## **Original Research**

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### Abstract

Background: The COVID-19 pandemic has raised concerns about the potential impact of SARS-CoV-2 infection on pregnancy outcomes. However, there is limited evidence regarding the association between COVID-19 and spontaneous abortion cases, particularly in Bangladesh. Methods: This retrospective observational study investigated the baseline characteristics of 48 cases of spontaneous abortion in pregnant women with laboratory-confirmed COVID-19 infection at Enam Medical College Hospital, Savar, Dhaka, Bangladesh between March and July 2020. Participants were included if they experienced fetal demise at 11 or more weeks of gestation, and potential confounding factors, such as fetal malformations or other obstetric disorders, were excluded. Data on demographic characteristics, gestational age, parity, gravidity, and COVID-19 severity were collected and analyzed.

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Results: The age distribution of participants ranged from 18 to 33 years, with 50% in the 26-30 year age group. A majority (58.33%) were obese, and 83.33% exhibited mild COVID-19 symptoms, while 16.67% were asymptomatic. Regarding gestational age at the time of spontaneous abortion, 50% were between 11-15 weeks, 41.67% were between 16-20 weeks, and 8.33% were between 21-25 weeks. All participants had at least one previous pregnancy, with 33.33% experiencing their second pregnancy, 41.67% their second pregnancy with a previous live birth, and 25% their third pregnancy with at least one previous live birth.

Conclusions: This study provides insights into the baseline characteristics and maternal outcomes of COVID-19 infected spontaneous abortion cases in Bangladesh. The findings suggest that severe COVID-19 illness may not be a prerequisite for adverse pregnancy outcomes and highlight the need for further investigations into the potential mechanisms of intrauterine SARS-CoV-2 transmission and the role of placental factors. Larger-scale studies are warranted to better understand the impact of COVID-19 on pregnancy outcomes and develop appropriate management strategies.

### Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has emerged as a global public health crisis. Declared a pandemic by the World Health Organization in March 2020, this novel coronavirus strain was first identified in Wuhan, China, in 2019. While the primary mode of transmission is through respiratory droplets, the possibility of perinatal remains uncertain<sup>1-3</sup>. Though transmission previous studies have suggested that pregnant

symptoms, some cases of acute maternal morbidity and mortality have been reported <sup>1,4-5</sup>. Pregnancy is a unique physiological state characterized by a delicate balance of immune tolerance towards the fetus's paternal antigens. This altered immune response can heighten susceptibility to infections, particularly respiratory illnesses like pneumonia<sup>3,6</sup>. Immunologists intricate continue explore to the factors women typically experience mild COVID-19 contributing to maternal immune tolerance, as changes in the immune system can render pregnant women vulnerable to various ailments. Physiological and mechanical modifications during pregnancy can further amplify infection rates, especially for respiratory tract infections. The early stages of pregnancy are a critical and vulnerable period, where any disturbance can impact embryogenesis and fetal organ development. Maternal ailments during pregnancy have been observed to affect neonates, contributing to neonatal morbidity and mortality. While COVID-19 is an infectious respiratory disease, its potential effects on neonates and child morbidity and mortality are still under investigation. Currently, there are limited guidelines for the critical care management of pregnant patients with COVID-19 infection. Furthermore, the association between COVID-19 and miscarriages or fetal demise is not well-established due to the scarcity of reported cases <sup>1,7-9</sup>. Consequently, there is a pressing need for evidence-based studies to elucidate the interrelationship between COVID-19 infection during pregnancy and the risk of miscarriages and fetal deaths, thereby informing suitable interventions. The present study focuses on cases of spontaneous abortion or fetal death in pregnant women infected with COVID-19. To the best of our knowledge, no other studies have been conducted on this subject in Bangladesh.

## **Methods**

The retrospective observational study was conducted on patients attending the Gynecology Emergency and Outpatient Department at Enam Medical College Hospital, Savar, Dhaka, Bangladesh, with hospital records from March 2020 to July 2020. The initial sample size was determined as 150 pregnant women with COVID-19 admitted to BSMMU. From this initial cohort, 48 cases of spontaneous abortion were selected and studied, following specific inclusion and exclusion criteria. The inclusion criteria were: 1) pregnant population, 2) confirmed COVID-19 cases, and 3) fetal demise with a gestational age of  $\geq$ 11 weeks. The exclusion criteria were: 1) other possible causes of abortion, such as fetal malformations, abruption. placenta placental previa. preeclampsia, diabetes, autoimmune disorders, or maternal trauma, and 2) COVID-19 negative cases. All cases of fetal demise had a gestational

age of  $\geq$ 11 weeks, determined clinically with the help of the earliest ultrasound (US) scan. Abortion was confirmed in the same manner, along with laboratory-confirmed COVID-19 via Real-Time Polymerase Chain Reaction (RT-PCR) assay of maternal nasal swab specimens. This case series aimed to acquire knowledge regarding pregnancy and the novel presentation of COVID-19, with the hope that this study would contribute to the pool of knowledge regarding COVID-19 infection in pregnancy and aid in developing appropriate interventions.

## Results

 Table 1: Baseline characteristics distribution of the participants

Variables	n=48	n(%)		
Age Range				
16-20	4	8.33		
21-25	12	25		
26-30	24	50		
31-33	8	16.67		
BMI				
Normal	20	41.67		
Obese	28	58.33		

The study involved a total of 48 participants who experienced spontaneous abortion during COVID-19 infection. Regarding the age distribution, half of the participants (50%) were in the 26-30 year age range, followed by 25% in the 21-25 year range, 16.67% in the 31-33 year range, and 8.33% in the 16-20 year range. In terms of body mass index (BMI), a majority of the participants (58.33%) were classified as obese, while 41.67% had a normal BMI.

