverage range nationwide at 2 September 2021, using as a reference for assessing herd immunity, recognizing that profound indirect protection can only be achieved in populations with more than 70% vaccine coverage.[18,19] Further detailed investigation of pre-vaccination and total post-vaccination periods mortality outcomes (**Table 2**),

Table 1. Demographic data of COVID-19 PCR-positive patients before 31 August 2021, and after 1 September 2021 setting the beginning of nationwide vaccination of pregnant patients.

Demographic data	Pre-vaccination period (before 31 August 2021) n=160	Post-vaccination period (after 1 September 2021) n=137	*P* value
Age	30.58 (5.66)	29.0 (5.52)	**.016**
Gravidity	2.0 (2.0-4.0)	2.0 (2.0-3.0)	.350
Parity	1.0 (1.0-2.0)	1.0 (0.25-2.0)	.270
Gestational week	36.10 (3.74)	36.39 (3.40)	.435
APGAR 1' score	8.0 (7.0-8.0)	8.0 (7.0-8.0)	.599
APGAR 5' score	9.0 (8.0-9.0)	9.0 (8.0-9.0)	.248
Indication placental anomaly	1 (0.6)	5 (3.6)	.098
Indication presentation anomaly/CPD	32 (20.0)	16 (11.7)	.052
Indication fetal distress	28 (17.5)	23 (16.8)	.871
Indication maternal ARDS	17 (10.6)	20 (14.6)	.301
Indication previous uterine surgery	82 (51.2)	73 (53.3)	.726
Additional chronic disease malignancy	2 (1.3)	0	.501
Additional chronic thyroid disease	7 (4.4)	13 (9.5)	.080
Additional chronic diabetes	10 (6.3)	9 (6.6)	.911
Additional chronic respiratory disorder	3 (1.9)	5 (3.6)	.478
Additional chronic hypertensive disorder	5 (3.1)	2 (1.5)	.458
Vaccinated patient	0 (0.0)	12 (8.8)	**<.001**
Variant	3 (1.9)	4 (2.9)	.707
ICU administration	35 (21.9)	26 (19.0)	.538
Mortality	13 (8.1)	9 (6.6)	.610

Results are presented as mean (SD) for normally distributed data, median (25-75 percentile) for non-normally distributed data. Number (percentage) for categorical variables. To compare independent categorical variables. The chi-square test was applied. CPD: cephalo-pelvic disproportion; ARDS: acute respiratory distress syndrome.

Table 2. Mortality data of COVID-19 PCR positive patients before 31 August 2021 and after 1 September 2021 setting the beginning of nationwide vaccination of pregnant patients.

Mortality	Pre-vaccination period (before 31 August 2021) n=13	Post-vaccination period (after 1 September 2021) n=9	*P* value
Age	33.23 (5.08)	29 (6.02)	.090
Gravidity	2.0 (1.0-2.0)	1.0 (0.0-2.5)	.149
Parity	1 (0.25-3.0)	1.0 (0.25-2.0)	.334
Gestational week	31.92 (3.73)	32.33 (3.7)	.788
APGAR 1' score	6.0 (1.0-7.5)	7.0 (3.0-8.0)	.154
APGAR 5' score	8.0 (5.5-8.0)	9.0 (6.0-9.0)	.169
Indication placental anomaly	0	0	>.99
Indication presentation anomaly/ CPD	1 (7.7)	0	.405
Indication fetal distress	5 (38.5)	1 (11.1)	.166
Indication maternal ARDS	6 (46.2)	1 (11.1)	**.045**
Indication previous uterine surgery	1 (11.1)	0	.405
Additional chronic disease malignancy	0	0	>.99
Additional chronic thyroid disease	2 (15.4)	0	.228
Additional chronic diabetes	1 (7.7)	3 (33.3)	.134
Additional chronic respiratory disorder	0	0	>.99
Additional chronic hypertensive disorder	1 (7.7)	0	.405
Vaccinated patient	0	0	>.99
Variant	2 (Delta variant) (15.4)	0	.228
ICU administration	13 (100)	9 (100)	>.99

Results are presented as mean (SD) for normally distributed data, median (25-75 percentile) for non-normally distributed data. Number (percentage) for categorical variables. To compare independent categorical variables. The chi-square test was applied. CPD: cephalo-pelvic disproportion; ARDS: acute respiratory distress syndrome.

detected SARS-CoV-2 variant outcomes, and detailed demographic data and clinical outcomes of detected COVID-19 PCR-positive vaccinated patients (**Table 3**) were conducted. Additionally, the monthly total numbers of new COVID-19 PCR-positive cesarean sections performed, ICU admissions after COVID-19 cesareans, mortality numbers, and total number of cesarean sections performed in our hospital during the study period are presented in **Figure 1**. Comparison of cesarean section rates among COVID-19 PCR-positive cases and the total number of COVID-19 PCR-positive and negative cesarean sections performed across three periods: pre-vaccination, early post-vaccination, and late post-vaccination are presented in **Table 4**.

