




Maternal outcomes in pregnant women with COVID-19: impact of disease severity, timing of intervention, and SARS-CoV-2 variants

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ABSTRACT: This study aimed to analyze maternal outcomes in pregnant women infected with COVID-19, focusing on the impact of disease severity, timing of medical intervention, and the effect of different SARS-CoV-2 variants. A retrospective analysis was conducted on 9,288 pregnant women diagnosed with COVID-19. Disease severity was classified as mild (30%), moderate (52%), severe (17%), and critical (2%). The study also examined the timing of medical care, with 41.6% of women seeking care within 7 days of symptom onset and 58.4% after 7 days. The average gestational age was 271.8 days, with the majority (93.8%) at full-term pregnancy. Results indicated that 88.2% of women continued their pregnancies during treatment, while 11.9% experienced pregnancy termination, including preterm deliveries and miscarriages. The study found a significant ($p < 0.01$) association between COVID-19 severity and adverse outcomes, such as preterm birth and maternal mortality. Severe and critical cases demonstrated increased risks of uteroplacental insufficiency (52.1% and 85.5%, respectively), the need for intensive respiratory support, and ICU admission. The differences in outcomes between the Delta and Omicron variants are also highlighted. The Delta variant was associated with more severe disease and higher rates of complications, including a higher need for cesarean sections, compared to the Omicron variant. The overall 30-day survival rate was 98.05%, with a noticeable drop to 43.59% in critically ill patients. This study underscores the importance of early medical intervention and continuous monitoring in managing COVID-19 in pregnant women. The findings also emphasize the need to consider the variant-specific effects of SARS-CoV-2 on maternal and neonatal outcomes, which can guide clinical decision-making and improve the prognosis for both mother and child.

KEYWORDS: COVID-19, pregnancy, maternal outcomes, SARS-CoV-2 variants, preterm birth, uteroplacental insufficiency, respiratory support, intensive care, maternal outcomes

INTRODUCTION

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has significantly impacted global health, with pregnant women being identified as a particularly vulnerable population [1-3]. The clinical course of COVID-19 in pregnancy presents unique challenges, with potential implications for both maternal and neonatal health. Initial studies suggested that pregnant women might not experience more severe COVID-19 than the general population; however, subsequent research has shown that pregnancy is associated with an increased risk of severe illness, preterm birth, and other complications [4-7].

Approximately 47% of pregnant women with COVID-19 may be asymptomatic, while others exhibit symptoms ranging from mild to severe, with common symptoms including fatigue, cough, and fever [8]. Severe cases can lead to hospitalization, the need for oxygen therapy, and in some instances, mechanical ventilation (MV) [9]. Moreover, COVID-19 has been associated with complications such as preeclampsia and hemolysis, elevated liver enzymes, low platelet (HELLP) syndrome, further complicating the course of pregnancy [10].

One of the significant concerns in managing pregnant women with COVID-19 is the increased risk of preterm birth, especially in those with severe disease. This has been observed in various studies, where COVID-19 infection in pregnancy was associated with a higher likelihood of preterm delivery and, in some cases, low birth weight in neonates [6, 7]. Although vertical transmission of the virus (from mother to fetus) is rare, it remains a concern, and

RESEARCH ARTICLE

PII: S225199392400007-14

Received: July 29, 2024

Revised: September 19, 2024

Accepted: September 21, 2024

the majority of newborns from mothers with COVID-19 are healthy, with only a small percentage testing positive for SARS-CoV-2 [10]. The timing of medical intervention is a critical factor in determining maternal and neonatal outcomes. Early medical intervention is associated with better outcomes, as prompt treatment can mitigate the progression of the disease and reduce the risk of severe complications, such as acute respiratory distress syndrome (ARDS) and the need for MV [9]. In contrast, delays in seeking care have been linked to worse outcomes, including higher rates of ICU admission and adverse neonatal outcomes [11].