**Table 2:** Previous Pregnancy report in parity and gravidity

 of the participants

Parity	n=48	n(%)
Gravida 1 Parity 0	16	33.33
Gravida 1 Parity 1	20	41.67
Gravida 2 Parity 1	12	25

The data on parity and gravidity revealed that the largest proportion of participants, 41.67%, were gravida 1 with parity 1, indicating they had been pregnant once before and had one previous live birth. Additionally, 33.33% of the participants were gravida 1 with parity 0, meaning it was their first pregnancy. The remaining 25% of participants were gravida 2 with parity 1, indicating they had been pregnant twice before and had one previous live birth.

 Table 3: Distribution of gestational weeks at abortion of participants

Gestational Week	n=48	n(%)
11-15	24	50
16-20	20	41.67
21-25	4	8.33

Half of the participants (50%) experienced spontaneous abortion between 11-15 weeks of gestation. Additionally, 41.67% of the abortions occurred between 16-20 weeks, while 8.33% of cases were between 21-25 weeks of gestation. Table 4: Covid-19 severity in the participants

Cov-19	n=48	n(%)
Asymptomatic	8	16.67
Mild	40	83.33
Severe	0	0

The majority of the participants (83.33%) exhibited mild COVID-19 symptoms at the time of spontaneous abortion. Meanwhile, 16.67% of the participants were asymptomatic, and none of the participants experienced severe COVID-19 illness.

## Discussion

The COVID-19 pandemic has emerged as a global crisis, affecting individuals across all walks of life. Pregnant women, in particular, face unique challenges due to the lack of proper guidelines for their management amidst the pandemic. The role of COVID-19 infection during pregnancy is yet to be fully established, although previous studies have reported predominantly mild cases with few instances of mortality and perinatal demise<sup>3,10-13</sup>. The present study focuses on the analysis of 48 cases of spontaneous abortion in pregnant women with laboratory-confirmed COVID-19 (via RT-PCR) at a single hospital in Dhaka, Bangladesh, between March and July 2020. To the best of our knowledge, no similar study has been conducted previously in Bangladesh. The cases included fetal demise at 11 or more weeks of gestation, with gestational age determined through case history ultrasound Potential and earlier scans. confounding factors, such as fetal malformations, placental abruption, placenta previa, preeclampsia, diabetes, autoimmune disorders, or maternal trauma, were excluded to isolate the potential impact of COVID-19 infection. The age distribution of the participants ranged from 18 to 33 years, with 50% falling within the 26-30 year age group, reflecting the common trend in Bangladesh of women becoming pregnant in their late twenties

or early thirties. Only 8.33% of the participants were under 20 years of age. Notably, 58.33% of the participants were obese, a factor that has been identified as a potential risk factor for COVID-19 in some studies<sup>16</sup>, while the remaining participants had a normal body mass index (BMI). Regarding previous pregnancy history, all participants had experienced at least one prior pregnancy. For 33.33% of the participants, the current pregnancy was their second, but their first fetus did not survive beyond 24 weeks of gestation. In 41.67% of cases, the first fetus had survived beyond 24 weeks, and this was their second pregnancy. The remaining 25% were in their third pregnancy, with at least one previous fetus surviving beyond 24 weeks of gestation. In terms of gestational age at the time of spontaneous abortion, 50% of the participants were between 11-15 weeks, 41.67% were between 16-20 weeks, and 8.33% were between 21-25 weeks, with all four cases in the latter group being at 21 weeks of gestation. Regarding COVID-19 severity, 83.33% of the participants exhibited mild symptoms, while 16.67% were asymptomatic, and none experienced severe illness. The study did not investigate the presence of SARS-CoV-2 in placental segments through histopathological analysis, limiting the understanding of the exact mechanism of intrauterine virus transmission. However, hypotheses suggest that angiotensinconverting enzyme 2 (ACE2), which acts as a surface receptor<sup>14,15</sup>, or placental barrier damage due to maternal hypoxemia<sup>16</sup>, could play a role. Additionally, reports indicate that COVID-19 can induce placental inflammatory reactions, acute chorioamnionitis. intervillositis, and intense neutrophil infiltration <sup>3</sup>. All cases were managed through a multidisciplinary approach.

Limitations of The Study: The retrospective nature of the current study created multiple limitations. One of the limitations of our study was that we could not collect an autopsy report of the placenta. Another limitation was contract tracing of all patients was not done and we could not conduct fetal autopsy. Here, more studies are needed to confirm the clinical causes of the disease and help to make appropriate management protocols in pregnancy during COVID-19 pandemic

Conflict of interest: None Declared.

# Conclusion

In conclusion, this study provides valuable insights into the baseline characteristics and maternal outcomes of COVID-19 infected spontaneous abortion cases in Bangladesh. The findings reveal that the majority of the participants were in their late twenties, with a significant proportion being obese, a known risk factor for COVID-19 complications. Notably, most participants experienced mild COVID-19 symptoms or were asymptomatic, suggesting that severe illness may not be a prerequisite for adverse pregnancy outcomes. The gestational age at the time of spontaneous abortion varied, with half of the cases occurring between 11-15 weeks, and a smaller proportion occurring later in pregnancy. The study also highlights the need for further investigations into the potential mechanisms of intrauterine SARS-CoV-2 transmission and the role of factors such as placental inflammation and hypoxemia. While the study provides valuable insights, largerscale studies with more comprehensive data collection are warranted to fully elucidate the impact of COVID-19 on pregnancy outcomes and develop appropriate management strategies. Nonetheless, this research contributes to the growing body of knowledge on the effects of COVID-19 during pregnancy and underscores the importance of multidisciplinary approaches in managing such cases.

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