Setting

The study design received approval from the hospital's ethics committee on December 22, 2022, and was designed in line with the principles of the Declaration of Helsinki. The research was carried out at a tertiary referral state hospital, encompassing data from the first COVID-19 PCR-positive cesarean section performed in October 2020 to the latest cesarean section conducted in July 2022. Data retrieval and clinical follow-up records were conducted from the hospital's digital archive and supplemented by public health surveillance data.

Participants

A total of 297 individuals who underwent cesarean

section at our hospital were included in the study cohort. Following our clinical protocol during pandemics, instead of routine screening of all patients upon admission, individuals displaying symptoms of COVID-19 infection or who had recent close contact with confirmed cases, or lived with a quarantined individual, underwent nasopharyngeal swab rapid antigen PCR testing for SARS-CoV-2 and variant status. Thus, inclusion criteria encompassed individuals with positive COVID-19 PCR testing results. Exclusion criteria included those with negative PCR testing but positive findings on chest computed tomography (CT).

The management of pregnant women with symptomatic respiratory infections due to COVID-19 was carried out through a multidisciplinary approach. Hospital admission criteria included moderate to severe disease, mild disease with comorbidities, and obstetric risks. Uncomplicated COVID-19 cases were monitored without antiviral treatment, while antiviral therapy was considered for more severe cases based on the risk-benefit ratio. Radiological imaging was performed with abdominal shielding if respiratory distress was present. Antibiotics were given for suspected bacterial pneumonia, and empirical treatment for influenza was administered if needed. Fetal lung maturation was induced with betamethasone or dexamethasone between 24-34 weeks. High-dose steroids were transitioned to prednisolone or hydrocortisone after lung maturation. Magnesium sulfate for neonatal neuroprotection was decided in consultation with a perinatologist. Anti-cytokine therapy was used for macrophage activation syndrome in life-threatening cases, and a multidisciplinary approach was adopted for ARDS. Delivery timing was determined based on obstetric indications, disease severity, maternal condition, comorbidities, gestational age, and fetal well-being. Cesarean delivery was performed for rapid clinical deterioration, acute organ failure, septic shock, mechanical ventila-

Table 3. Variant and vaccinated patient data of COVID-19 PCR positive cesarean section patients.

Variants	Delta (n=5)	Omicron (n=1)	English (n=1)
Age	32.4 (5.22)	39	37
Gravidity	3.0 (1.5-5.0)	4	3
Parity	2.0 (0.5-4.0)	3	2
Gestational week	34.8 (4.71)	37	35
APGAR 1' score	8.0 (2.5-8.0)	8	7
APGAR 5' score	9.0 (6.5-9.0)	9	8
Indication placental anomaly	0	0	0
Indication presentation anomaly/ CPD	0	0	0
Indication fetal distress	1	0	0
Indication maternal ARDS	2	1	0
Indication previous uterine surgery	2	0	1
Additional chronic disease malignancy	0	0	0
Additional chronic thyroid disease	0	0	0
Additional chronic diabetes	0	0	0
Additional chronic respiratory disorder	0	0	0
Additional chronic hypertensive disorder	0	0	0
Vaccinated patient	0	0	0
ICU administration	4 (80)	1 (100)	0
Mortality	2 (40)	0	0

Table 3 (cont.) Variant and vaccinated patient data of COVID-19 PCR-positive cesarean section patients.

Vaccinated patients	Biontech (1 dose) (n=1)	Biontech (2 doses) (n=7)	Biontech (3 doses) (n=1)	Sinovac (2 doses) (n=3)
Age	40	30.8 (5.27)	29	31.6 (5.03)
Gravidity	3	2.0 (2.0-3.0)	1	2.0 (2.0-2.0)
Parity	2	1.0 (1.0-2.0)	0	1.0 (1.0-1.0)
Gestational week	32	37.5 (1.68)	27	37.0 (1.0)
APGAR 1' score	6	7.0 (7.0-8.0)	4	8.0 (8.0-9.0)
APGAR 5' score	8	9.0 (8.0-9.0)	7	9.0 (9.0-9.0)
Indication placental anomaly	0	0	1	0
Indication presentation anomaly/ CPD	0	2	0	0
Indication fetal distress	0	0	0	0
Indication maternal ARDS	0	0	0	0
Indication previous uterine surgery	1	5	0	3
Additional chronic disease malignancy	0	0	0	0
Additional chronic thyroid disease	0	1	0	0
Additional chronic diabetes	0	0	0	0
Additional chronic respiratory disorder	0	2	0	0
Additional chronic hypertensive disorder	0	0	0	0
Variant	0	0	0	0
ICU administration	0	0	0	0
Mortality	0	0	0	0

Results were presented as mean (SD) for normally distributed data, median (25-75 percentile) was used for non-normally distributed data, and number (percentage) for categorical variables. To compare independent categorical variables, the chi-square test was applied, and the results were reported as numbers and percentages. CPD: Cephalo-pelvic disproportion; ARDS: acute respiratory distress syndrome; ICU: Intensive care unit

tion difficulties, and fetal distress. Postpartum analgesia was provided with acetaminophen, and venous thromboembolism prophylaxis was administered with low molecular weight heparin. Depending on the maternal clinical condition, continuous or frequent electronic fetal monitoring and biophysical profile assessments, including ultrasonography and/or Doppler studies, were conducted to monitor fetal well-being in cases of maternal desaturation or assessed fetal intrapartum compromise risk factors.[20]