The emergence of different SARS-CoV-2 variants, such as Delta and Omicron, has further complicated the clinical management of COVID-19 in pregnancy. The Delta variant has been associated with more severe disease and higher rates of hospitalization and mortality compared to earlier variants, including the Alpha variant [12]. In contrast, the Omicron variant, although more transmissible, appears to cause milder disease, resulting in better maternal and neonatal outcomes [11]. Understanding the impact of these variants on pregnancy outcomes is essential for guiding clinical management and public health strategies.

Given these challenges, this study aims to analyze maternal outcomes in pregnant women with COVID-19, with a focus on the impact of disease severity, the timing of medical intervention, and the effects of different SARS-CoV-2 variants.

MATERIAL AND METHODS

In a study involving 9,288 pregnant women with COVID-19, mild disease severity was identified in 30% (2,755 patients), moderate severity in 52% (4,794 patients), and severe disease in 17.0% (1,574 patients), with only 2.0% (165 patients) experiencing a critical condition. The mean age of participants was 31.5 years (SD ±4.9), ranging from 18 to 53 years. The largest proportion of women (47.7%) were aged 25-29 years, followed by those aged 18-24 years (29.1%), 30-34 years (15.4%), and women aged 35 years and older (7.8%). The average time from symptom onset to seeking care was 11.6 days (SD ±3.8), with a range of 2 to 22 days, indicating that most women delayed seeking medical attention, possibly due to underestimating the severity of the disease or difficulty accessing healthcare services (Table 1). A total of 3,860 women (41.6%) sought care within 7 days of symptom onset, potentially reflecting earlier detection and a more favorable prognosis. However, 5,428 women (58.4%) sought care more than 7 days after symptom onset, often after receiving unsuccessful treatment at other regional maternity hospitals, which may be linked to the later initiation of specialized treatment, increasing the risk of complications, particularly during pregnancy.

Table 1. COVID-19 course and severity in pregnant women admitted to Zangiota-1

Parameter	n=9288	
	n	%
Time from COVID-19 symptom onset to maternity complex admission		
Mean	11,6±3,8 суток	
Range	2-22 суток	
<7 days	3860	41,6%
>7 days	5428	58,4%
Lung involvement		
Up to 50%	6120	65,9%
More than 50%	3168	34,1%
COVID-19 severity at initial assessment		
Mild	2755	30%
Moderate	4794	52%
Severe	1574	17%
Extremely severe	165	2%

A total of 6,120 women (65.9%) had lung involvement of up to 50%, while 3,168 women (34.1%) had lung involvement exceeding 50%, indicating a greater health risk for the mother and fetus, necessitating more intensive monitoring and treatment. The period from December 2020 to the end of 2023 encompasses several pandemic waves, allowing for an analysis of how changes in treatment strategies, vaccination, and the emergence of new variants impacted outcomes. Out of the total number of women, 646 (7.0%) were nulliparous, while 8,642 (93.0%) had previous childbirth experience. The predominance of multiparous women may indicate a higher likelihood of complications in this group or that they were more likely to seek medical care (Table 2).

Table 2. Pregnancy profile and gestational age of women with COVID-19 admitted to Zangiota-1

Parameter	n=9288	
	n	%
Parity		
Nulliparous	646	7,0%
Multiparous	8642	93,0%
Gestational age		
Mean gestational age (days)	271,8±13,5	
Range (days)	152-302 days	
Gestational weeks		
22 to <32 weeks	113	1,2%
32 to <35 weeks	241	2,6%
35 to <42 weeks	8715	93,8%
≥42 weeks	219	2,4%

The mean gestational age was 271.8 days (± 13.5), corresponding to approximately 39 weeks, close to full-term pregnancy. The range of gestational ages varied from 152 to 302 days, encompassing both preterm and post-term pregnancies. A total of 8,715 women (93.8%) were at a gestational age of 35 to less than 42 weeks, indicating full-term pregnancy. This suggests that most women were admitted late in their pregnancies, possibly due to preparation for delivery or exacerbation of COVID-19 symptoms at this stage. Preterm deliveries, between 22 to less than 32 weeks, were observed in 113 women (1.2%), and between 32 to less than 35 weeks in 241 women (2.6%). These data highlight the risk of preterm birth among women with COVID-19. In 219 cases (2.4%), pregnancies extended beyond 42 weeks, indicating post-term pregnancy. Preexisting comorbidities were identified in 646 women (7.0%). The presence of comorbid conditions before pregnancy can significantly complicate the course of COVID-19, increasing risks for both the mother and fetus.

