ORIGINAL ARTICLE

Preterm Birth Outcomes in COVID-positive and COVID-negative Pregnancies during SARS-CoV-2 Pandemic in a Tertiary Care Center in India: A Cohort Study

Rao Preethi Venkatachala[1], Shashikala Karanth[2], Christy Vijay[3], Sivakami Sundari S[4]

Abstract

Objective: To compare the maternal and neonatal outcomes, particularly the incidence of preterm birth, and identify their risk among pregnant women who were seropositive or seronegative for SARS-CoV-2, during the pandemic.

Method: Pregnant women who got admitted to an urban tertiary care center for delivery during the period August 1, 2020, to October 30, 2020, and consented to participate in the study were recruited and followed up until delivery. Among 230 women, 73 pregnant women who tested positive for SARS-CoV-2 were included in the positive cohort and the remaining in the negative cohort. Demographic details, symptoms at presentation, gestational age, laboratory tests done, and treatment given were noted.

The outcome measures studied were the incidence of preterm birth, gestational age at admission and delivery, risk factors for preterm birth (PTB), obstetrics/medical complications, drugs given, mode of delivery, and neonatal outcomes, such as birth weight, Apgar scores at 1 and 5 minutes, neonatal complications, need for NICU admission, and SARS-CoV-2 positivity.

Results: Among the 73 SARS-CoV-2 pregnant women, 95% were asymptomatic. The incidence of preterm birth was similar in the SARS-CoV-2-positive and SARS-CoV-2-negative cohorts (20.5 vs 22.5%). There were four SARS-CoV-2-positive babies in the positive cohort and none in the negative cohort. The distribution of known risk factors of preterm births and other maternal and neonatal outcomes were also comparable between the positive and negative cohorts.

Conclusion: There is no increase in incidence of preterm births in SARS-CoV-2-positive compared to SARS-CoV-2-negative cohort, during the pandemic. Majority of them have asymptomatic infection, and good pregnancy outcomes can be anticipated.

Keywords: Coronavirus disease-2019, Maternal outcome, Neonatal outcome, Perinatal outcome, Preterm birth.

Journal of South Asian Federation of Obstetrics and Gynaecology (2021): 10.5005/jp-journals-10006-1984

Introduction

Pregnant women are at high risk of SARS-CoV-2 infection due to changes in their cardiopulmonary and immune system.[1–3] An increased maternal and perinatal morbidity and mortality has been reported with severe infection, especially in the presence of comorbidities, such as obesity, diabetes, and hypertension.[2]

Evidence suggests that severe coronavirus disease-2019 (COVID-19) in pregnancy is associated with a higher prevalence of abortions, preterm premature rupture of membranes (PPROM), preterm birth (PTB), preeclampsia, cesarean section, fetal growth restriction (FGR), intrauterine demise (IUD), disseminated intravascular coagulation (DIC), neonatal intubation, and need for admission to neonatal intensive care unit (NICU).[4–9]

Previous studies have reported a high rate of PTB ranging from 12 to 47%[10–13] with the prevalence being three times higher in symptomatic than asymptomatic patients. Majority were indicated PTB rather than due to spontaneous preterm labor.[4,6,14] The increased risk of medical and obstetrical complications and cardiopulmonary compromise with SARS-CoV-2 infection may necessitate early termination of pregnancy to improve maternal prognosis leading to indicated PTB.[4,6,14]

There is insufficient evidence to support the vertical transmission of COVID-19 infection from mother to fetus, though some cases have been reported.[4,6]

Though most authors report increased risk of PTB, there are very few studies comparing the outcomes between SARS-CoV-2-positive and SARS-CoV-2-negative pregnant women. Hence, we aimed to study the effect of SARS-CoV-2 infection on pregnancy outcomes, particularly PTB, between SARS-CoV-2-positive and SARS-CoV-2-negative pregnant women during the peak of the first wave of the pandemic as there is scant Indian literature available.

