



RETROSPECTIVE COMPARATIVE STUDY BETWEEN COVID-19 POSITIVE AND COVID-19 NEGATIVE PREGNANT WOMEN: MATERNAL AND FETAL OUTCOME

Obstetrics & Gynaecology

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ABSTRACT

Objectives: This retrospective comparative study aims to compare maternal and fetal outcomes in COVID-19 positive and negative pregnant women. **Material and Methods:** Our study is a single centre retrospective comparative study conducted in Department of obstetrics and Gynaecology, Lalla Ded hospital. **Results:** Of the 362 COVID-19 positive pregnant women, 37.6% had a vaginal delivery, and 62.4% underwent LSCS, while in the control group, 70.3% had a vaginal delivery, and 29.7% underwent LSCS. The (mean $\pm$ SD) gestational age at delivery was (35.2 $\pm$ 2.8) weeks in the COVID-19 positive group and (37.4 $\pm$ 2.2) weeks in the control group. Preterm labor was significantly higher in the COVID-19 positive group ($p=0.0032$), with a rate of 5.5% compared to 2.5% in the control group. The incidence of maternal mortality showed no significant difference and was 0.6% in the COVID-19 positive group and 0.4% in the control group ($p=0.6072$). In the perinatal outcomes, there was no significant difference in the Apgar score and still births between the two groups. However, the birth weight and neonatal ICU admission were found to be significantly different between COVID-19 positive group and COVID-19 negative group with ($p=0.0133$) and ($p=0.0001$) respectively. The SARS-CoV.2 screening was carried out for all pregnant women admitted for delivery using RT-PCR. All neonates born from SARS-CoV.2 positive mothers were isolated and tested for SARS-CoV.2 infection. On the basis of the RT-PCR result (negative vs. positive), statistically significant differences were found for maternal characteristics, such as mean gestational age (37-38 vs. 35-36), medical comorbidity (4% vs. 8%), and maternal outcomes like the C-section rate (25% vs. 62.4%), preterm delivery (2.5% vs. 5.5%), Deaths ICU Admissions (1.5% vs. 0.7%) Anemia (69% vs 45%) Deaths (0.01% vs 0.5%) and perinatal outcomes like mean Low birth weight (1.9% vs 4.1%), low Apgar score (1.8% vs. 3.9%), IUD (1.5% VS 2.2%) and fetal distress (9% vs. 23.2%) among SARS-CoV.2 negative and positive cases, respectively. No neonate from SARS-CoV.2 positive pregnant women was found to be positive for SARS-CoV.2 infection. **Conclusions:** This retrospective comparative study highlights the significant impact of COVID-19 on maternal and neonatal outcomes. The incidence of preterm labor and admission to the neonatal intensive care unit were significantly higher in the COVID-19 positive group. Therefore, it is crucial to provide adequate care and management for pregnant women infected with COVID-19 to improve maternal and fetal outcomes

KEYWORDS

COVID.19, maternal outcomes, neonatal outcomes, Obstetrical outcomes , Pregnancy complications, NICU admission in COVID-19 pregnancy

INTRODUCTION

The novel coronavirus is responsible for the coronavirus disease 2019 (COVID-19) pandemic. This is a highly infectious respiratory disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [1] which has caused an unprecedented public health emergency all around the world. The very first case was identified in December 2019 at Wuhan, China, and since then COVID-19 has spread to almost every country in the world. COVID-19 pandemic, is also termed as a "Systematic Human Development Crisis" by the United Nations Development Programme. It was declared a global pandemic on March 11, 2020, by the World Health Organization. [2,3]. The COVID-19 pandemic has had a significant impact on healthcare worldwide, including obstetrics and gynecology. Pregnant women are considered to be at an increased risk of severe illness and adverse outcomes from COVID-19. However, there is limited data available on the impact of COVID-19 on maternal and neonatal outcomes. This retrospective comparative study aims to compare maternal and neonatal outcomes in COVID-19 positive and negative pregnant women. Pregnant women with Gestational diabetes mellitus (GDM) or overt DM, hypertension, asthma, HIV, chronic liver disease, chronic kidney disease, blood dyscrasias and those with organ transplant and malignancies have been identified as being more vulnerable to severe effects of COVID 19 infection. [4] Reports from the beginning of the COVID-19 pandemic have characterized pregnant women as a vulnerable group in comparison to the general population for developing severe SARS-CoV-2 infection with adverse maternal-perinatal outcomes as well. More than 100 million pregnant women across the globe were at high risk of SARS-CoV 2 infection due to various physiological conditions, such as elevation of the diaphragm, decrease residual lung functional capacity, increased oxygen consumption, edema of mucosal membrane of the respiratory tract, and immunomodulation during pregnancy. Moreover, reports suggest that with viral respiratory infections pregnant women were at a higher

risk of obstetric and perinatal complications due to changes in their immune response.[5] SARS-CoV-2 infection during pregnancy may lead to mother to child vertical transmission and unfavorable maternal and perinatal outcomes as well. Although, there is no conclusive evidence of vertical transmission of Covid-19. [6,7]. Current studies on the susceptibility of pregnant women to infection by Covid-19 are still developing.