Variables

Key variables examined in the study included maternal and gestational age, vaccination and variant strains, indications for surgery, maternal complications (acute respiratory distress syndrome [ARDS], mortality), neonatal outcomes (APGAR scores, fetal distress), ICU admission, and the overall monthly number of cesarean sections performed during the study period. These variables were analyzed to determine the mortality rate of SARS-CoV-2 before 31 August 2021, and after 1 September 2021, marking the beginning of nationwide vaccination of pregnant individuals. Additionally, the late post-vaccination period specifically refers to the timeframe aligned with 70% of the median immunization coverage range nationwide at 2 September 2021.[17,18]

Data sources/measurement

Data were extracted from electronic medical records, encompassing demographic information, clinical history, and outcomes. COVID-19 vaccination status and variant strains were documented based on patient re-

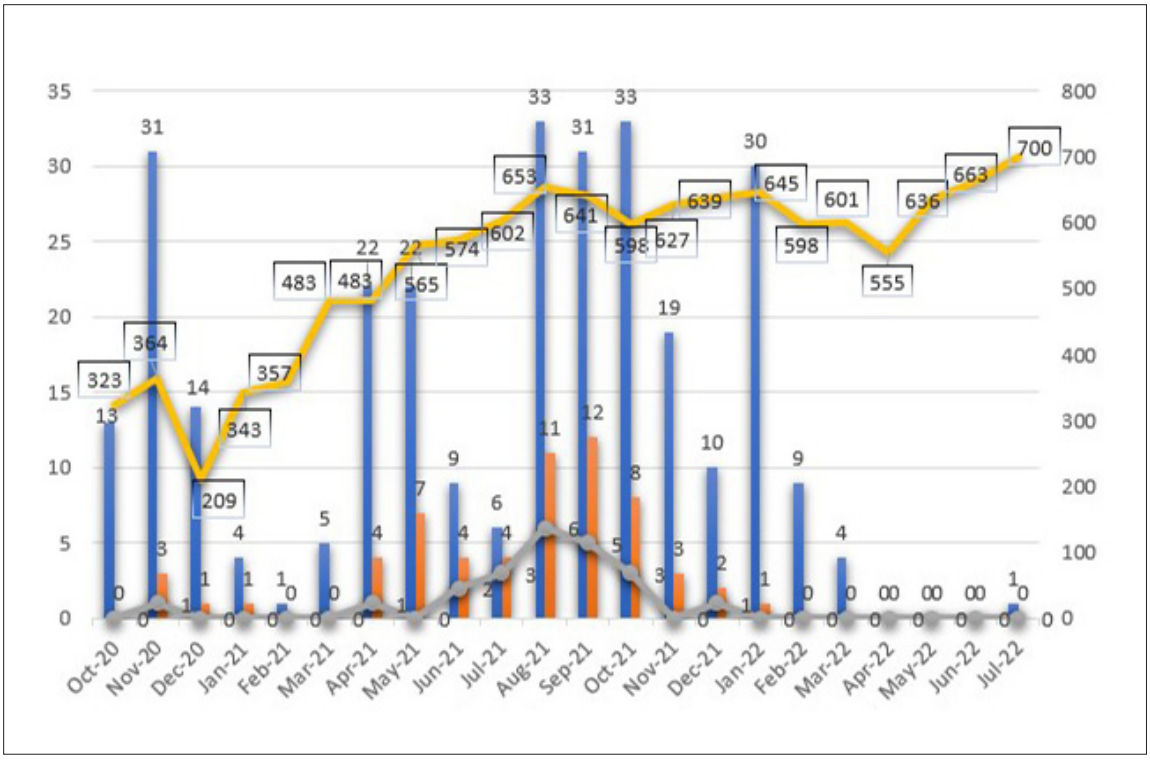


Figure 1. COVID-19 PCR-positive cesarean sections and subsets (see color coding). Blue: COVID-19 (total number); Orange: ICU admissions; Yellow: total cesarean patients (boxed); Grey: COVID-19 mortality.

cords and supplemented by public health surveillance data. Maternal and neonatal outcomes were categorized based on clinical management protocols established during the pandemic, with periodic updates in response to evolving evidence and guidelines.[20]

Bias

Potential sources of bias in this retrospective study include the reliance on hospital records and public health data, which may be subject to documentation errors. Efforts to mitigate potential sources of bias included excluding individuals with negative PCR testing but positive findings on chest CT scans to ensure a more objective cohort.

Study size

The study included PCR-positive COVID-19 cesarean sections conducted within the study period, spanning from the beginning of the pandemic. Given the observational nature of the study, a power calculation was not conducted.

