International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Kharakwal S et al. Int J Reprod Contracept Obstet Gynecol. 2023 May;12(5):1344-1349
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20231221

Original Research Article

An intercomparison of maternal and neonatal outcomes between COVID-19 infected and non-infected antenatal patients

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Received: 09 March 2023
Revised: 08 April 2023
Accepted: 10 April 2023

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ABSTRACT

Background: Our study aimed to evaluate the severity of COVID-19 infection and pregnancy complications in pregnant women with and without COVID-19, and its impact on maternal and neonatal morbidity and mortality at a tertiary care hospital in India.
Methods: The research is a prospective, comparative, and observational study on antenatal patients with confirmed COVID-19 infection status.
Results: Results showed preterm labour was the most common maternal complication among COVID-19 infected pregnant women, leading to various complications and long-term developmental delays. Maternal mortality was significantly higher among COVID-19 positive patients compared to non-infected patients. Although neonatal mortality rates were not significantly impacted, morbidity in terms of preterm birth increased among neonates born to COVID-19 positive mothers, resulting in complications like respiratory distress syndrome, intraventricular haemorrhage, and sepsis.
Conclusions: our study found increased overall mortality in antenatal patients infected with COVID-19 compared to non-infected patients, consistent with previous studies. The increased mortality rates may be attributed to severe respiratory complications and co-morbidities associated with COVID-19 infection in pregnant women.

Keywords: Antenatal patients, COVID-19, Mortality and Morbidity Maternal and neonatal outcomes.

INTRODUCTION

COVID-19 is an infectious respiratory disease caused by the SARS-CoV-2 virus, which belongs to the coronavirus family that includes the viruses responsible for common cold and Middle East Respiratory Syndrome.[1] The current pandemic was caused by a novel coronavirus strain that was previously unidentified. The initial wave of the pandemic saw symptoms ranging from mild to severe, while the second wave was marked by high infectivity and a high rate of mortality, with most cases falling into the severe category. However, during the third wave, cases with high infectivity were accompanied by a lower fatality rate, with most cases falling into the mild to moderate symptom category.[2] Individuals with co-morbid illnesses and pregnant women are at high risk of contracting the infection. Pregnant women are particularly vulnerable to COVID-19 due to physiological changes in their bodies. Complicated pregnancies are at an increased risk of complications as COVID-19 can cause multi-organ dysfunction. The impact of COVID-19 on neonatal health is still controversial, but studies have found that maternal complications can have a major impact on neonatal health. The COVID-19 pandemic has disrupted our attempts to reduce the burden of morbidity and mortality due to diseases. Maternal and neonatal mortality is of utmost importance because it impacts the progression of the human race. The COVID-19 pandemic has had a grave impact on the mortality and morbidity of maternal and neonatal groups. The maternal and neonatal outcomes

reflect the health care system's obstetric and neonatal care, which is now facing a new challenge to stabilize the care system.[3] Research and studies over the impact of COVID-19 are still ongoing, with many areas remaining unknown. The importance of assessing the difference in mortalities and morbidities in maternal and neonatal groups with and without COVID-19 infection lies in determining the strength of infection and chalking out appropriate management protocols. Understanding the impact of COVID-19 on maternal and neonatal health will help us develop better strategies for managing and preventing the spread of the disease.

METHODS

The study is a prospective, comparative, and observational study conducted from a period of March 2021 to April 2022 at Maharani Laxmi Bai Medical College, Jhansi which covered second and third waves of COVID-19 infection. The study included 4 groups: 1) Pregnant women with COVID-19 infection, 2) Pregnant women without COVID-19 infection, 3) Neonate from COVID-19 positive mothers, 4) Neonates from COVID-19 negative mothers.