To facilitate the understanding of pregnancy in COVID-19, the aim of this retrospective study is to review the perinatal outcome in pregnant women affected by COVID-19, its psychological impact and its wider implications on healthcare services.

MATERIALS AND METHODS

This study was a single centre, retrospective comparative study performed in Postgraduate Deptt. Of Obstt.&Gynea LD Hospital located in Kashmir, Jammu and Kashmir (India) between MARCH, 2020 and MARCH 30, 2022. This is one of the largest maternity hospitals in the Kashmir region that provides obstetrical care to nearly 800 patients/week. For the first six months of COVID when Rapid Antigen Test (RAT) was not available whole Kashmir was divided in to three zones (RED, GREEN and ORANGE) and admitted pregnant women were segregated on basis of zones they came from. LALA DED HOSPITAL was not a designated COVID hospital, but all the admitted pregnant patients who came from RED ZONE were segregated and were tested for covid infection by RTPCR. An isolation facility, separate from the main hospital had been set up to cater to the COVID positive pregnant women amid the ongoing pandemic. A total of 1080 patients turned out COVID positive among the total of 9820 suspected patients who presented to the isolation facility. Out of these, 1080 patients only 362 were included in this study as only 362 covid positive women underwent LSCS/ vaginal deliveries & 718 were excluded as they were far from Term and were

conservatively managed and are discharged home after completion of isolation period. All of these pregnant women were compared with controls in the ratio of 1:4. Controls were all pregnant women who were tested COVID negative and delivered during the same time frame.

Data were collected about various clinico-epidemiological parameters, maternal and fetal outcome of the selected patients. Data collected from individual case records included maternal characteristics like age, gestational age at delivery, gravidity, parity, and presence of medical comorbidities like hypertension, diabetes, thyroidism, and so on. Data about pregnancy outcomes such as mode of delivery (C-section or vaginal), type of delivery (term or preterm), and obstetric complications, such as hemoglobin (HB<10), gestational diabetes mellitus (GDM), pregnancy induced hypertension (PIH), along with perinatal outcomes (birth weight, Apgar score, neonatal intensive care unit (ICU) Admission, and neonatal deaths). These were compared between SARS-CoV-2-positive and SARS-CoV-2-negative pregnant women admitted for delivery..

Statistical Analysis

The statistical analysis was performed using Statistical Package for the Social Sciences version 19 software (IBM, Armonk, NY, USA). $P < 0.05$ was considered to be statistically significant at a 95% confidence interval. data were analyzed using descriptive statistics to summarize the characteristics of the study population. Continuous variables, such as gestational age, were reported as means and standard deviations, while categorical variables, such as maternal comorbidity, were reported as frequencies and percentages.

To compare the maternal and neonatal outcomes between COVID positive and COVID negative mothers, we used chi-square tests and Fisher's exact tests for categorical variables and t-tests for continuous variables

RESULTS

During the period of our study, the pregnant women admitted for delivery in Postgraduate Deptt. Of Obstt.&Gynaecology Hospital SRINAGAR KASHMIR, 9820 were suspected COVID-19 positive patients and sent to isolation facility. Out of these, 1080 patients turned out to be COVID-19 positive on RT-PCR. We included 362 of these women in this study as only 362 COVID-19 positive women underwent LSCS /Vaginal deliveries & 718 were excluded as they were far from delivery and were conservatively managed and discharged home after isolation period. Against these 362 cases we selected 1448 controls in the ratio of 1:4

Maternal Characteristics

Maternal characteristics of all pregnant women included in our study has been summarized in Table 1. When comparing the baseline characteristics between COVID positive and COVID negative patients. The mean gestational age at delivery was 35.2 ± 2 weeks and 37.4 ± 2.2 weeks respectively. Among COVID-19 positive cases 94 (25.9%) were nullipara, 268 (74.1%) were multipara, 194 (53.6%) were with Gravia 1, 133 (36.8%) were with Gravia 2, 35 (9.6%) were with Gravia ≥ 3 and 32 (8.8%) of pregnant women had medical comorbidities.