Statistical analysis

In this study, the following statistical methods were applied:

Descriptive statistics: Calculated means, standard deviations, and percentages for baseline characteristics like age, gestational age, and COVID-19 severity to provide an overall summary of the sample. **Comparative analysis:** T-tests and chi-square tests were used to compare outcomes across groups with different COVID-19 severities and SARS-CoV-2 variants (Delta vs. Omicron), assessing the significance of differences in complications and outcomes. **Logistic regression:** Employed to identify risk factors for adverse outcomes (e.g., ICU admission, respiratory support needs), considering the impact of disease severity, timing of intervention, and viral variant. **Kaplan-Meier Survival analysis:** Analyzed 30-day survival rates to compare outcomes based on COVID-19 severity and variant type, highlighting survival differences in severe and critical cases.

RESULTS

A total of 8,196 women (88.2%) continued their pregnancies while undergoing COVID-19 treatment, indicating successful disease management in most patients. However, 1,102 women (11.9%) ended their pregnancies, including deliveries and cases of premature pregnancy termination, such as miscarriages (Table 3). Among women who completed their pregnancies, 694 (63.0%) delivered at term, indicating a favorable outcome for most women. A total of 391 women (35.5%) had preterm births, linked to COVID-19 complications or other infection-related risk factors. Sixteen women (1.5%) experienced miscarriages before 22 weeks, a small percentage, but one that underscores the risks associated with early pregnancy infection.

Spontaneous delivery occurred in 241 women (22.2%), reflecting a natural birth process without the need for intervention. Labor induction was performed in 127 women (11.7%), possibly necessary to prevent complications for both mother and child. Cesarean section was performed in 717 women (66.1%), constituting the majority of deliveries. The high percentage of cesarean sections is linked to the need for rapid delivery due to COVID-19 complications or other medical indications.

In mild COVID-19 cases, uteroplacental insufficiency (UPI) occurred in 0.9% (25 out of 2,755). In moderate cases, UPI frequency increased to 4.1% (197 out of 4,794). Among severe COVID-19 cases, UPI was observed in 52.1% (819 out of 1,574). In critical cases, UPI was recorded in 85.5% (141 out of 165) (Figure 1).

In mild COVID-19, respiratory support was rarely needed, with less invasive methods like non-invasive ventilation (NIV) predominating (2.7%, 75 cases). In moderate COVID-19, there was an increase in the use of all forms of respiratory support, particularly ICU admissions (8.6%, 413 cases) and NIV (3.9%, 188 cases). In severe COVID-19, a significant portion of patients required intensive care, with 53.6% (843 cases) needing ICU treatment, and 22.2% (349 cases) requiring MV. In critical COVID-19 cases, nearly all patients required MV (95.8%, 158 cases), and almost all were in the ICU (100.0%, 165 cases). These data underscore the significant increase in the need for intensive respiratory support as COVID-19 severity increases in pregnant women (Figure 2).