Materials and Methods

A prospective cohort study to compare the incidence of PTB, the risk factors, and maternal and neonatal outcomes, among pregnant women who were seropositive or seronegative for SARS-CoV-2, during the pandemic, was carried out in an urban tertiary

[1–3]Department of Obstetrics and Gynaecology, St Johns Medical College and Hospital, Bengaluru, Karnataka, India

[4]Division of Epidemiology and Biostatistics, St Johns Research Institute, Bengaluru, Karnataka, India

Corresponding Author: Rao Preethi Venkatachala, Department of Obstetrics and Gynaecology, St Johns Medical College and Hospital, Bengaluru, Karnataka, India, Phone: +91 9480333488, e-mail: preethibhat77@gmail.com

How to cite this article: Venkatachala RP, Karanth S, Vijay C, *et al*. Preterm Birth Outcomes in COVID-positive and COVID-negative Pregnancies during SARS-CoV-2 Pandemic in a Tertiary Care Center in India: A Cohort Study. J South Asian Feder Obst Gynae 2021;13(6):396–402.

Source of support: Nil

Conflict of interest: None

care center, between August 1, 2020, and October 30, 2020, after obtaining Institutional Ethics Committee approval.

Universal testing for SARS CoV-2 at the time of delivery was started in July 2020 in our institute as per Government orders. All pregnant women who consented for the study were recruited. All those who tested positive for SARS-CoV-2 and were admitted or delivered during the study period were included in the COVID-19-positive cohort; the remaining who tested negative for SARS-CoV-2 were included in the COVID-19-negative cohort. The recruitment of the participants into COVID-19-positive and COVID-19-negative cohorts is depicted in Flowchart 1. Among 230 women, 73 pregnant women who tested positive for SARS-CoV-2 were included in the positive cohort and the remaining were included in the negative cohort. SARS-CoV-2 infection was confirmed by the use of qualitative real-time polymerase chain reaction on maternal nasopharyngeal swab specimens or by rapid antigen testing. Neonatal throat swabs were collected at birth or Day 3 of life.

Data Collection

Maternal characteristics, such as age, parity, body mass index (BMI), and comorbid conditions; risk factors for PTB, such as previous history of PTB and low socioeconomic status (as per BG Prasad classification); infections, such as periodontal or genital or urinary tract infections (UTI); medical disorders, such as anemia, hypertension, and diabetes mellitus; and obstetrics complications, such as PPROM, hypertension, fetal growth restriction, previous abortions or intrauterine deaths, previous cesarean delivery, oligo- or polyhydramnios, multiple pregnancy, uterine anomalies, and treatment for infertility were noted.

Data relating to COVID-19, including presence or absence of symptoms (i.e., fever/chills, cough, dyspnea, chest pain, myalgia, nausea, vomiting, diarrhea, headache), temperature >100.4°F, and treatment given like oxygen, steroids, antibiotics, and anticoagulants were recorded.

Disease severity was classified as asymptomatic, mild, moderate, or severe based on our hospital protocol. Mild cases were defined as those who were symptomatic with respiratory rate (RR) ≤ 24 cycles per minute (CPM) and SpO_2 >94% at room air; moderate cases as symptomatic with pneumonia, RR 24–30 CPM, and SpO_2 90–94% at room air; and severe cases as those with pneumonia, RR >30 CPM, and SpO_2 <90% on room air.

Obstetrical symptoms were noted, and examination was performed. Gestational age was calculated by a reliable menstrual history or ultrasound. Preterm was defined as births with <37 weeks of gestation.

The outcome measures studied were the incidence of PTB, gestational age at admission/delivery, risk factors for PTB, obstetrics/medical complications, drugs given, mode of delivery, and neonatal outcomes, such as birth weight, Apgar scores at 1 and 5 minutes, neonatal complications, need for NICU admission, and SARS-CoV-2 positivity.

Sample Size Calculation

The paper by Khoury et al. reported 20% PTB among SARS-CoV-2-positive mothers in the USA.[7] We expected a slightly higher incidence at 35%. To compare this rate with the expected preterm rate of 10% among SARS-CoV-2-negative mothers with 5% level of significance and 80% power, the sample size required was 43 per group (43 positive and 43 negative).