Table 1 Maternal Characteristics Of Pregnant Women At The Time Of Admission

Maternal characteristic	SARS.CoV.2 positive pregnant women (n=362)	SARS.CoV.2 negative pregnant women (n=1448)	Estimated effect (95% CI)	P-value
Gestational age at delivery (weeks)	35.2 ± 2.8 weeks	37.4 ± 2.2 weeks	0.14 (1.93–2.47)	$p < 0.0001$
Gravidity				
1	194 (53.6%)	715 (49.4%)	4.2 (–1.56 to 9.88)	$p = 0.1530$
2	133 (36.8%)	598 (41.3%)	4.5 (–1.17 to 9.94)	$p = 0.1187$
≥ 3	35 (9.6%)	135 (9.3%)	0.3 (–2.77 to 4.04)	$p = 0.8609$
Medical Comorbidity	32 (8.8%)	59 (4.1%)	4.7 (1.95–8.19)	$p = 0.0003$

Maternal Outcomes And Obstetric Complications

SARS-CoV-2 negative and SARS-CoV-2 positive pregnant women have also been characterized on the basis of maternal outcomes such as type of delivery (term, preterm), mode of delivery (vaginal, cesarean), maternal ICU admission, maternal deaths, and obstetric complications, such as HB < 10, GDM, PIH

Table 2 Maternal Outcomes Of SARS-COV-2 Positive And SARS-COV-2 Negative Pregnant Women

Maternal outcome	SARS.CoV.2 positive pregnant women (362)	SARS.CoV.2 negative pregnant women (1448)	Estimated effect (95% CI)	P-value
Pregnancy outcomes				
Term	342 (94.5%)	1412 (97.5%)	3.0 (0.87–5.93)	$p = 0.0032$
Preterm	20 (5.5%)	36 (2.5%)	3.0 (0.87–5.93)	$p = 0.0032$
Mode of delivery				
LSCS	226 (62.4%)	430 (29.7%)	32.7 (27.06–38.05)	$p < 0.0001$
Vaginal delivery	136 (37.6%)	1018 (70.3%)	32.7 (27.06–38.05)	$p < 0.0001$
Maternal ICU admission	6 (1.6%)	10 (0.71%)	0.89 (–0.16–2.81)	$p = 0.1065$
Maternal death	2 (0.6%)	6 (0.4%)	0.2 (–0.44–1.68)	$p = 0.6072$

Abbreviations: ICU, Intensive Care Unit; LSCS, Lower Segment Cesarean Section.

Table 3 Obstetric Complications Among SARS-COV-2 Positive And SARS-COV-2 Negative Pregnant Women

Obstetric complications	SARS.CoV.2 positive pregnant women (362)	SARS.CoV.2 negative pregnant women (1448)	Estimated effect (95% CI)	P-value
Hemoglobin (HB<10)	235 (65%)	623 (43%)	22 (16.34–27.36)	$p < 0.0001$
GDM	49 (13.6%)	125 (8.6%)	3.9 (–1.70 to 11.87)	$p = 0.2037$
PIH	37 (10.2%)	113 (7.8%)	5.0 (1.48–9.14)	$p = 0.0039$

Abbreviations: GDM, Gestational Diabetes Mellitus; PIH, Pregnancy Induced Hypertension

Perinatal Outcomes

Neonates from SARS-CoV-2 positive and SARS-CoV-2 negative pregnant women were also evaluated on the basis of perinatal characteristics such as birth weight (g), 5th min Apgar score ≤ 7 , neonatal ICU admission, still births.

TABLE 4 Perinatal Outcomes Of SARS-COV-2 Positive And SARS-COV-2 Negative Pregnant Women

Perinatal outcome	SARS.CoV.2 positive pregnant women (362)	SARS.CoV.2 negative pregnant women (1448)	Estimated effect (95% CI)	P-value
Birth weight < 2500g	14 (4.1%)	26 (1.9%)	2.2 (0.38–4.83)	$p = 0.0133$
5th min Apgar score ≤ 7	18 (4.9%)	32 (2.2%)	1.7 (–0.37–4.54)	$p = 0.111$
Neonatal ICU admission	21 (5.9%)	30 (2.1%)	3.8 (1.62–6.78)	$p = 0.0001$
Still Births	8 (2.2%)	22 (1.5%)	0.7 (–0.62–2.84)	$p = 0.3484$

Apart from that, no neonate from SARS-CoV-2 positive showed positive test for SARS-CoV-2 infection.

DISCUSSION

The COVID-19 pandemic has significantly impacted the healthcare

system worldwide, with pregnant women being a particularly vulnerable group. Previous studies have shown that COVID-19 infection in pregnant women can lead to adverse maternal and neonatal outcomes, including preterm labor, fetal distress, and even maternal death (8, 9).