Table 3. Pregnancy outcome and delivery characteristics in women with COVID-19

Parameter	n=9288	
	n	%
Pregnancy outcome		
Continued pregnancy during COVID-19 treatment	8196	88,2%
Pregnancy completed	1102	11,9%
Delivery characteristics		
Full-term delivery	694	63,0%
Preterm delivery	391	35,5%
Miscarriage before 22 weeks	16	1,5%
Delivery mode		
Spontaneous delivery	241	22,2%
Induced labor	127	11,7%
Cesarean section	717	66,1%

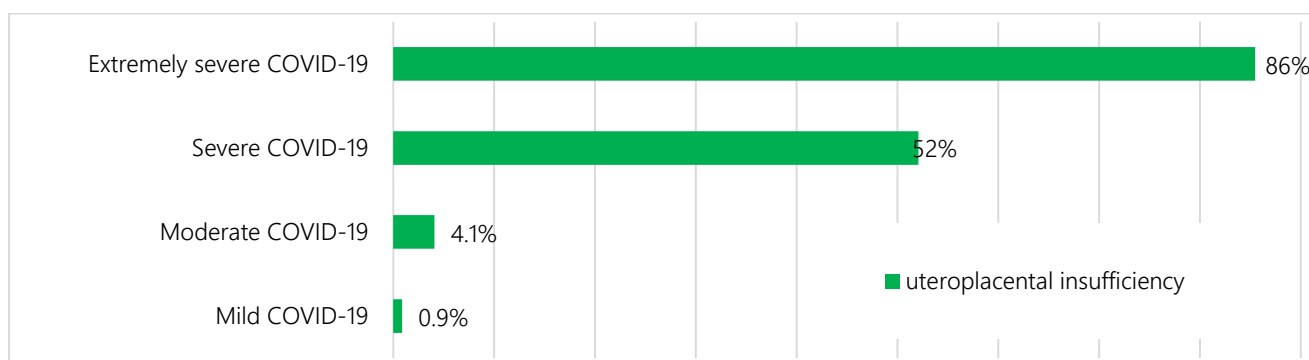


Figure 1. Uteroplacental insufficiency frequency by COVID-19 severity in pregnant women