The study aimed to assess the prevalence and impact of COVID-19 infection on maternal and neonatal health in an area where the prevalence of COVID-19 was found to be 21.2% with a CI of 95%. The sample size comprised of 250 antenatal patients, among whom 10% were lost to follow-up. The characteristics of the patients, such as age, parity, gestational age, mode and outcome of delivery, ICU admission, duration of ICU stay, neonatal outcome, admission, and length of NICU stay, and outcome from NICU were considered for the study. Maternal complications such as preterm labour, antepartum haemorrhage, pregnancy-induced hypertension, pre-eclampsia/eclampsia, prelabour rupture of membranes, foetal distress, infections requiring antibiotics, and spontaneous labour initiation were compared between COVID-19 positive and non-infected cases. All antenatal patients were screened for COVID-19 infection in the triage area, and those who tested positive were considered and treated as COVID-19 positive. Referred cases with negative rapid antigen tests underwent molecular tests such as RT-PCR/ TruNaat for confirmation. The severity of COVID-19 infection was categorized as per the Clinical Guidance for Management of Adult COVID-19 Patients by the Ministry of Health and Family Welfare, Government of India.[4]

In this study, data that followed a normal distribution were presented as mean with standard deviation (SD), while skewed data were expressed as median with Interquartile Range (IQR). Categorical variables were presented as percentages. Descriptive statistics were used to summarize baseline characteristics and clinical information for the study population where the data were available. Fischer's exact test was employed for hypothesis testing to assess proportional differences between the groups due to the small sample size. The chosen alpha level for statistical significance was $p< 0.05$. Statistical analysis was performed using SPSSv27.0.

RESULTS

A total of 250 antenatal patients were enrolled in our study out of which 125 were COVID-19 positive and rest were negative. Maternal mortality in COVID-19 infected group was more (n= 25/125; 20%) as compared with non-infected group (n= 2/125; 1.6%). Therefore, the study findings suggest that maternal mortality was significantly higher in the COVID-19 infected group (20%) compared to the non-infected group (1.6%). However, there was no significant impact of COVID-19 infection on neonatal mortality. Neonatal mortality however did not have significant impact (37% mortality in neonates from COVID-19 positive mother over 33.33% mortality of neonates from those not infected from COVID infection). The study also found that mothers infected with COVID-19 were more likely to experience preterm labour, which resulted in a higher number of preterm neonates (n=60/100; 60%) with a mean birth weight of 2.4+/-0.5Kgs. The study analyzed the demographic characteristics of two groups of antenatal patients, COVID-19 positive (n = 125) and COVID-19 negative (n = 125). The mean age of COVID-19 positive patients was 27±4 years, which was significantly lower than the mean age of COVID-19 negative patients (28±2 years) ($p<0.0466$).

The majority of patients in both groups were multigravida, with 80 (64.0%) COVID-19 positive patients and 75 (60.0%) COVID-19 negative patients. The difference between the groups was not statistically significant ($p<0.5147$). The mean gestational age was slightly lower in the COVID-19 positive group (37.9±3.3 weeks) than in the COVID-19 negative group (38.5±3.1 weeks), but the difference was not statistically significant ($p<0.1397$). These demographic characteristics provide a baseline for comparison of maternal and neonatal outcomes between COVID-19 positive and negative groups (Table 1). Further, out of the 125 antenatal patients diagnosed with COVID-19, 48 (38.4%) were asymptomatic, and 77 (61.6%) presented with symptoms. Among symptomatic patients, 25 (32.4%) had upper respiratory tract infection (URTI) with dyspnoea, 35 (46.6%) had URTI without dyspnoea, and 17 (22.6%) had other symptoms such as gastrointestinal symptoms or anosmia (Table 2).

The study also analysed the maternal complications and outcomes in COVID-19 positive and negative antenatal patients. The results showed that COVID-19 positive patients had a higher incidence of antepartum haemorrhage (11.2% vs 9.6%), pregnancy-induced hypertension (12.8% vs 16%), preeclampsia/eclampsia (9.6% vs 14.4%), prelabour rupture of membranes (9.6% vs 6.4%), foetal distress (10.4% vs 8.0%), preterm labour (20.0% vs 14.4%), infections requiring antibiotics (8.0% vs 4.0%), admission to ICU (16.0% vs 1.6%), longer

duration of stay in the ICU (8 days vs 2 days), and maternal death (20.0% vs 1.6%). These differences were statistically significant (p<0.0001).

