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Original Research Article

Maternal and foetal outcome in COVID-19 infection: what we learnt and what lies ahead

Ambreen Shaikh, Niranjan Mayadeo, Jyotsna Dwivedi, Madhura Mandlik*

Department of Obstetrics and Gynaecology, Seth G S Medical College and KEMH, Mumbai, Maharashtra, India

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***Correspondence:**
Dr. Madhura Mandlik,
E-mail: madhuramandlik13@yahoo.in

ABSTRACT

Background: The world has seen 16 major pandemics since its inception. COVID-19 (coronavirus disease 2019), being the most recent one, was a pandemic the world faced, due to a new coronavirus called the SARS-CoV-2. It originated in Wuhan, China and soon grappled the whole world. The World Health Organization (WHO) declared COVID-19 a global pandemic on March 11, 2020. This pandemic lasted for three years, with the WHO finally declaring an end to the global health emergency on May 5, 2023 Pregnant women remain a vulnerable population for such respiratory illnesses that pose a risk to not only the mother but also the foetus.
Methods: This was a retrospective study conducted in a tertiary care, premium institute in Mumbai, during the third wave of COVID 19 in India. Primary objective was to assess maternal and foetal outcome in COVID 19 positive patients. Secondary objective was to assess rate of preterm delivery in COVID 19 positive patients.
Results: 103 COVID 19 positive women were included in the study. 74.7% patients who had tested positive, were asymptomatic. There was no statistical difference between the mode of delivery of patients. The most common comorbidity in the positive patients was pre-eclampsia (15.53%). 2.9% patients received Remdesivir and 2.9% received Favipravir. 58.2% were transferred to a dedicated COVID 19 hospital post-delivery. There were three intrauterine foetal demises. 18 (17.47%) women delivered preterm under 37 weeks. The rate of preterm delivery was significantly higher in COVID-positive patients (p-value <0.00025).
Conclusions: The COVID-19 pandemic posed significant challenges for healthcare workers and policymakers. It is crucial for clinicians to learn from this experience to enhance preparedness and mitigate future adversities.

Keywords: COVID 19, Third wave, Maternal outcome, Foetal outcome, Preterm birth

INTRODUCTION

We were taken by surprise, in December 2019, when the emergence of a new strain of coronavirus, made the world come to a standstill. Viruses are known to be circulating and mutating and are responsible for epidemics of flu or respiratory infections. Coronaviruses are known to cause respiratory, enteric, hepatic and neurologic diseases in humans, birds and other mammals.1) Out of the myriad coronavirus species, six have been causing diseases in humans, namely 229E, OC43, NL63 and HKU.[1] They mainly infect the immunocompetent and are known to cause symptoms of common cold.[2] The two other strains-severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV)-are zoonotic in origin and have been linked to sometimes fatal illness. In 2019, Wuhan, China a novel beta coronavirus was identified in patients of pneumonia.

This was a new virus, different from the MERS-CoV and SARS-CoV. India alone had witnessed 6.4 million deaths till 2021. Even today, in 2024, the virus continues to circulate and SARS-CoV-2 PCR percent positivity was found to be around 7.3% across 79 countries during the week ending on 28 April 2024. Due to their ability to mutate, viruses have different variants and variants of

concern with regard to SARS-CoV-2 were Alpha, Beta, Gamma, Delta and Omicron. The Omicron strain came into being in November 2021, was associated with higher transmission rates leading to surges in case numbers, but was associated with less severe complications.[3]

SARS-CoV-2 infection in pregnancy was associated with worsening of maternal and neonatal outcomes. Increased risk of severity of illness, need for critical care unit, mechanical birth and preterm birth. This study was conducted from January 2022 to March 2022, during the third wave, in a premier teaching institute in Mumbai, India. This research aimed at studying the maternal and foetal outcome in women with coronavirus infection and to highlight lessons learnt, so as to strengthen preparedness, for tackling virus epidemics and pandemics.

METHODS

Study type

This study was a retro-prospective, cross-sectional study.

Study place

Study was conducted in the Department of Obstetrics and Gynaecology, Seth G S Medical college and KEM Hospital.

Sample size

During the study period, 1445 women were admitted to the hospital, 103 were COVID 19 positive and 1342 were negative.

Study duration

Study was carried out from January 2022 to March 2022, during the third wave of COVID 19.

Inclusion criteria

Pregnant patients who tested positive for COVID 19 on RTPCR (Reverse transcriptase polymerase chain reaction) swab taken from the nasopharynx, were included in study. These patients were either admitted from the outpatient department, were referred or had presented to the emergency room.

Exclusion criteria

Patients who were COVID 19 positive who were transferred to other hospitals or who were not in labour were excluded from the study.

Data collection

Data was collected using a pre-validated case record form.