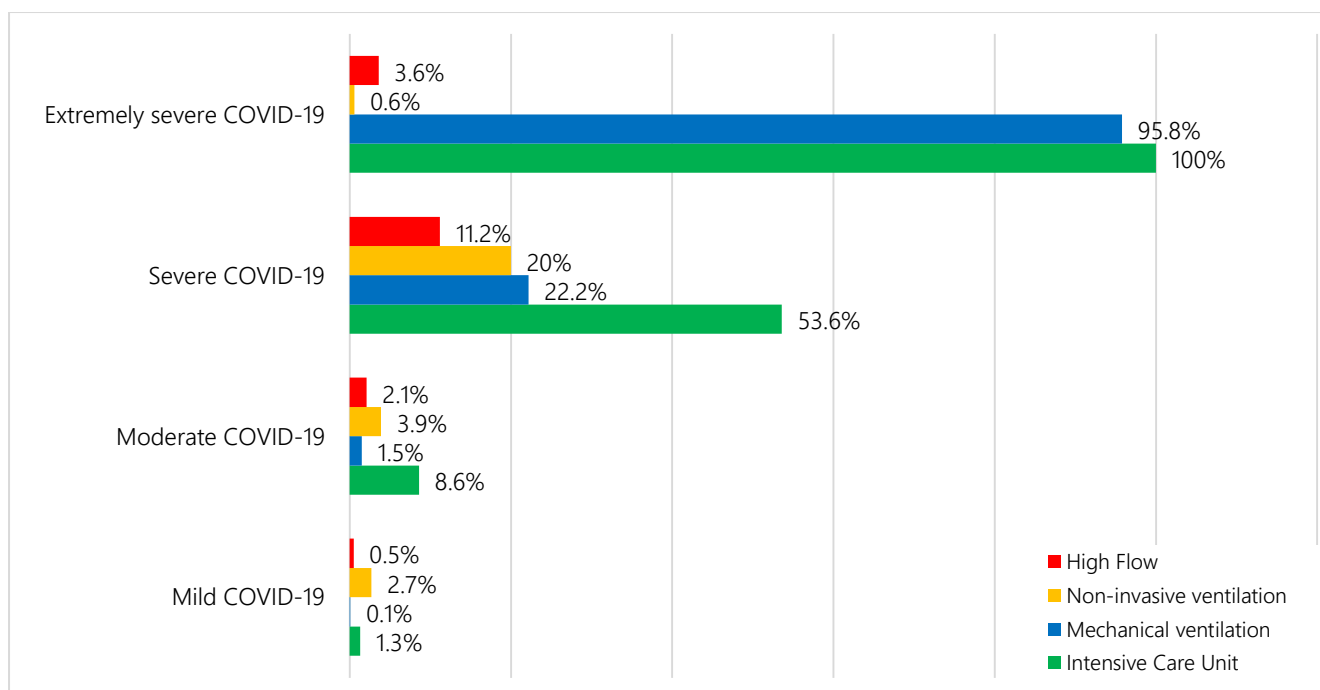


Figure 2. Analysis of respiratory support use by COVID-19 severity in pregnant women

Further analysis of hospital treatment outcomes showed that outcomes were strongly dependent on COVID-19 severity in pregnant women (Figure 3). For mild and moderate COVID-19, there was an almost 100% favorable treatment outcome (99.9%, 2,753 out of 2,755 and 4,790 out of 4,794 cases, respectively). In severe cases, mortality increased to 1.2% (19 out of 1,574 cases). In critical cases, mortality rose significantly to 26.7% (44 out of 165 cases).

This highlights the importance of early intervention and close monitoring of pregnant women with COVID-19, especially in the presence of risk factors and signs of worsening condition. Analysis of mortality among pregnant women with COVID-19 identified several immediate causes of death linked to complications from the infection.

Acute respiratory distress syndrome (ARDS), diagnosed in 29 cases, was a primary cause of death in severe and critical COVID-19 cases. The developing hypoxemia and worsening lung function led to acute respiratory failure, requiring intensive therapy, including MV. Multiple organ failure, observed in 24 patients, was characterized by the dysfunction of several vital organs, such as the heart, kidneys, and liver. Throughout the treatment course, 18 fatal cases were associated with an increased risk of thromboembolic complications, such as pulmonary embolism. Infectious complications, such as sepsis, were the direct cause of death in 37 pregnant women with COVID-19. Additionally, in women with pre-existing chronic conditions, such as diabetes, hypertension, or cardiovascular diseases, COVID-19 triggered the decompensation of these conditions, contributing to fatal outcomes.

The analysis of cumulative 30-day survival in pregnant women infected with COVID-19 by severity showed that patients with critical disease had significantly worse survival prospects compared to other groups (Figure 4). Mortality in severe COVID-19 was 1.2% (19 out of 1,574). In critical cases, mortality was 26.7% (44 out of 165). Overall, the 30-day survival among pregnant women with COVID-19 was 98.05%. For those with critical COVID-19, 30-day survival dropped to 43.59%.