Statistical Analysis

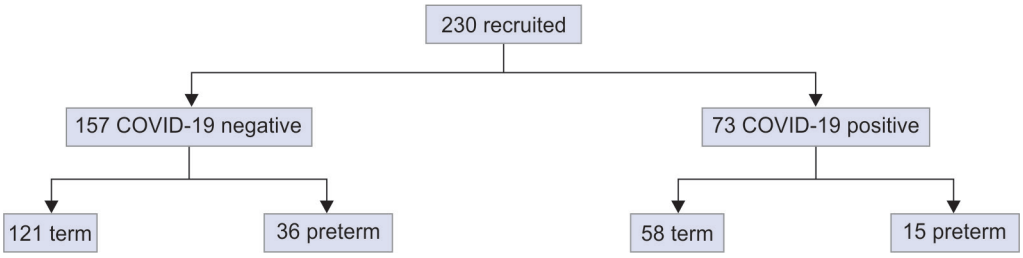
MS Excel was used to enter the data, and IBM SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, New York: IBM Corp.) was used for data analysis. The incidence of known risk factors of adverse outcomes in positive and negative cohorts was compared using Chi-square test or Fisher's exact test. Continuous variables were compared by *t* test or Mann-Whitney *U* test based on the distribution being normal. Normality of the distribution was assessed using Q-Q plot. Statistical significance was defined as a *p*-value <0.05.

Results

The SARS-CoV-2-positive and SARS-CoV-2-negative cohorts were comparable in terms of demographic features as shown in Table 1. Among the SARS-CoV-2-positive women, 70 (95.8%) women were asymptomatic; two (2.7%) had fever and dyspnea each; none had cough, myalgia, anosmia, diarrhea, or chest pain; and one had moderate COVID-19, who was also admitted to ICU, recovered, and subsequently delivered. Fifty-eight (79.5%) were detected in the third trimester. The gestational age at the time of recruitment and testing for the SARS-CoV-2-positive group was 36.92 ± 3.84 and 36.99 ± 3.49 weeks in the negative group. The average gestational age at delivery was 38.5 ± 7.2 weeks and 37.2 ± 2.7 weeks in the positive and negative groups, respectively (Table 1).

The overall incidence of PTB during the study period was 51/230 (22.1%; 95% Confidence Interval: 17–28%); 20.5% (95% CI: 12–32%) and 22.9% (95% CI: 17–30%), respectively, in SARS-CoV-2-positive mothers and SARS-CoV-2-negative mothers ($p = 0.686$) (Table 2). Indicated PTB was higher than spontaneous PTB in both cohorts. There were more late preterms (73 and 63%) than early preterms

Flowchart 1: Recruitment of participants



in both groups ($p = 0.514$). Neonatal outcomes were similar in both cohorts. Fetal distress was observed in slightly higher proportion of babies in the positive group (8.2 vs 2.5%, $p = 0.077$). There were four SARS-CoV-2-positive babies in the positive cohort and none in the negative cohort (Table 2). All babies were breastfed, and none had neonatal sepsis. Neither group had IUD or abortions.

Cesarean delivery was comparable between the two groups (53.4% in positive and 54.1% in negative groups). Emergency sections were done in 37.6% of negative group and 35.6% in the positive group—only three done at maternal request for SARS-CoV-2-positive status; all the others were done for obstetric indications like 3 (7.7%) for severe preeclampsia, 8 (26.5%) for previous cesarean delivery, nonreactive nonstress test (NRNST); 10 (25.6%) for non-progression of labor; and 6 (15.4%) for cephalopelvic disproportion (CPD). Eleven (15.9%) had postpartum hemorrhage (PPH) which was managed with oxytocics in the SARS-CoV-2-positive group. None had puerperal sepsis. Three mothers died in the SARS-CoV-2-negative cohort due to hemolysis, elevated liver enzymes, and low platelets (HELLP), dilated cardiomyopathy, or cerebellopontine angle tumor; only one succumbed in SARS-CoV-2-positive cohort to PPH—she was found to be RAT-negative initially and was later detected to be positive on RT-PCR, after mortality. There was no maternal mortality due to SARS-CoV-2 positivity.

The risk factors for PTB were similar in both the cohorts as shown in Table 3. None had uterine or congenital fetal anomalies, nor were treated for infertility or had a history of bleeding in the first trimester; two had multiple pregnancies in the SARS-CoV-2-negative cohort. However, the prevalence of hypertension was significantly higher in the SARS-CoV-2-negative ($p = 0.032$) compared to the SARS-CoV-2-positive cohort.

The obstetric and medical complications were similar in both groups as shown in Table 4. Though the prevalence of obstetrics complications, such as oligohydramnios, PPROM, gestational diabetes mellitus (GDM), Rh-negative pregnancy, and anemia, was slightly higher in the SARS-CoV-2-positive group, it was not significantly different from the SARS-CoV-2-negative group. 42.5 and 35.7% had induced labor in the SARS-CoV-2-positive and SARS-CoV-2-negative groups, respectively, but not statistically different. Laboratory parameters were similar in both groups (Table 5). A significant increase in lymphocytes was noted in the SARS-CoV-2-positive cohort.