Statistical analysis

Data recorded in Microsoft Excel sheet. Categorical data expressed by percentage and comparisons made by the $\chi 2$ test. Open Epi version 3, an online statistical tool was be used for calculations.

RESULTS

During the study period a total of 1445 women were admitted and out of them 103 women had tested positive for COVID-19.

The average age of women included in this study was 27.19 years. The average education was up to 10th grade, while most were homemakers. Table 1 shows the distribution of age, education and occupation of COVID-19-positive women.

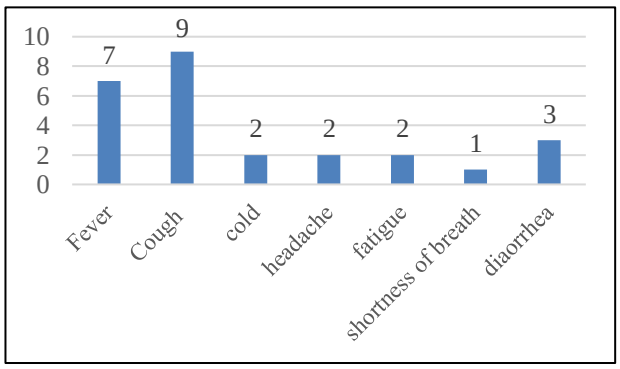

Figure 1: Symptoms of COVID 19 positive women.

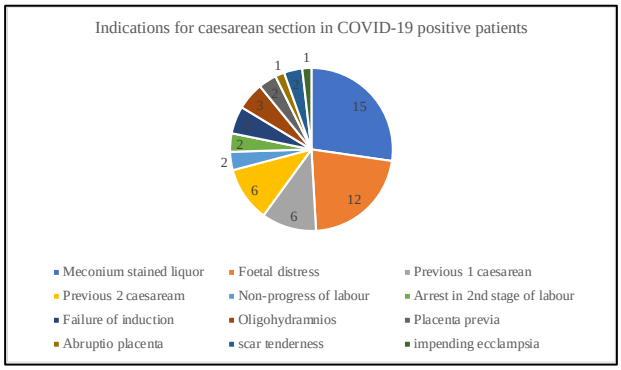

Figure 2: Indications of caesarean section in COVID 19 positive patients.

44 were primigravida and the average gestational age was 37.2. 18 (17%) out of 103 women presented with preterm labour. 90 women out of 103 had pain in abdomen on admission, whereas only 6 had complain of decreased foetal movement. 3 women had an intrauterine foetal demise. 77 (74.74%) women who tested positive for COVID-19 were asymptomatic. Most common symptom was cough (8.7%) and shortness of breath (1%) was the least common. Figure 1 showing symptoms of COVID 19 positive women. 15.53% women had pre-eclampsia. Out

of 103 women, 6 had anaemia, 3 had thrombocytopenia,1 had history of deep vein thrombosis, 1 had extrahepatic portal-venous obstruction and 1 had Anti phospholipid antibody syndrome. 55 women had an emergency lower segment caesarean section.

Table 3 shows the mode of delivery in COVID-19 positive vs COVID-19 negative women. On comparing with COVID-19 negative women, difference in mode of delivery was not statistically significant (p value>0.06). The most common indication for caesarean section amongst the COVID-19 patients was meconium-stained amniotic fluid (27%) followed by foetal distress (21%). Figure 2 highlights the various indications for caesarean delivery in COVID-19 positive patients.

Only 2 patients in the postpartum period had postpartum haemorrhage, severe enough to warrant transfusion of blood and blood products. Antipyretics like paracetamol, hydrartion vitamin C formed the backbone of the supoortive treatment that was given to all COVID-19 positive patients. Only 13 (12.6%) women needed anti-viral treatment. Remdesevir was given to only 3 patients who were treated in an intensive care setting. Table 4 highlights the antiviral therapy and place of treatment for COVID-19 positive patients.

Only 2 patients had abnormalities on a chest X-ray. 100 babies born had an APGAR of 9/10, whereas, there were 3 intrauterine foetal demises. Average baby weight was 2.55 kg. 5 babies were COVID-19 positive and 22 babies were small for gestational age. 66 out of 103 babies were admitted in the neonatal intensive care unit for observation. 18 (17.47%) women delivered preterm under 37 weeks. Table 5 shows preterm births in COVID19 positive vs COVID-19 negative patients. The rate of preterm delivery was significantly higher in COVID-positive patients (p value<0.00025).

Table 1: Patient characteristics of COVID 19 positive patients.

Age	Number of women
</=20	8
21-25	26
26-30	43
>30	26
Education	
Uneducated	5
Primary	17
Secondary	60
Higher secondary	18
Graduate	3
Occupation	
Homemaker	78
Private	25
Government	0

Table 2: The associated maternal co-morbidities in COVID-19 positive pregnant women.