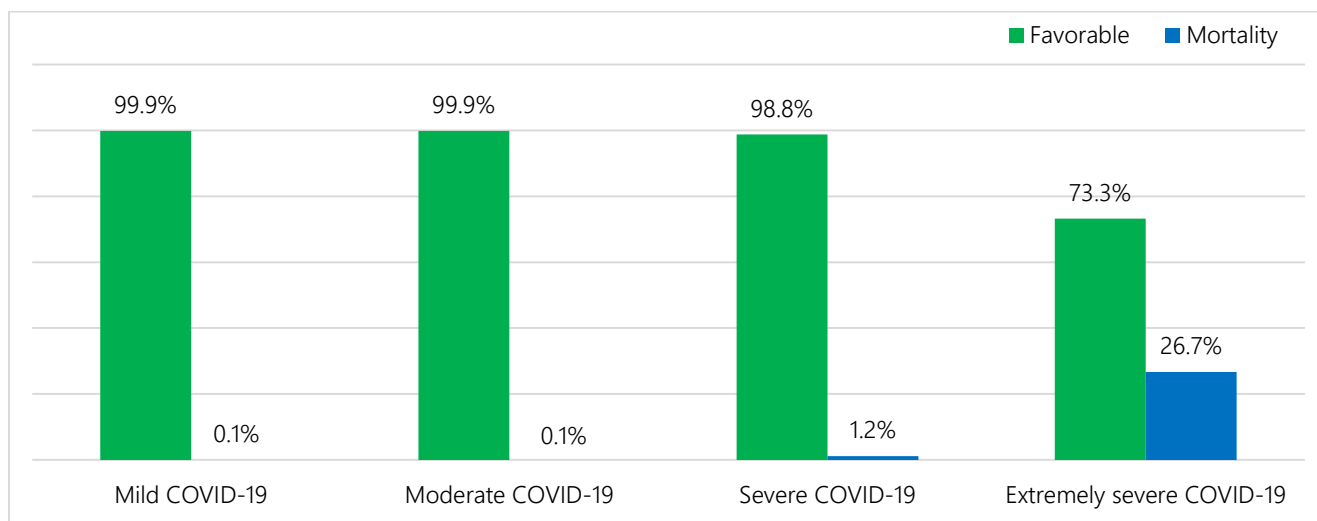


Figure 3. Treatment outcomes by COVID-19 severity in pregnant women

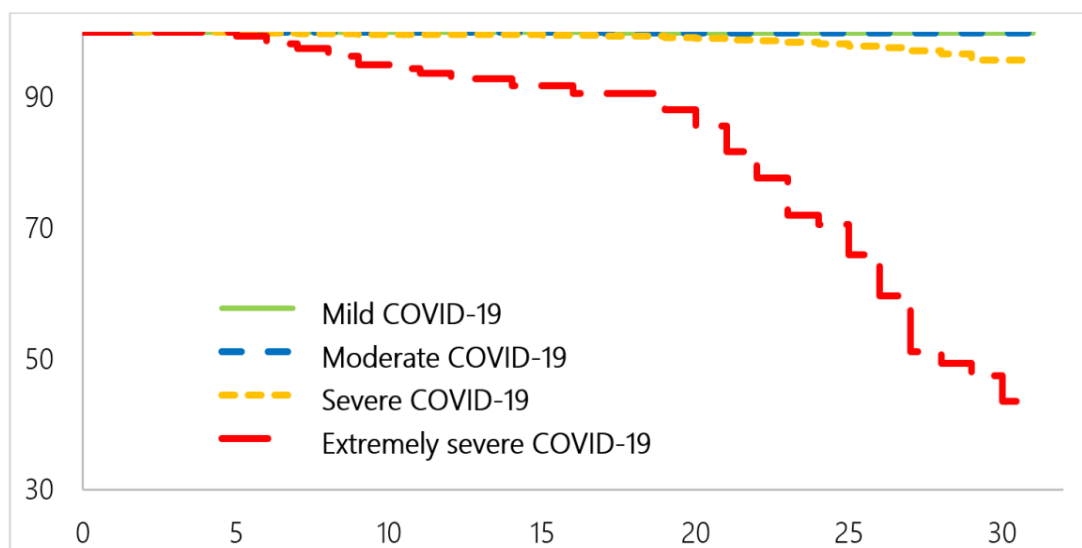


Figure 4. Cumulative 30 days survival in pregnant women by COVID-19 severity

Thus, this study showed that the severity of the clinical course of COVID-19 in pregnant women significantly impacts pregnancy outcomes, delivery, and newborn health. The largest proportion of patients had moderate to severe COVID-19. Early medical intervention correlated with mild disease, whereas later care, particularly after 7 days from symptom onset, was associated with more severe forms of COVID-19. Overall survival among pregnant women infected with the Omicron variant was higher (99.71% by day 30) compared to the Delta variant (95.63% by day 30) (Figure 5).