Statistical methods

The normality of distributions was assessed employing the Kolmogorov-Smirnov test. In cases where normal distribution was not evident within two independent groups, the Mann-Whitney U test was utilized. Conversely, if normal distribution was observed within the two groups, the t-test was employed. Results were presented as mean (SD) for normally distributed data and median (25-75 percentile) for non-normally distributed data. For comparing independent categorical variables, the chi-square test was applied, with results reported as numbers and percentages. The z-test was employed to compare means or proportions between groups and to test hypotheses about population parameters.

All statistical analyses were conducted using IBM SPSS 26.0 for statistical analysis, with *P* values <.05 considered statistically significant.

RESULTS

Participants

The demographic characteristics of the study population are detailed in **Table 1**. Prior to 31 August 2021, 160 patients (53.9%) were included in the analysis, whereas from 1 September 2021, the number decreased to 137 (46.1%). Gravidity, parity number, mean gestational age

Table 4. Presentation of the monthly total numbers of new COVID-19 PCR positive patients, ICU admissions, mortality numbers, total number of COVID-19 PCR-positive and negative cesarean sections performed in our hospital, and comparison of cesarean section rates among COVID-19 PCR-positive cases and the total number of COVID-19 PCR-positive and negative cesarean sections performed across three periods: pre-vaccination, early post-vaccination, and late post-vaccination, analyzed using a one-proportion z-test.

Group	Month/Year	COVID-19 cesarian (n)	COVID-19 ICU admission (n)	COVID-19 mortality (n)	Total cesarian (n)
Pre-vaccination period	October 2020	13	0	0	323
	November 2020	31	3	1	364
	December 2020	14	1	0	209
	January 2021	4	1	0	343
	February 2021	1	0	0	357
	March 2021	5	0	0	483
	April 2021	22	4	1	483
	May 2021	22	7	0	565
	June 2021	9	4	2	574
	July 2021	6	4	3	602
	August 2021	33	11	6	653
Early post-vaccination period	September 2021	31	12	5	641
Late post-vaccination period	October 2021	33	8	3	598
	November 2021	19	3	0	627
	December 2021	10	2	1	639
	January 2022	30	1	0	645
	February 2022	9	0	0	598
	March 2022	4	0	0	601
	April 2022	0	0	0	555
	May 2022	0	0	0	636
	June 2022	0	0	0	663
	July 2022	1	0	0	700
	Pre-vaccination period	**Proportion**	**95% CI**	***P* value**	
Early post-vaccination period	COVID-19 PCR positive cesarian section	0.0484	0.0318-0.0650	**.021**	
	ICU admission	0.0187	0.0082-0.0292	**.004**	
	Fatality rate	0.0026	0.0010-0.0146	**.009**	
Late post-vaccination period	COVID-19 PCR positive cesarian section	0.0169	0.0137-0.0201	**<.001**	
	ICU admission	0.0022	0.0010-0.0034	**<.001**	
	Fatality rate	0.0006	0.0000-0.0012	**.0019**	

(Rates in Pre-vaccination period; COVID-19 PCR positive cesarian section: 0.0323, ICU administration: 0.0071, Mortality: 0.0026). ICU: Intensive care unit; CI: Confidence interval.

Note: One proportion z-test was employed to compare means or proportions between groups and to test hypotheses about population parameters *P* values.

at presentation, indications for surgery, or presence of additional chronic diseases showed no statistically significant differences between the pre-vaccination and post-vaccination periods. Concerning maternal and fetal complications; for neonatal outcomes, 28 patients (17.5%) in the pre-vaccination period experienced fetal distress necessesited cesarean section, compared to 23 patients (16.8%) in the post-vaccination period (*P*=.871). Additionally, mean APGAR scores at 1 minute (*P*=.599) and 5 minutes (*P*=.248) after birth did not exhibit any significant variation between the two periods. Regarding maternal outcomes, 17 patients (10.6%) in the pre-vaccination period and 20 patients (14.6%) in the post-vaccination period experienced ARDS necessitating cesarean section (*P*=.301). Similarly, there were no discernible differences in ICU admissions (*P*=.538) or mortality rates (*P*=.610) between the two periods.

Mortality data of COVID-19 PCR-positive patients

Table 2 offers insights into the mortality outcomes of COVID-19 PCR-positive patients undergoing cesarean sections during pre-vaccination and post-vaccination periods. In the pre-vaccination group, a total of 13 mortalities (8.1%) were observed, compared to 9 mortalities (6.6%) in the post-vaccination group (*P*=.610). Although, there was no significant difference in the mean age of patients, gravidity, parity numbers, or the presence of additional chronic diseases between the two cohorts, notabibly differences in maternal complications were observed. Maternal ARDS was noted in 46.2% (n=6) of mortalities in the pre-vaccination group compared to 11.1% (n=1) in the post-vaccination group (*P*=.045). Among the entire mortality cohort of COVID-19 PCR-positive patients, 2 Delta variants (15.4%) were observed in the pre-vaccination group. None of the mortalities were vaccinated, and all deaths occurred during ICU admission after the cesarean section operation.