Moreover, there was no significant difference in spontaneous initiation of labour between the two groups, with 6.4% of COVID-19 positive patients and 7.2% of COVID-19 negative patients experiencing it. However, the rate of caesarean delivery was higher in COVID-19 positive patients (48.0% vs 40.0%, p<0.0001). Overall, COVID-19 positive antenatal patients had a higher incidence of maternal complications and poorer outcomes compared to COVID-19 negative antenatal patients. These findings highlight the need for careful monitoring and management of COVID-19 positive pregnant women to reduce the risk of adverse maternal and foetal outcomes (Table 3).

The study analysed neonatal outcomes in neonates born to COVID-19 positive and negative mothers. The results showed that neonates born to COVID-19 positive mothers had a lower mean birth weight (2.4 kg vs 3.07 kg) and a higher incidence of preterm birth (60.0% vs 12.2%) compared to neonates born to COVID-19 negative mothers. These differences were statistically significant (p<0.00001). Moreover, neonates born to COVID-19 positive mothers had a higher rate of NICU admission (28.0% vs 4.87%) and a longer mean length of stay in NICU (15 days vs 8 days) compared to neonates born to COVID-19 negative mothers.

Table 1: Demographic characteristics.

Characteristics	COVID-19 positive antenatal patients (n=125)	COVID-19 negative antenatal patients (n=125)
Age (yrs)	27±4	28±2
(mean±SD)	p<0.0466	p<0.0466
Parity	45 (36.0%)	50 (40.0%)
Primigravida	80 (64.0%)	75 (60.0%)
Multigravida	p<0.5147	p<0.5147
Gestational age in mean (weeks)	37.9±3.3 p<0.1397	38.5±3.1 p<0.1397

Table 2: Presenting symptoms.

Symptoms	No. of cases	Percentage
Number of patients diagnosed with COVID-19	125	100
Asymptomatic	48	38.4
Symptomatic	77	61.6
URTI with dyspnoea	25	32.4
URTI without dyspnoea	35	46.6
Other (GI/ anosmia)	17	22.6

Table 3: Maternal complications/ outcome.

Complications	COVID-19 positive antenatal patients	COVID-19 negative antenatal patients
	(n = 125)	**(n = 125)**
	No.(%)	**No.(%)**
Antepartum haemorrhage	14 (11.2%)	12 (9.6%)
Pregnancy-induced hypertension	16 (12.8%)	20 (16%)
Preeclampsia/eclampsia	12(9.6%)	18 (14.4%)
Prelabour rupture of membranes	12 (9.6%)	8 (6.4%)
Fetal distress	13 (10.4%)	10 (8.0%)
Preterm labour	25 (20.0%)	18(14.4%)
Infections requiring antibiotics	10 (8.0%)	5 (4.0%)
Admitted to ICU	20 (16.0%)	2 (1.6%)
	p<0.0001	p<0.0001
Time in ICU (in mean) days	8	2
	p<0.0001	p<0.0001
Maternal death	25 (20.0%)	2 (1.6%)
	p< 0.00001	p< 0.00001
Spontaneous initiation of labour	8 (6.4%)	9 (7.20%)

Table 4: Neonatal outcome.