Comparative analysis of the clinical course and outcomes in pregnant women infected with the Delta and Omicron variants of SARS-CoV-2 revealed that the Delta variant was characterized by more severe disease and a higher frequency of complications (Table 3), such as UPI (OR=1.55, 95%CI 1.35-1.79, p<0.001), ARDS (OR=1.65, 95%CI 1.24-1.78, p<0.001), multiple organ failure (OR=2.28, 95%CI 1.87-2.78, p<0.001), preterm birth (OR=2.35, 95%CI 1.86-2.98, p<0.001), and maternal mortality (OR=3.13, 95%CI 1.2-8.15, p<0.001).

Accordingly, women with the Delta variant more frequently required intensive care, including ICU admissions (OR=1.88, 95%CI 1.63-2.17, p<0.001), MV (OR=1.59, 95%CI 1.34-1.89, p<0.001), and cesarean section (OR=1.92, 95%CI 1.63-2.27, p<0.001).

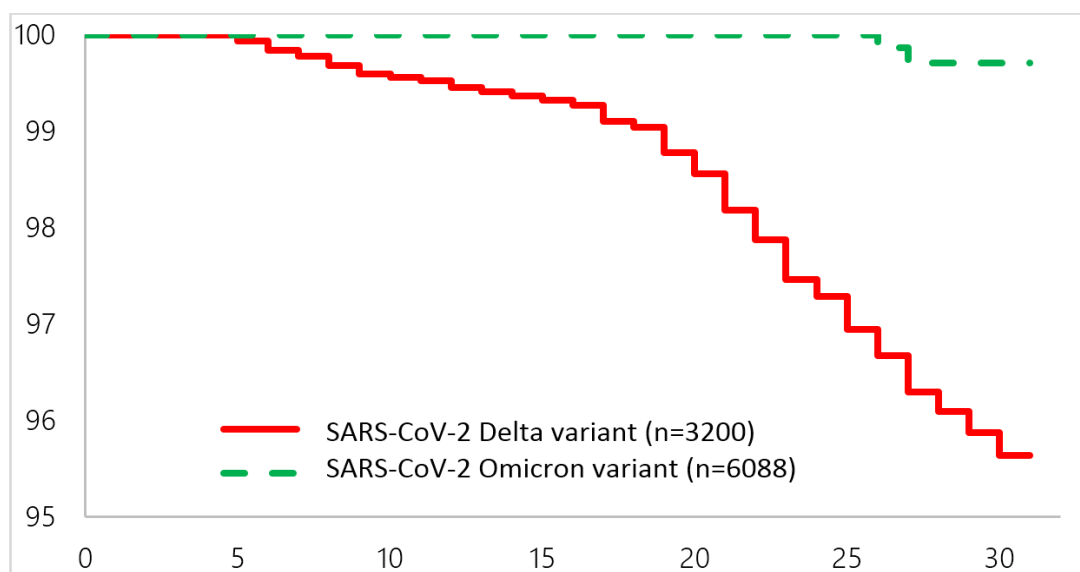


Figure 5. Comparative cumulative 30-Day survival in pregnant women infected with COVID-19

Table 4. Risk of specific outcomes associated with the Delta variant compared to the Omicron variant

Outcome	Odds Ratio	95% CI Lower	95% CI Upper	p-value
UPI	1.55	1.35	1.79	<0.001
ARDS	1.65	1.24	1.78	<0.001
Multiple Organ Failure	2.28	1.87	2.78	<0.001
Preterm Birth	2.35	1.86	2.98	<0.001
Maternal Mortality	3.13	1.2	8.15	<0.001
ICU Admission	1.88	1.63	2.17	<0.001
Mechanical Ventilation	1.59	1.34	1.89	<0.001
Cesarean Section	1.92	1.63	2.27	<0.001

DISCUSSION

This study provides a comprehensive analysis of maternal outcomes in pregnant women with COVID-19, emphasizing the effects of disease severity, the timing of medical intervention, and the impact of different SARS-CoV-2 variants. Our findings are consistent with, and add to, the growing body of literature on the subject.