Variant and vaccinated patient data of COVID-19 PCR-positive patients

Table 3 presents variant data, vaccinated patients data of COVID-19 PCR-positive patients undergoing cesarean sections. The Delta variant was the most prevalent, accounting for 5 cases, followed by the Omicron and English variants with 1 case each. Patients infected with the Delta variant exhibited a higher incidence of ICU admission of 4 patients (80%) and mortality of 2 patients (40%) compared to those infected with other variants. Additionally, 2 Delta PCR-positive patients (40%) experienced severe maternal complications such as ARDS. The single patient with the Omicron variant also required ICU admission but had no mortality, indicating that Omicron can still lead to severe outcomes. Conversely, the patient with the English variant did not require ICU admission and had no mortality, observed less severe outcomes compared to Delta and Omicron. Notably, among the 12 vaccinated patients, none required ICU admission or experienced mortality, regardless of the type of vaccine or doses administered. Among vaccinated patients, 11 patients (91.6%) were fully vaccinated, having received two or more doses.[18]

Comparison of outcomes in pre-vaccination and post-vaccination groups

Figure 1 illustrates the monthly occurrence of new COVID-19 PCR-positive cesarean sections, along with data on ICU admissions and mortality among COVID-19 PCR-positive cesarean section patients. It also includes the total number of COVID-19 PCR-positive and negative cesarean sections performed in our hospital.

Comparison of rates among new COVID-19 PCR-positive cesarean sections, ICU admissions, mortality numbers, and the total number of COVID-19 PCR-positive and negative cesarean sections performed across pre-vaccination, early post-vaccination, and late post-vaccination periods using a one proportion z-test. During the early post-vaccination period, there was a significant decline in the rates of COVID-19 PCR-positive cesarean sections (*P*=.021), ICU admissions (*P*=.004), and fatality (*P*=.009) compared to the pre-vaccination period. Moreover, in the late post-vaccination period, there were further statistically significant reductions in the rates of COVID-19 PCR-positive cesarean sections (*P*<.001), ICU admissions (*P*<.001), and fatality (*P*=.0019) compared to the pre-vaccination period (**Table 4**).

DISCUSSION

The COVID-19 pandemic continues to pose significant challenges worldwide, with the cumulative total number of cases surpassing 775 million as reported by the WHO. Among pregnant individuals, the seroprevalence of SARS-CoV-2 in reached up to 21.4% during the first wave of the pandemics.[21] The recent surge, exemplified by 242 845 new cases reported in April 2024 alone, underscores the ongoing threat posed by the virus despite vaccination efforts. Since the initiation of global COVID-19 vaccination campaigns on 22 July 2020, a remarkable 13.59 billion doses have been administered, signifying substantial progress in vaccine

distribution.[22] As of 26 November 2023, approximately 67% of the global population had completed their primary vaccination series, with 32% having received at least one booster dose. Notably, significant strides have been made in our country, administering over 152 million vaccine doses, with 85.70% of individuals aged 18 and above having received at least two doses.[23] However, the discussion must acknowledge the existence of regional disparities in vaccination coverage rates, as evidenced by variations nationwide.[18] Contrasts between regions, such as the West Marmara and Southeast, highlight the complex interplay of socio-demographic factors, healthcare infrastructure, and vaccine accessibility, emphasizing the need for targeted intervention strategies.

COVID-19 vaccines employ diverse platforms, each with unique mechanisms and efficacy profiles. Vaccines like Pfizer-BioNTech and Moderna use mRNA technology to encode the SARS-CoV-2 spike protein, prompting host cells to produce it. This triggers immune responses, generating neutralizing antibodies and activating T cells, akin to natural infection.[24] Pfizer-BioNTech and Moderna vaccines have received emergency use authorization (EUA) and have demonstrated high efficacy rates in clinical trials, exceeding 94% efficacy in preventing symptomatic COVID-19.[25,26] Real-world data further support their effectiveness in reducing severe disease, hospitalization, and mortality. Pfizer-BioNTech and Moderna vaccines had effectiveness in 91.2% and 98.1%, respectively.[27] Protein subunit vaccines, like Novavax, employ purified SARS-CoV-2 spike protein fragments to activate the immune system. Novavax, with its Matrix-M adjuvant, has received EUA and demonstrated efficacy in trials. Real-world data affirm its ability to prevent COVID-19 infections and severe outcomes.[24-28] Inactivated virus vaccines, such as Sinovac's CoronaVac and Sinopharm's BBIBP-CorV, use chemically inactivated SARS-CoV-2 viruses to trigger an immune response. While clinical trial efficacy rates varied, real-world data from Chile, Brazil, Indonesia, and Turkey confirm their effectiveness in reducing severe illness, hospitalization, and mortality.[29] These diverse vaccine platforms offer flexibility in addressing the global demand for COVID-19 vaccines and contribute to the collective effort to control the pandemic.

Extensive genomic sequencing of the virus since its identification in late 2019 has unveiled the emergence of several variants, some classified as VOCs due to their heightened transmissibility, potential for immune evasion, or increased severity of illness.[5,6] Mutations in the spike (S) protein, vital for viral entry into human cells, especially in the receptor-binding domain, have led to the emergence of these variants. Notable VOCs include Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (B.1.617.2), known for heightened transmissibility. Of particular concern is the Delta variant, with enhanced infectivity and potential immune evasion. Recently, the Omicron variant (B.1.1.529) has emerged, highly transmissible and immune-evading, emphasizing the need for robust surveillance and containment efforts to curb its global impact.[30-33] These variants pose challenges due to increased transmissibility, potential immune evasion, and severity of illness, highlighting the need for robust surveillance and containment measures. Adjustments to vaccination strategies and ongoing research efforts are essential to effectively control the spread of the virus in the face of evolving variants.

