

Maternal and Neonatal Outcomes in COVID-19-Positive Pregnant Women

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Introduction

Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, poses significant risks to pregnant women. The physiological and immunological alterations during pregnancy render them more vulnerable to severe complications, and fetal health is also a concern due to the presence of SARS-CoV-2.¹ The maternal and neonatal outcomes associated with coronavirus infections, including SARS, MERS, and SARS-CoV-2, remain unclear. Although numerous studies have investigated the impact of COVID-19, there is a lack of data on the effects of gestational age at the time of diagnosis. This information is crucial for implementing trimester-specific interventions. Our clinical observation compared maternal, perinatal, and neonatal outcomes among COVID-19-infected patients across different pregnancy trimesters.

Clinical manifestations and patient characteristics

This clinical observation on SARS-CoV-2-infected pregnant women at Kamali Hospital, Iran (from May to November 2021) included hospitalized, polymerase-chain-reaction-positive pregnant women (excluding postpartum cases). Data on demographics, medical history, and clinical aspects were extracted from records, covering maternal age, comorbidities, infertility, abortion, stillbirth, pregnancy complications, delivery mode, gestational age (GA), COVID-19 symptoms, hospitalization duration,

intensive care unit (ICU) admission, intubation, treatment, and neonatal complications. The study was approved by the Research Ethics Committee of Alborz University of Medical Sciences (IR.ABZUMS.REC.1399.316) and was conducted by the Declaration of Helsinki. Informed written consent was obtained from all participants.

Maternal complications included gestational diabetes mellitus (GDM), preeclampsia, hypertension, and COVID-19-related mortality. Fetal or neonatal outcomes such as abortion, stillbirth, neonatal death, preterm birth, low birth weight (LBW), Apgar score, malformations, and infant health were assessed. Trimesters were defined by GA (first trimester: 0–13 weeks, second trimester: 14–26 weeks, third trimester: 27–40 weeks). Participants were grouped according to the trimester of COVID-19 symptom onset. The primary outcomes were the maternal, perinatal, and neonatal outcomes in COVID-19-infected pregnant women, exploring the trimester-related differences of SARS-CoV-2 infection.

The follow-up was from hospitalization to 28 days post-delivery. Obstetric, maternal, and neonatal outcomes were evaluated during hospitalization, at the end of pregnancy (from records), and 28 days post-delivery (by phone). The phone follow-up inquired about maternal postpartum outcomes (COVID-19 reinfection/symptoms, rehospitalization, surgery, pre-eclampsia signs, death) and neonatal outcomes (jaundice, hospitalization, infant death).

Statistical analysis

Data were presented as mean $\pm$ standard deviation or median (interquartile range, IQR) for continuous variables and percentage (frequency) for categorical variables. Chi-squared or Fisher's exact test was used for categorical variables (Fisher's exact test for small samples), the Kruskal-Wallis test for non-normally distributed data, and analysis of variance (ANOVA) for normally distributed data. Analyses were performed using SPSS 26.0 (Chicago, USA), and a *P*-value less than 0.05 was considered statistically significant.

Outcomes and complications analysis

Our study encompassed 172 hospitalized COVID-19-infected pregnant women. Two deaths occurred at admission and one-day post-hospitalization. Data was analyzed on 170 surviving, moderately or severely COVID-19 patients according to the clinical and imaging criteria. The trimester distribution indicated that 58.2% (99/170) were in the

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third trimester, 30.6% (52/170) in the second, and 11.2% (19/170) in the first. The median (IQR) age was 32.5 (27.8–37.0) years with no statistical difference among trimesters. Median GA at infection was 28 weeks ranging from 5–40. 27.1% had an abortion history ($n = 46$), and 8.2% had an infertility history ($n = 14$), with no statistically significant difference between trimesters. Eight infertile patients were conceived with IVF during this pregnancy. GDM occurred in 17 cases (8 post-COVID-19), preeclampsia in 5, and gestational hypertension in 2. Hydrocortisone and remdesivir were administered in 83.1% and 86.0% of cases, respectively. Common symptoms included cough (61.8%), fever (50.6%), dyspnea (57.6%), myalgia (22.4%), and fatigue (31.8%), with fatigue higher in the second trimester ($P = 0.01$). ICU admission was required in 30 cases (17.6%), with 8 intubations (7 in the third trimester, 1 in the second; $P = 0.215$). Nearly 60% had cesarean sections, more often in the third trimester group ($P = 0.004$). No congenital malformations were observed. Abortion occurred in 14.0% (7/50), more frequently in the first trimester (21%, 4/19) compared to the second trimester group (9.7%, 3/31), without statistically significant difference. Stillbirth or intrauterine fetal death (IUFD) occurred in 8 cases (7 in the second trimester, 1 in the first), with six abortions and four stillbirths/IUFDs in the acute infection phase. One infant died from pulmonary hemorrhage. The median hospital stay was 5 days (IQR: 3–8), and all patients were discharged in stable condition. No COVID-19 reinfections were reported during follow-up (see Supplemental Tables 1–3, <http://links.lww.com/MFM/A59>).