The data from our study reveal a strong correlation between COVID-19 severity and adverse maternal outcomes. Severe and critical cases were associated with higher rates of uteroplacental insufficiency, preterm birth,

and maternal mortality. These findings align with previous research indicating that severe COVID-19 significantly increases the risk of adverse pregnancy outcomes. For instance, [Allotey et al. \[6\]](#) conducted a systematic review and meta-analysis showing that pregnant women with severe COVID-19 are more likely to require ICU admission and experience preterm birth compared to those with mild or moderate disease.

Similarly, a study by [Knight et al. \[7\]](#) reported that pregnant women with severe COVID-19 had an increased risk of preterm birth and stillbirth, with ICU admission rates significantly higher among those with more severe illness. Our findings reinforce the need for vigilant monitoring and early intervention in pregnant women presenting with COVID-19 symptoms, especially those at risk of severe disease progression.

Our study highlights the critical importance of early medical intervention in improving maternal outcomes. Women who sought medical care within 7 days of symptom onset had better outcomes compared to those who delayed care. This is consistent with the findings of other studies like [Vousden et al. \[9\]](#), who found that early hospitalization and treatment were associated with reduced severity and better outcomes in pregnant women with COVID-19.

The delay in seeking medical care, as observed in our study, may contribute to the progression of the disease, leading to worse outcomes, including higher rates of ICU admission, mechanical ventilation, and adverse neonatal outcomes. This underscores the importance of public health messaging and education for pregnant women about the risks of delaying medical care if COVID-19 symptoms develop.

The study also compared outcomes between women infected with the Delta and Omicron variants of SARS-CoV-2. The Delta variant was associated with more severe disease and higher rates of complications, including an increased need for intensive care, mechanical ventilation, and cesarean sections. These findings are consistent with those reported in the literature, where the Delta variant has been noted to cause more severe disease compared to earlier variants, including the Alpha variant [\[12\]](#).

In contrast, the Omicron variant, while more transmissible, has generally been associated with milder disease outcomes. This is reflected in our findings, where women infected with Omicron had better survival rates and fewer severe complications compared to those infected with Delta. The differential impact of these variants on pregnant women is an important consideration for clinical management and public health strategies. A study done by [Adhikari et al. \[11\]](#) similarly reported that the Omicron variant was associated with less severe outcomes in pregnant women compared to the Delta variant.

When compared to similar studies, our findings align with the global experience regarding the risks of COVID-19 in pregnancy. For instance, a large study conducted in the United States by [Ellington et al. \[8\]](#) found that pregnant women with COVID-19 were more likely to be admitted to the ICU and require mechanical ventilation than non-pregnant women of reproductive age. Our study adds to this by highlighting the impact of variant-specific differences on maternal and neonatal outcomes, providing a more nuanced understanding of the risks posed by COVID-19 in pregnancy. Additionally, [Villar et al. \[10\]](#) in a study involving pregnant women across multiple countries reported similar findings regarding the increased risk of severe maternal outcomes and preterm birth in those with COVID-19.

Our study's findings further support these observations and contribute additional insights into the influence of SARS-CoV-2 variants on these outcomes.

CONCLUSION

This study underscores the critical role of early intervention and variant-specific management in improving outcomes for pregnant women with COVID-19. The severity of the disease significantly impacts maternal and neonatal outcomes, and the emergence of different SARS-CoV-2 variants has further complicated the clinical management of these patients. Future research should continue to explore the long-term effects of COVID-19 in pregnancy, particularly as new variants emerge, to inform guidelines and optimize care for this vulnerable population.

DECLARATIONS

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Ethical approval

The review board and ethics committee of Republican Specialized Hospital Zangiota-1 approved the study protocol and informed consents were taken from all the participants.

Acknowledgements

This work was supported by Republican Specialized Hospital Zangiota-1, Tashkent, Uzbekistan.

Authors contributions

All authors contributed equally to this work.

Funding support

None.

Competing interests

All authors declare that they have no conflict of interest.

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