Future directions and recommendations

It is crucial to highlight the significance of COVID-19 vaccination for pregnant individuals within the broader context of global vaccination efforts. Pregnant individuals face heightened risks associated with COVID-19 infection, including severe illness and pregnancy complications. The risk of maternal mortality can be as much as thirty times higher compared to the general population, with increased rates of cesarean delivery, neonatal care unit admissions and stillbirth rates particularly in low- and middle-income countries, highlighting the critical need for access to high-quality maternity care. These adverse outcomes underscore the importance of vaccination in this population.[34-37]

In line with updated recommendation on 5 December 2023 from WHO, priority groups for COVID-19 vaccination include pregnant individuals, along with older adults, immunocompromised individuals, healthcare workers, and children above six months of age.[38] These priority groups are recommended to receive both primary vaccination series and booster doses, with intervals between doses as per guidelines.

In line with CDC recommendations on 12 September 2023, COVID-19 vaccination during pregnancy is strongly advised due to the heightened risk of severe illness from COVID-19 in pregnant individuals. Additionally, recent WHO guidance on 13 December 2023 underscores the broad cross-reactive neutralizing antibody responses elicited by monovalent XBB.1.5 COVID-19 vaccines against circulating variants, emphasizing the importance of vaccination in protecting against evolving strains of the virus. Furthermore, CDC recommendations for updated COVID-19 vaccines highlight the critical role of vaccination in mitigating the potentially serious outcomes of COVID-19 illness during pregnancy.[38-41]

In a study of 196470 pregnancies in Sweden and

Norway, where 48% of pregnant women had been vaccinated, there was no increase in the odds of adverse neonatal outcomes.[42] However, further studies are crucial to evaluate the effects of newly developed COVID-19 vaccines developed on various platforms on SARS-CoV-2 variants and VOCs, particularly in community-based populations that include pregnant individuals.

In conclusion, in light of the evolving epidemiology of COVID-19 and the emergence of new variants, ongoing surveillance efforts are crucial to inform future vaccination strategies and effectively control the pandemic. Research endeavors aimed at understanding the immune response to variant strains and advancing the development of next-generation vaccines play a pivotal role in mitigating the enduring impact of SARS-CoV-2 infection. Additionally, integrating COVID-19 vaccination with existing influenza vaccination programs, including extension to pregnant individuals, holds promise in maximizing vaccine coverage and providing comprehensive protection, particularly among vulnerable populations like older adults.[43] While significant immunity to SARS-CoV-2 suggests the conclusion of the pandemic's acute phase, COVID-19 persists as a global threat and endemic, particularly in regions with inadequate vaccine coverage and public health systems. Outbreaks persist, and the threat of variant strains remains a concern.

Limitations

Our study provides valuable insights, and enriches the existing literature, while also serving as a contemporary resource for clinicians by integrating recent data to support informed decision-making and management of pregnant patients, its reliance on retrospective data from a single hospital may limit its broader applicability to populations with diverse healthcare settings and demographics. Despite a significant sample size, a larger and more varied sample could enhance the robustness and statistical power of our findings. Efforts to gather data from electronic medical records and public health surveillance were made, yet data accuracy and completeness may still be subject to limitations. One notable example is the unavailability of patients' Robson-10 values, which could have been useful to objectively assess the characteristics of the cesarean cases.

REFERENCES

1. Gorbalenya A, Baker S, Baric RS, de Groot R, Drosten C, Gulyaeva AA, et al. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nature microbiology. 2020 Mar 2;5(4):536-44.doi:10.1038/s41564-020-0695-z

2. Meyerowitz EA, Richterman A, Gandhi RT, Sax PE. Transmission of SARS-CoV-2: a review of viral, host, and environmental factors. Annals of internal medicine. 2021 Jan;174(1):69-79. doi:10.7326/m20-5008

3. World Health Organization (2020) Statement on the second meeting of the International Health Regulations Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV).

4. World Health Organization (2020) WHO Director-General's opening remarks at the media briefing on COVID-19—11 March 2020 Geneva, Switzerland. 2020:3-5.

5. Hayawi K, Shahriar S, Serhani MA, Alashwal H, Masud MM. Vaccine versus variants (3Vs): are the COVID-19 vaccines effective against the variants? A systematic review. Vaccines. 2021 Nov 10;9(11):1305. DOI: 10.3390/vaccines9111305

6. La Rosa G, Mancini P, Ferraro GB, Veneri C, Iaconelli M, Lucentini L, et al. Rapid screening for SARS-CoV-2 variants of concern in clinical and environmental samples using nested RT-PCR assays targeting key mutations of the spike protein. Water research. 2021 Jun 1;197:117104. DOI: 10.1016/j.watres.2021.117104

7. Piret J, Boivin G. Pandemics throughout history. Frontiers in microbiology. 2021 Jan 15;11:631736. DOI: 10.3389/fmicb.2020.631736

8. World Health Organization (2020) Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected: interim guidance, 25 January 2020. 9240000917.