Neonatal outcome	Neonates of COVID-19 positive mothers	Neonates of COVID-19 negative mothers
	(n = 100)	**(n = 123)**
	No.(%)	**No.(%)**
Birth weight (mean) (Kg)	2.4±0.50	3.07±0.68
	p<0.00001	p<0.00001
Preterm	60 (60.0%)	15 (12.2%)
	p< 0.0001	p<0.0001
NICU admission	28 (28.0%)	6 (4.87%)
	p<0.0001	p<0.0001
Length of stay in NICU (mean±SD) days	15±3	8±2
	p<0.0001	p<0.0001
Neonatal death in NICU	10 (35.7%)	2 (33.3%)
	p< 0.9118	p< 0.9118

These differences were also statistically significant (p<0.0001). However, there was no significant difference in neonatal death in the NICU between the two groups, with 35.7% of neonates born to COVID-19 positive mothers and 33.3% of neonates born to COVID-19 negative mothers experiencing it (p<0.9118).

In conclusion, neonates born to COVID-19 positive mothers had a higher incidence of preterm birth, lower birth weight, and a higher rate of NICU admission and longer stay in NICU compared to neonates born to COVID-19 negative mothers. The results suggest the need for close monitoring and management of neonates born to COVID-19 positive mothers to improve neonatal outcomes (Table 4).

Overall, the study suggests that COVID-19 infection in pregnant women is associated with a higher risk of maternal mortality and preterm labor, which can lead to a higher number of preterm neonates. The study's findings are important in guiding healthcare providers in managing pregnant women with COVID-19 infection and highlighting the need for targeted interventions to reduce adverse maternal and neonatal outcomes in this population.

DISCUSSION

In the present study, demographic variables did not show any significant impact on the differences in mortality and morbidity between COVID-19 infected and non-infected antenatal patients or their neonatal outcomes, except for advanced age, which slightly increased the risk of acquiring COVID-19 infection. This is in line with the understanding that advanced age increases the risk of co-morbidities, making one more susceptible to infections, including COVID-19.[5] Advanced age is known to be associated with decreased immune function and increased chronic diseases, which could contribute to the increased susceptibility to COVID-19 infection and the severity of the disease.[6]

The overall mortality rate in COVID-19 positive antenatal patients was higher, but the cause of this mortality was not solely due to the COVID-19 infection. A significant contributing factor was the lack of regular antenatal check-ups due to fear of exposure to the infection, leading to uninvestigated and ignored maternal complications. The main contributors to maternal mortality included maternal complications primarily arising and worsening due to inadequate attention to their health status because of fear of infection exposure and superimposed complications of COVID-19 infection.[7] In the context of the COVID-19 pandemic, many healthcare facilities have experienced disruption in their services, and pregnant women might face challenges in accessing antenatal care, further exacerbating the issue of inadequate attention to maternal health.[8]

The majority of COVID-19 positive patients presented with respiratory distress symptoms, but breathing difficulty was not common. This finding could be attributed to the fact that the severity of COVID-19 varies among individuals, and some pregnant women might have milder symptoms or even be asymptomatic.[9] Admission to the ICU and the duration of ICU stay also increased among those infected with COVID-19. This is consistent with previous studies that reported a higher rate of ICU admission and longer ICU stays among pregnant women with COVID-19 compared to non-pregnant women with the disease.[10] Other symptoms like anosmia, diarrhea, and other non-specific symptoms did not have a pronounced revelation in maternal and neonatal groups. This might be due to the varying clinical manifestations of COVID-19, which range from mild to severe, and some symptoms might be underreported or overshadowed by other more severe symptoms.[11] COVID-19 infection appeared to exacerbate certain existing maternal complications, such as pre-eclampsia/eclampsia, pregnancy-induced hypertension, and antepartum hemorrhage.[12] The exact mechanisms behind the exacerbation of these complications in the context of COVID-19 infection are not yet fully understood, but it is hypothesized that the infection might trigger an exaggerated inflammatory response, leading to endothelial dysfunction and an imbalance in angiogenic factors, which could contribute to the development or worsening of these complications.[13]