97.3% received anticoagulants; 97.3% received multivitamins; and 43.8% received antibiotics in the SARS-CoV-2-positive group. None received remdesivir or convalescent plasma.

When the subgroup of preterm babies was examined separately in both cohorts, they were comparable in terms of risk factors, medical/obstetrical complications, mode of delivery, and neonatal outcomes as shown in Table 6.

Table 1: Demographic details of SARS-CoV-2-positive and SARS-CoV-2-negative group

Mean	*COVID-19-positive (n = 73)*	*COVID-19-negative (n = 157)*	*p value*
Maternal age (years)	27.21 ± 4.73	26.15 ± 4.97	0.123
Parity—Primi	39 (53.4%)	95 (60.5%)	0.596
Multi	26 (35.6%)	47 (29.9%)	
Grand-multi	8 (11%)	15 (9.6%)	
Low socioeconomic status	5 (6.8%)	20 (12.7%)	0.182
Consanguinity	11 (15.3%)	20 (12.7%)	0.630
Mean gestational age at delivery (weeks)	38.48 ± 7.19	37.18 ± 2.74	0.445
Gestational age at delivery (weeks)			
<28	2 (2.7%)	5 (3.2%)	
$28–33^{+6}$	2 (2.7%)	8 (5.1%)	
$34–36^{+6}$	11 (15.1%)	23 (14.6%)	
$37–39^{+6}$	55 (75.3%)	116 (73.9%)	
>40	3 (4.1%)	5 (3.2%)	

Table 2: Pregnancy outcomes by SARS-CoV-2-positive status

Pregnancy outcomes	*COVID-19-positive (n = 73)*	*COVID-19-negative (n = 157)*	*p value*
Mode of delivery			
Vaginal delivery	34 (46.6%)	72 (45.9%)	0.919
Cesarean delivery	39 (53.4%)	85 (54.1%)	
PPH	11 (15.9%)	22 (14%)	—
Maternal mortality	1	3	—
Neonatal outcomes			
Term	58 (79.5%)	121 (77.1%)	0.686
Preterm	15 (20.5%)	36 (22.9%)	0.686
Spontaneous PTB	3 (20%)	3 (8.3%)	0.343
Indicated PTB	12 (80%)	33 (91.7%)	
Mean birth weight (kg)	2.68 ± 0.71	2.55 ± 0.55	0.179
LBW (<2.5 kg)	20 (27.4%)	41 (26.1%)	0.792
Low Apgar score (<7/10)			
At 1 minute	29 (39.7%)	60 (38.2%)	0.827
At 5 minutes	7 (9.6%)	17 (10.8%)	0.775
Fetal distress	6 (8.2%)	4 (2.5%)	0.077
NRNST	1 (1.4%)	3 (1.9%)	1
Meconium stained liquor	1 (1.4%)	4 (2.5%)	—
NICU admission	17 (23.3%)	43 (27.4%)	0.510
COVID-positive babies	4 (5.4%)	0 (0%)	—

Table 3: Risk factors for preterm birth by SARS-CoV-2-positive status

Risk factors	*COVID-19-positive (n = 73)*	*COVID-19-negative (n = 157)*	*p value*
History of PTB	3 (4.1%)	5 (3.2%)	0.711
Low socioeconomic status	5 (6.8%)	20 (12.7%)	0.182
Oligohydramnios	4 (5.5%)	3 (1.9%)	0.212
PPROM	6 (8.2%)	11 (7%)	0.743
HTN	4 (5.5%)	25 (15.9%)	0.032
Infections	49 (67.12%)	93 (59.23%)	0.997
Anemia	11 (7%)	6 (8.2%)	0.743
Obesity (BMI >25.5 kg/m^2)	24 (32.9%)	53 (33.8%)	0.895
Low BMI (<18.5 kg/m^2)	1 (1.4%)	2 (1.3%)	1
DM	10 (13.7%)	14 (8.9%)	0.270
FGR	3 (4.1%)	7 (4.5%)	1
Previous IUD	4 (5.5%)	2 (1.2%)	—
Previous history of abortions	21 (28.7%)	37 (23.56%)	—