Co-morbidities	Number of patients
Gestational diabetes	2 (1.3%)
Pre-ecclampsia	16 (15.53%)
Hypothyroidism	8 (7.70%)
Heart disease	3 (2.9%)

Table 3: Comparing the mode of delivery in COVID 19 positive patients vs COVID 19 negative patients.

	COVID-19+	COVID-19-	Total
LSCS	55	590	645
Vaginal delivery	48	752	800
Total	103	1342	1445

Table 4: The distribution of administering anti-viral therapy and place of treatment.

Anti-viral therapy	Number of COVID-19 positive mothers
Remdesevir	3 (2.9%)
Favipravir	3 (2.9%)
Oseltamavir	5 (4.8%)
Ritonavir	2 (1.9%)
Place of treatment	
COVID-19 positive ward	32 (31.06%)
Intensive care unit	11 (10.6%)
Dedicated covid care hospital	60 (58.2%)

Table 5: Preterm birth in COVID19 positive vs COVID 19 negative patients.

	COVID +	COVID -
Preterm births	18 (8.27) (11.45)	98 (107.73) (0.88)
Full term births	85 (94.73) (1)	1244 (1234.27) (0.08)
Total	**103**	**1445**

DISCUSSION

The world has seen 16 major pandemics since its inception. COVID-19 (coronavirus disease 2019), being the most recent one, was a pandemic the world faced, due to a new coronavirus called the SARS-CoV-2. The world health organization, labelled it a pandemic on the global level on 11th March 2020.[4] It lasted for three years and the World health organisation declared the global health emergency had come to an end on 5th May 2023. Besides the mild "common cold" coronaviruses already present in humans, SARS-CoV-2 is the third highly infectious and disease-causing coronavirus to emerge in the past two decades. This follows the outbreaks of SARS-CoV in 2002-2003 and MERS-CoV, which first appeared in 2012

Statistics from the World Health Organization state that, till May 2023 there were 765 million confirmed cases of COVID 19, worldwide, with India recording around 45 million cases.[5] A staggering 6.9 million people had lost their lives in their fight against COVID-19.

The World Health Organization (WHO) states that a new wave of infection requires a significant increase in cases after the previous wave has been brought under control. Standardized terminology is crucial to differentiate and understand the epidemic, reducing confusion among healthcare providers, researchers and policymakers.[6] In this study we present the data from the third wave of COVID-19 pandemic in India.

As a RNA virus, SARS-CoV-2 is prone to genetic evolution as it adapts to human hosts. Over time, mutations accumulate, leading to the emergence of new variants with distinct characteristics that differ from the original strain. Variants of Concern (VOCs) are characterized by increased transmissibility or virulence, reduced effectiveness of antibodies from natural infection or vaccination, ability to evade detection and decreased effectiveness of treatments or vaccines. The variants of concern were Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2) and Omicron (B.1.1.529).[7,8] Adhikari et al, divided the dominant variant as follows pre-Delta epoch: 17 May 2020 to 26 June 2021; Delta epoch: 27 June 2021 to 11 December 2021; Omicron epoch: 12 December 2021 to 29 January 2022.[9]

Pregnant women were a vulnerable group, which posed high morbidity with COVID-19 infection. Pregnancy's anatomical and physiological changes, such as the enlarged uterus elevating the diaphragm, reduced lung capacity, increased oxygen demand and airway swelling, may increase susceptibility to severe respiratory infections and reduce tolerance to low oxygen levels, as observed in a Hong Kong study on SARS-CoV-19 patients.[10] Pregnant women infected with pre-delta and omicron variants were majorly asymptomatic, while those infected with the delta variant were symptomatic. The Omicron variant which came into being in the later 2021, was more rapidly transmissible and spread rampantly across borders.

74.75% patients who tested positive for COVID 19 were asymptomatic. A population-based study was conducted by Crovetto et al, and it showed that around 68.5% were asymptomatic.[11] Study conducted in Sweden by Ahlberg et al, highlighted that out of the 156 COVID-19 positive patients, 65 % patients had no symptoms.

In our study, out of 103 patients 29 (28.15%) had co-morbidities and 16 women (15.53%) had pre-ecclampsia. Pre-eclampsia is characterised by endothelial dysfunction which leads to increase in blood pressure, proteinuria and associated complications.[12] Infection with SARS-CoV-2 increases risk of pulmonary endothelial damage which further increases risk of pre-eclampsia, when infection occurs during pregnancy.[13] Pre-eclampsia is characterised by abnormal placentation leading to placental ischaemia, which in turn leads to an anti-angiogenic environment. There is increase in inflammatory cytokines like FMS-like tyrosine kinase 1 (sFlt-1), which leads to endothelial damage.[14] The pathophysiology of COVID-19 infection is akin to pre-eclampsia. In SARS-CoV-2 infection, there is alveolar epithelial damage and pneumonia with respiratory distress syndrome causes hypoxia, leading to activation of cytokine storm and the renin angiotensin system (RAS).[15] Activation of RAS is central to the pathophysiology of both pre-eclampsia and COVID-19. Thus, there is a chance of increased risk of pre-eclampsia with COVID 19 infection in pregnancy.