Delivery methods in COVID-19 positive pregnant women have been a topic of much debate. According to guidelines from the American College of Obstetricians and Gynecologists (ACOG), vaginal delivery is recommended for most COVID-19 positive women, except in cases where the mother's respiratory status is severely compromised (3). However, some studies have suggested that cesarean delivery (LSCS) may be more appropriate for COVID-19 positive women, as it reduces the risk of maternal-fetal transmission and may also prevent the need for emergency LSCS due to maternal deterioration (10).

A systematic review and meta-analysis of 22 studies involving 2,100 COVID-19 positive pregnant women found that LSCS rates were higher in COVID-19 positive women compared to COVID-19 negative women (11).

In our study out of 362 COVID positive pregnant women 226 (62.4%) underwent LSCS as compared to 430(29.7%) LSCS among 1448 controls, value was significant ($p < 0.0001$)

However, the review also found that there was no difference in perinatal outcomes between the two groups, including Apgar scores, neonatal resuscitation, and NICU admission rates. Other studies have shown conflicting results regarding the impact of COVID-19 infection on perinatal outcomes. A study of 64 COVID-19 positive pregnant women in the UK found that neonates born to these women were more likely to be admitted to the neonatal unit than neonates born to COVID-19 negative women, even after adjusting for potential confounders (12). However, a larger study of 1,800 pregnant women in the US found no significant difference in perinatal outcomes between COVID-19 positive and negative women (13).

There are still many gaps in the literature regarding the impact of COVID-19 on pregnancy and delivery outcomes.

Further research is needed to better understand the optimal delivery method for COVID-19 positive pregnant women and the long-term effects of COVID-19 infection on neonatal health.

In our study, such as gestational age at delivery (in weeks) and medical comorbidity, showed a statistically significant difference between and SARS-CoV-2 positive and SARS-CoV-2 negative pregnant women ($p < 0.0001$) and ($p = 0.0003$) respectively. As per some reports comparing these two characteristics between two groups admitted for delivery (19, 20, 21). However only a few studies (19) observed a statistically significant difference between the high and low risk pregnancy groups on the basis of characteristics, such as gestational age at delivery and medical comorbidity.

At present there is insufficient evidence to determine any correlation between spontaneous preterm labor and COVID-19 infection in pregnancy (14).

In our study 20 (5.5%) out of 362 COVID positive pregnant women had preterm delivery as compared to 36 (2.5%) out of 1448 in COVID negative group, p value was significant ($p = 0.0032$). A systematic review of 33 studies by Gillian A Ryan et al described the outcome of 385 pregnant women with COVID-19 with period of gestation ranging from 30 to 41 weeks, a preterm birth rate of 15.2% was noted (15).

In our study, we found a significant difference between SARS-CoV-2 positive and SARS-CoV-2 negative pregnant women on the basis of outcomes such as C-section rate, birth weight (g), prematurity. Some reports suggest a risk of low birth weight, low Apgar score, and preterm delivery in SARS-CoV-2 infected pregnant women (22, 23, 24).

In our study no statistically significant difference was found between the two comparison groups in terms of 5th min Apgar score ($p = 0.111$).

In our study, both COVID positive and negative pregnant women were treated using antibiotics only where dexamethasone was given in COVID positive pregnant women having moderate illness needing no oxygen support and 1.5% needed ventilator support.

In our study, no neonate from COVID positive pregnant women showed positive tests for COVID-19 similar to other studies.

Limitations Of Study

This study has some limitations. The study was conducted in a single tertiary care hospital, which may limit the generalizability of the findings and the study was retrospective, which may affect the accuracy of the data. Further multicentre studies with larger sample sizes are needed to validate our findings. The study did not assess the impact of vaccination on the outcomes of pregnant women. No maternal serological testing and non availability of radiological data were the key limitations.

CONCLUSION

In conclusion, this retrospective comparative study provides important insights into the clinical outcomes of COVID-19 positive and COVID-19 negative pregnant women. COVID-19 positive pregnant women had a higher incidence of preterm delivery and caesarean section. Overall, the literature suggests that COVID-19 positive pregnant women may be at a higher risk of adverse maternal and perinatal outcomes compared to COVID-19 negative pregnant women. Further research is needed to explore the long-term effects of COVID-19 infection on maternal and neonatal health, the impact of COVID-19 vaccination on pregnancy outcomes, the effect of COVID-19 infection on fetal growth and development, and the optimal management of COVID-19 positive pregnant women. The retrospective comparative study proposed in this paper aims to contribute to the existing literature by comparing the outcomes of COVID-19 positive and negative pregnant women in a specific population of 362 cases and controls chosen in the ratio of 4 against 1 case.

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