Table 4: Obstetric and medical complications by SARS-CoV-2-positive status

Variables	*COVID-19-positive (n = 73)*	*COVID-19-negative (n = 157)*	*p value*
Obstetric complications			
No obstetric complication	33 (45.2%)	69 (43.9%)	—
Previous cesarean delivery	5 (6.8%)	13 (8.3%)	0.707
Hypertension	4 (5.5%)	25 (15.9%)	0.032
Oligohydramnios	4 (5.5%)	3 (1.9%)	0.212
PPROM	6 (8.2%)	11 (7%)	0.743
GDM	10 (13.7%)	14 (8.9%)	0.27
FGR	3 (4.1%)	7 (4.5%)	1
Anemia	11 (7%)	6 (8.2%)	1
Rh-negative	4 (5.5%)	2 (1.3%)	0.082
CPD	1 (1.4%)	8 (5.1%)	0.279
Fetal distress	6 (8.2%)	4 (2.5%)	0.077
NR NST	1 (1.4%)	3 (1.9%)	1
Medical complications			
No medical complication	45 (61.6%)	119 (75.8%)	—
Cardiac disease	2 (2.7%)	3 (1.9%)	1
Respiratory disease	2 (2.7%)	4 (2.5%)	1
Hypothyroidism	13 (17.8%)	17 (10.8%)	0.143
Seizure disorder	1 (1.4%)	0%	—

Table 5: Comparison of laboratory parameters by SARS-CoV-2-positive status

Parameter	*COVID-19-positive (n = 73)*	*COVID-19-negative (n = 157)*	*p value*
Leukopenia (<4500 cells/cumm)	24 (32.9%)	65 (41.4%)	0.202
Lymphocytes (cells/cumm)	16.75 (10.38, 23)	13 (0.00, 19)	0.010
Increased D-dimer (>256 µg/dL)	17 (23.3%)	27 (17.2%)	—
Increased FBS (>95 mg/dL)	5 (16.1%)	6 (10.9%)	0.486
Increased PPBS (>140 mg/dL)	10 (6.8%)	37 (25%)	0.943
HbA1C (%)	5.26 ± 0.71	5.57 ± 0.97	0.292
Blood Urea (mg/dL)	15.40	13	0.688
Creatinine (mg/dL)	0.59	0.61	0.207
AST (U/L)	18	17	0.413
ALT (U/L)	11	11	0.595
Increased PT (>14.2 seconds)	2 (7.4%)	3 (5.1%)	0.766
INR	0.93 (0.88, 1)	0.91 (0.89, 1)	0.789
Urine culture—growth	35 (47.9%)	68 (43.3%)	0.511
Cervical swab—growth	14 (19.2%)	25 (15.9%)	0.540

Table 6: Comparison of maternal characteristics of preterm babies by maternal SARS-CoV-2-positive status

Parameters	*COVID-19-positive (n = 15)*	*COVID-19-negative (n = 36)*	*p value*
Mean maternal age (years)	27 ± 4.42	27.53 ± 4.13	0.686
Parity			
Primi	4 (26.7%)	25 (69.4%)	0.016
Multi	8 (53.3%)	9 (25%)	
Mean gestational age at birth (weeks)	36 ± 0.8	34 ± 0.8	0.211
Gestational age in weeks			
Early preterm (28–34 weeks)	4 (26.7%)	13 (36.1%)	0.514
Late preterm (34.1–36.6 weeks)	11 (73.3%)	23 (63.9%)	
Spontaneous PTB	3 (20%)	3 (8.3%)	0.343
Indicated PTB	12 (80%)	33 (91.7%)	
Risk factors			
Low socioeconomic status	0 (0%)	3 (8.3%)	—
History of preterm births	1 (6.7%)	3 (8.3%)	1
Previous cesarean delivery	5 (33.3%)	13 (36.1%)	—
Obesity	6 (40%)	12 (33.3%)	0.650
Infections	10 (66.7%)	20 (55.6%)	0.543
Urine culture growth	4 (26.7%)	6 (16.7%)	0.454
Cervical swab growth			
Mode of delivery			
Vaginal	7 (46.7%)	12 (33.3%)	0.526
Cesarean	8 (53.3%)	24 (66.7%)	
PPH	0	3 (37.5%)	—
Mean birth weight (kg)	2.15 ± 0.59	2.08 ± 0.68	0.721
Low birth weight (kg)	3 (20%)	14 (38.9%)	0.328
Low Apgar scores			
At 1 minute	6 (40%)	12 (33.3%)	0.650
At 5 minutes	3 (20%)	4 (11.1%)	0.406
NICU admission	3 (20%)	10 (27.8%)	0.730