Villar et al, conducted a cohort, multicentre study, which included 706 COVID 19 positive and 1424 COVID 19 negative pregnant patients. Women with COVID 19 were at a higher risk of developing pre-eclampsia (relative risk [RR], 1.76; 95% CI, 1.27-2.43).[16] This study also highlighted an increased risk of pre-term birth (RR, 1.59; 95% CI, 1.30-1.94).

Xiong et al, conducted a single-centred retrospective study with 116 COVID-19 positive patients. They stated that the occurrence of new onset hypertension was higher in cases of severe COVID-19 infection.[17] Presence of pre-eclampsia on the background of infection with SARS-CoV-2, was associated with poorer maternal and neonatal outcome.

55 out of COVID-19 positive women (53%) had an emergency caesarean section and the most common indication was meconium-stained amniotic fluid. A retrospective cross-sectional study conducted by Miyamoto et al, included 98 COVID 19 positive patients to 388 patients who were negative. Both groups had a similar rate of caesarean delivery and vaginal delivery.[18] We found a similar finding in our study, difference in mode of delivery was not statistically significant (p value>0.06). Magawa et al, conducted a cross sectional observational retrospective study in Japan and found that COVID 19 infection was associated with higher rate of caesarean section and increased rate of caesarean with no medical indications. They also found poorer neonatal outcome in the caesarean section group.[19]

Remdesivir is a nucleoside prodrug that exhibits broad-spectrum antiviral activity against various human and zoonotic coronaviruses. As the first licensed treatment for COVID-19, remdesivir has demonstrated efficacy in reducing the time to recovery in hospitalized patients requiring oxygen therapy.[20] In our study only three patients received Remdesivir.

4.8% neonates born to COVID 19 positive mothers tested positive in our study. Adhikari et al, conducted a prospective study which included 1919 infants. Out of them 1015 infants were tested with a RT-PCR swab and 3% of infants were positive. These rates are similar to what we found in our study.[9] In our study, we came across 3

still births. A meta-analysis conducted by Smith et al, included 12 studies and they found a relative risk 1.08 (0.53 to 2.16).[21]

Our study found an increased risk of preterm birth (p value<0.00025). A meta-analysis highlighted the increased risk of preterm birth (RR 1.27, 95% CI 1.07 to 1.49) and moderate preterm birth (RR 1.37, 95% CI 1.05 to 1.79). They also explained that COVID 19 infection during pregnancy was associated with a three times increased risk of moderate preterm birth (RR 2.92, 95% CI 1.88-4.54) and two times increased risk of preterm birth (RR 1.71, 95% CI 1.28-2.29).[21] A population based cohort study in England included 3527 COVID 19 positive patients and it highlighted that SARS-CoV-2 infected women had more frequent preterm births (adjusted odds ratio, 2.17; 95% confidence interval, 1.96–2.42; P<.001).[22] On the other hand, a systematic review conducted with 33 studies failed to find an increased risk of preterm birth.[23]

This study was conducted in a high prevalence area of COVID 19 infection and an apex referral centre. The limitation of the study was its limited sample size. The task of managing COVID 19 infection was monumental in terms of infrastructure, health care personnel, proper referral linkage and healthcare equipment availability. Pregnant women will always remain a vulnerable population who could be at an increased risk of such viral infections. Compared to SARS CoV and MERS- Cov infections, the maternal and neonatal outcome were better with SARS CoV-2 infection. There was lower rate of need for intensive care admission, ventilatory support and maternal death.[24]

This pandemic was a major lesson to the health care profession, it urged us into action and come up with new ways of manging adversity. It highlighted the importance of multidisciplinary approach. This time also highlighter the importance of research clinical as well as paraclinical, as the world tried to device treatment strategies to manage this menace. It has also highlighted the importance of looking at what we learnt from past pandemics and viral epidemics. Agreed, it would remain a dark time in human history, but the silver lining would be the gain of knowledge to manage such emergencies, establishment of guidelines to manage such viral infections in pregnancy and would enhance healthcare preparedness to battle future challenges.

CONCLUSION

COVID 19 was a monumental challenge for health care workers and policy makers alike. So as clinicians it is imperative, that we hone the lessons taught by this battle and improve our preparedness for future challenges and in a way mitigate adversity. This study highlighted the patient characteristics in COVID 19 pandemic during the third wave and Omicron epoch. Majority patients were asymptomatic. There was no statistically significant difference between modes of delivery. Rate of preterm birth was statistically higher in COVID 19 positive patients.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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