9. World Health Organization (2020) Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected Interim guidance, 19 March 2020.

10. Control CfD Overview of testing for SARS-CoV-2 (COVID-19)., Prevention. (2020)

11. McNamara LA, Wiegand RE, Burke RM, Sharma AJ, Sheppard M, Adjemian J, et al. Estimating the early impact of the US COVID-19 vaccination programme on COVID-19 cases, emergency department visits, hospital admissions, and deaths among adults aged 65 years and older: an ecological analysis of national surveillance data. The Lancet. 2022 Jan 8;399(10320):152-60. doi:10.1016/s0140-6736(21)02226-1

12. Thompson MG, Stenehjem E, Grannis S, Ball SW, Naleway AL, Ong TC, et al. Effectiveness of Covid-19 vaccines in ambulatory and inpatient care settings. New England Journal of Medicine. 2021 Oct 7;385(15):1355-71. doi:10.1056/NEJMoa2110362

13. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, et al. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. The Lancet. 2021 May 15;397(10287):1819-29. doi:10.1016/s0140-6736(21)00947-8

14. Vasileiou E, Simpson CR, Shi T, Kerr S, Agrawal U, Akbari A, et al. Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. The Lancet. 2021 May 1;397(10285):1646-57. doi:10.1016/s0140-6736(21)00677-2

15. Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, Het al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. New England Journal of Medicine. 2021 Apr 15;384(15):1412-23.

16. Péju E, Belicard F, Silva S, Hraiech S, Painvin B, Kamel T, et al. Management and outcomes of pregnant women admitted to intensive care unit for severe pneumonia related to SARS-CoV-2 infection: the multicenter and international COVIDPREG study. Intensive Care Medicine. 2022 Sep;48(9):1185-96. doi:10.1007/s00134-022-06833-8

17. T.C. Sağlik Bakanliği (2021) Covid-19 Aşisi Bilgilendirme Platformu. https://covid19asi.saglik.gov.tr Accessed 15 July 2021

18. Erdal D, Şaşmaz CT. EN AZ İKİ DOZ COVID-19 AŞI KAPSAYICILIK HIZI İLE VAKA İNSİDANSI ARASINDAKİ KORELASYONUN DEĞERLENDİRİLMESİ: EKOLOJİK TİPTE BİR ÇALIŞMA. ESTÜDAM Halk Sağlığı Dergisi. 2023 May 1;8(2):142-50.

19. Tsaban G, Ben-Shimol S. (2017) Indirect (herd) protection, following pneumococcal conjugated vaccines introduction: A systematic review of the literature. Vaccine. 35(22):2882-91. Epub 2017/04/30. doi: 10.1016/j.vaccine.2017.04.032. PubMed PMID: 28449971.

20. TC Sağlık Bakanlığ (2021) COVID-19 Solunum Sistemi Hastalıklarının Yaygın Olduğu Dönemde Sağlık Kuruluşlarında Gebe Takibi, https://covid19.saglik.gov.tr/TR-75284/covid-19-solunum-sistemi-hastaliklarinin-yaygin-oldugu-donemde-saglik-kuruluslarinda-gebe-takibi.html (Accessed 06 August 2024)

21. Villalaín C, Herraiz I, Luczkowiak J, Pérez-Rivilla A, Folgueira MD, Mejía I, et al. Seroprevalence analysis of SARS-CoV-2 in pregnant women along the first pandemic outbreak and perinatal outcome. PLoS One. 2020 Nov 30;15(11):e0243029.

22. World Health Organization (2024) WHO coronavirus (COVID-19) dashboard. https://data.who.int/dashboards/covid19. Accessed 02 May 2024

23. T.C. Sağlik Bakanliği (2024) Covid-19 Aşisi Bilgilendirme Platformu. https://covid19asi.saglik.gov.tr. Accessed 02 May 2024)

24. Firouzabadi N, Ghasemiyeh P, Moradishooli F, Mohammadi-Samani S. Update on the effectiveness of COVID-19 vaccines on different variants of SARS-CoV-2. International immunopharmacology. 2023 Apr 1;117:109968. DOI: 10.1016/j.intimp.2023.109968

25. Fortner A, Schumacher D. First COVID-19 vaccines receiving the US FDA and EMA emergency use authorization. Discoveries. 2021 Jan;9(1). DOI: 10.15190/d.2021.1

26. Branswell H. A side-by-side comparison of the Pfizer/BioNTech and Moderna vaccines. STAT, Boston, Retrieved. 2021 Jan;14.