Insights and implications

In this study, we observed 172 COVID-19 infected pregnant women, 60% were infected in their third trimester. Higher rates of preterm labor, cesarean delivery, and ICU admissions occurred in the third trimester group. LBW rate increased with GA. Pregnancy loss/infant death was highest in the first trimester (1/3), followed by the second (1/5), with none in the third. Our findings also suggest no significant difference in the COVID-19 case fatality rate between pregnant women and the general population.² Previous studies have likewise demonstrated that pregnancy does not elevate the risk of COVID-19-related mortality.³ In contrast, pregnant women infected with SARS-CoV or MERS-CoV exhibited a 25% to 30% higher case mortality.⁴ The discrepancy may be attributed to the differential immunological responses elicited by SARS-CoV-2 compared to those elicited by SARS-CoV or MERS-CoV. In our study, patients who infected in the third trimester were more prone to developing severe disease. During pregnancy, as oxygen consumption increases, uterine enlargement and hormonal effects induce anatomical changes in the thoracic cage, resulting in a decrease in functional residual capacity.⁵ These alterations in respiratory function render pregnant women in the last trimester less tolerant to hypoxia.

Similar to our study, prior research found a direct association between pregnancy trimester at COVID-19 diagnosis.⁶ In our observation, around 70% of third-trimester-infected pregnant women had cesareans, thrice the global rate.⁷ This may be due to COVID-19 pneumonia or vertical transmission concerns. Data on the impact of maternal SARS-CoV-2 infection on pregnancy outcomes by

gestational age at diagnosis is limited. First-trimester fetal development makes maternal infections more harmful. Some early viral infections are associated with higher fetal loss/death and abnormality risks. The first-trimester abortion risk is about 10%–15%.⁸ Some case series reported increased abortion risk in SARS-CoV-2-positive mothers. Our study had a 21% first-trimester fetal loss without congenital defects. A recent study noted a higher incidence of adverse fetal outcomes in first-trimester COVID-19-diagnosed pregnant women.⁹

The preterm birth rate in the second and third trimesters of COVID-19-infected pregnant women exceeded the global rate (~10%), while the first trimester did not. Similar studies reported a higher preterm labor incidence. Karasek *et al.*¹⁰ noted increased risks of very preterm, preterm, and early-term birth, especially in patients with COVID-19. Pathological changes in the placenta after COVID-19, like decidual arteriopathy, fibrinoid deposition, inflammation, and maternal vascular malperfusion, may lead to adverse pregnancy outcomes. The vertical transmission of SARS-CoV-2 remains controversial.

This study has limitations. The lack of a control group, due to the COVID-19 pandemic peak and testing resource scarcity, restricts direct outcome comparison, though within-group trimester comparisons were made. Also, a small first-trimester sample size from recruitment challenges. However, a strength is the comprehensive trimester comparison of clinically important pregnancy complications and outcomes in COVID-19 patients, providing insights into the impact on pregnancy via within-group analysis.

Conclusion

Pregnant women in the third trimester may have a greater susceptibility to severe COVID-19. Third-trimester infection correlates with higher preterm labor, cesarean delivery, and LBW rates. In contrast, first-trimester infection is linked to an increased risk of pregnancy loss.

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Author Contributions

Mahnaz Seifi Alan: Supervised study design, drafted manuscript. Elmira Jafari Afshar: Led patient recruitment, offered clinical expertise, interpreted data. Parham Samimisedeh: Contributed to design, recruitment, reviewed manuscript. Somaye Moghadam: Aided patient enrollment, managed data, provided clinical insights. Mahya Dorri: Contributed to literature review and manuscript discussion. Bitah Bاده-noosh: Contributed to design, screened patients, revised manuscript. Maedeh Jahansooz: Assisted recruitment, reviewed manuscript. Hadith Rastad: Provided statistical expertise, analyzed data, prepared manuscript.

Conflicts of Interest

None.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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