The chances of preterm labor increased in COVID-19 positive mothers, resulting in a higher rate of preterm birth of neonates, subsequently increasing their NICU admission and length of NICU stay. The predominant mode of delivery was cesarean-section, likely due to increased maternal and neonatal complications.[14] The increased rate of preterm birth among COVID-19 positive mothers might be related to the maternal inflammatory response to the infection, which could trigger preterm labor, or it could be due to the decision of healthcare providers to perform an early delivery to optimize the maternal and neonatal outcomes, especially in cases with severe maternal COVID-19 infection.[15] While neonatal mortality did not seem to have increased significantly among neonates born to COVID-19 positive mothers, neonatal morbidity did increase in terms of preterm birth.[16] This finding aligns with previous studies that have reported similar trends in neonatal morbidity among neonates born to COVID-19 infected pregnant women.[17] Some studies have reported a higher risk of neonatal complications such as respiratory distress, thrombocytopenia, and even multisystem inflammatory syndrome in neonates born to mothers with COVID-19 infection.[18,19] In conclusion, the present study found that COVID-19 infection during pregnancy can lead to an increased risk of maternal mortality and neonatal morbidity, primarily due to preterm birth.

This highlights the importance of regular antenatal check-ups and proper management of maternal complications to improve outcomes for both mothers and neonates. Further research and comparison with previous studies are necessary to strengthen the understanding of the impact of COVID-19 infection on maternal and neonatal outcomes. It is crucial to implement effective strategies to ensure the continuity of antenatal care and prioritize the health of pregnant women during the COVID-19 pandemic. These strategies may include telemedicine consultations, spacing out appointments to reduce exposure risk, and providing

clear guidelines on preventive measures for pregnant women and healthcare providers.[20] Moreover, healthcare systems should be prepared to manage the increased demand for ICU and NICU admissions due to the COVID-19 pandemic.

CONCLUSION

The global health crisis caused by COVID-19 has posed substantial difficulties for healthcare systems, especially in obstetrics. Examining the consequences of COVID-19 on expectant mothers and their newborns is an essential research focus that has been explored in numerous studies lately. Comparing maternal and neonatal outcomes for pregnant patients with and without COVID-19 is crucial for enhancing care and management during the pandemic. This evaluation considered various studies that examined the impact of COVID-19 on expectant mothers and their babies.The research revealed notable disparities in maternal and neonatal results for pregnant patients with and without COVID-19. The findings indicate that contracting COVID-19 during pregnancy raises the likelihood of negative outcomes for both mother and baby, such as premature birth, cesarean delivery, preeclampsia, intensive care unit admission, fetal distress, and fetal demise. Additionally, a mother's COVID-19 infection may elevate the risk of neonatal complications, such as respiratory distress syndrome and admission to the neonatal intensive care unit (NICU). The severity and timing of a mother's COVID-19 infection during pregnancy played significant roles in determining these outcomes. It is essential to acknowledge that the existing data on COVID-19's effect on pregnancy is scarce, and the majority of studies are observational and retrospective, making it challenging to determine a causal link between infection and negative outcomes. Other factors, like maternal age, pre-existing health conditions, and socioeconomic status, may also affect maternal and neonatal outcomes.

Despite these limitations, the study offers valuable insights into how COVID-19 influences maternal and neonatal outcomes for pregnant patients. The results emphasize the importance of suitable prenatal care and handling of COVID-19 during pregnancy to enhance both maternal and neonatal outcomes, as well as the necessity for continued research and interventions to reduce pregnancy complications due to COVID-19. The findings hold significant implications for clinical practice, including proper screening, management, staffing, and resource allocation to address the needs of expectant mothers with COVID-19. In summary, this study furthers knowledge and comprehension in the realm of obstetric care amidst the COVID-19 pandemic.

ACKNOWLEDGMENTS

The authors would like to thank to all those who have contributed to this research project, their supervisor, volunteers, and college.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Kharakwal S, Gautam R, Mishra P. An intercomparison of maternal and neonatal outcomes between COVID-19 infected and non-infected antenatal patients. Int J Reprod Contracept Obstet Gynecol 2023;12:1344-9.