27. Zheng C, Shao W, Chen X, Zhang B, Wang G, Zhang W. Real-world effectiveness of COVID-19 vaccines: a literature review and meta-analysis. International journal of infectious diseases. 2022 Jan 1;114:252-60. DOI: 10.1016/j.ijid.2021.11.009

28. Parums DV. First approval of the protein-based adjuvanted nuvaxovid (NVX-CoV2373) novavax vaccine for SARS-CoV-2 could increase vaccine uptake and provide immune protection from viral variants. Medical science monitor: international medical journal of experimental and clinical research. 2022;28:e936523-1, DOI: 10.12659/MSM.936523

29. Wilder-Smith A, Mulholland K. Effectiveness of an inactivated SARS-CoV-2 vaccine. New England Journal of Medicine. 2021 Sep 2;385(10):946-8. DOI: 10.1056/NEJMe2111165

30. Chen J, Wang R, Gilby NB, Wei GW. Omicron variant (B. 1.1. 529): infectivity, vaccine breakthrough, and antibody resistance. Journal of chemical information and modeling. 2022 Jan 6;62(2):412-22. DOI: 10.1021/acs.jcim.1c01451

31. Zhang M, Xiao J, Deng A, Zhang Y, Zhuang Y, Hu T,et al. Transmission dynamics of an outbreak of the COVID-19 Delta variant B. 1.617. 2—Guangdong Province, China, May–June 2021. China CDC weekly. 2021 Jul 7;3(27):584. DOI: 10.46234/ccdcw2021.148

32. Sanches PR, Charlie-Silva I, Braz HL, Bittar C, Calmon MF, Rahal P, et al. Recent advances in SARS-CoV-2 spike protein and RBD mutations comparison between new variants alpha (B. 1.1. 7, United Kingdom), Beta (B. 1.351, South Africa), Gamma (P. 1, Brazil) and delta (B. 1.617. 2, India). Journal of virus eradication. 2021 Sep 1;7(3):100054. DOI: 10.1016/j.jve.2021.100054

33. Radvak P, Kwon HJ, Kosikova M, Ortega-Rodriguez U, Xiang R, Phue JN, et al. SARS-CoV-2 B. 1.1. 7 (alpha) and B. 1.351 (beta) variants induce pathogenic patterns in K18-hACE2 transgenic mice distinct from early strains. Nature communications. 2021 Nov 12;12(1):6559.DOI: 10.1038/s41467-021-26803-w

34. Rahmati M, Yon DK, Lee SW, Butler L, Koyanagi A, Jacob L, et al. Effects of COVID-19 vaccination during pregnancy on SARS-CoV-2 infection and maternal and neonatal outcomes: A systematic review and meta-analysis. Reviews in Medical Virology. 2023 May;33(3):e2434. doi:10.1002/rmv.2434

35. Hameed BH, Thamir AR, Jassim H, Ali H. Maternal and perinatal outcome of pregnant women with COVID 19, a tertiary centre experience in Iraq-A Case Series. JPMA The Journal of the Pakistan Medical Association. 2021 Dec 1;71(12):S174-8.

36. Mohan M, Appiah-Sakyi K, Oliparambil A, Pullattayil AK, Lindow SW, Ahmed B, et al. A Meta-Analysis of the Global Stillbirth Rates during the COVID-19 Pandemic. J Clin Med. 12(23). 2023 Nov 21;12(23):7219. Epub 2023/12/09. doi: 10.3390/jcm12237219. PubMed PMID: 38068270; PubMed Central PMCID: PMCPMC10707675.

37. Demir BC, Albayrak O, Aslan K. The impact of Coronavirus disease-19 on pregnancy outcomes, a case series. Gynecology Obstetrics & Reproductive Medicine. 2023 Mar 17;29(1):30-5.

38. World Health Organization (2024) COVID-19 advice for the public: Getting vaccinated https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-

19-vaccines/advice. Accessed 02 May 2024
39. US Centers for Disease Control and Prevention. (2024) CDC Recommends Updated COVID-19 Vaccine for Fall/Winter Virus Season https://www.cdc.gov/media/releases/2023/p0912-COVID-19-Vaccine.html. Accessed 02 May 2024
40. World Health Organization (2023) Statement on the antigen composition of COVID-19 vaccines https://www.who.int/news/item/13-12-2023-statement-on-the-antigen-composition-of-covid-19-vaccines. Accessed 02 May 2024
41. US Centers for Disease Control and Prevention (2024) COVID Data Tracker https://covid.cdc.gov/covid-data-tracker/#pregnancy-data. Accessed 02 May 2024
42. Norman M, Magnus MC, Söderling J, Juliusson PB, Navér L, Örtqvist AK, et al. Neonatal Outcomes After COVID-19 Vaccination in Pregnancy. Jama. 2024 Feb 6;331(5):396-407. Epub 2024/02/06. doi: 10.1001/jama.2023.26945. PubMed PMID: 38319332; PubMed Central PMCID: PMCPMC10848052 Research Council of Norway, NordForsk, and European Research Council during the conduct of the study. No other disclosures were reported.
43. Carnalla M, Stern D, Colchero MA, Rangel-Moreno K, Basto-Abreu A, Alpuche-Aranda CM, et al. Who is getting COVID-19 boosters? A latent class analysis in a nationally representative sample of Mexican adults 60 years and over. Vaccine. 2024 May 22;42(14):3273-6.