Discussion

Most pregnant women acquire SARS-CoV-2 infection in the third trimester of pregnancy[15,16] as was found in our study too. During the pandemic, there was mass exposure of pregnant population at varied periods of gestation to SARS-CoV-2 infection. Only symptomatic women accessed healthcare facility. Due to lockdowns and economic and social reasons, antenatal checkups were infrequent. A vast majority of asymptomatic women missed out on antenatal care and the only time of testing for SARS-CoV-2 was at the time of delivery, as was mandated by the Government.

We have a higher rate of asymptomatic infection (95%) compared to other authors who have reported asymptomatic or mild infection rates of 80–87%.[10,17] The liberal use of spices, vegetables, and fruits in Indian diet could boost the immunity and modulate immune responses, causing mild or asymptomatic infection.[18] It could also be due to the prevalence of a less virulent SARS-CoV-2 strain, though further studies are needed to verify this.

Pregnant women are especially susceptible to respiratory pathogens and severe pneumonia, because of the physiological

changes in the immune and cardiopulmonary systems, rendering them more prone to severe infection and hence severe maternal and neonatal morbidity and mortality.[14,19]

Though increasing maternal age, high BMI and pre-existing comorbidities have been implicated as risk factors for severe COVID-19 infection in pregnancy,[10,11,20] it was not so in our study.

As pregnancy is an immunosuppressed state, an exaggerated COVID-19 response due to pro-inflammatory cytokines alters the fragile balance between a controlled immune response and host damaging reaction.[21] The release of inflammatory markers, such as ferritin, and cytokines, such as IL 6, is responsible for severe COVID-19 infections.[21] However, IL 6 has also been implicated in the etiopathogenesis of preterm labor. Also, the leukopenia caused by the SARS-CoV-2 virus predisposes the mother to other infections leading to preterm labor and PPROM.[22]

Some authors have reported a high prevalence rate of PTB ranging from 12 to 47%.[10–13] The incidence of PTB in our study was 20.5% among SARS-CoV-2-positive and 22.5% among SARS-CoV-2-negative pregnant women, demonstrating that there was no significant increase in preterm births. Though this is higher than our national average of 12.9% (3.5 million out of 27 million babies born per year),[23] this could be attributed to the expertise and facilities available at a tertiary care center, in addition to the referrals.

A decrease in PTB compared to the previous years has been reported due to the COVID-19 mitigation measures and rest taken by the pregnant working women during the lockdown.[24,25] An Irish study reported an unprecedented 73% reduction in PTB involving extremely low birth weight (ELBW) and very low birth weight (VLBW) infants.[26] We noted that there was no increase in PTB among SARS-CoV-2-positive pregnancies despite the risk factors for PTB being similarly distributed in both cohorts.

Symptomatic COVID-19 is associated with an increased risk of PTB compared with asymptomatic COVID-19, with the prevalence increasing with severity of infection.[27] Our study concurs with Adhikari et al. who have found that there is no difference in PTB between women with SARS-CoV-2 compared to those without.[28]

Yan et al. have reported a PTB rate of 2% before 34 weeks and 21.2% before 37 weeks among 116 pregnant women with COVID-19.[19] The likelihood of preterm delivery during hospitalization is significantly lower in the early preterm period compared to the late preterm period[10] as majority of them are discharged home undelivered. We too found that the number of late PTB was greater than early PTB, though this was not statistically significant as complications due to COVID-19 infection or obstetric complications are more common in late pregnancy.

Our study concurs with Villar et al. and other authors who found medically indicated PTB (83%) were more frequent than spontaneous PTB.[14,27,29] Eighty percent in SARS-CoV-2-positive and 92% in SARS-CoV-2-negative groups were indicated PTB in our study.

SARS-CoV-2 infection in pregnancy is associated with increased prevalence of preeclampsia, stillbirth, PTB, PPROM, gestational diabetes, and low birth weight.[9,22,27] However, other authors have reported that there is no significant effect of SARS-CoV-2 infection on maternal and fetal outcomes in pregnancy.[6,8,30,31]

We found that majority had no obstetrical or medical complications, as most of them had asymptomatic COVID-19. Among the complications, preeclampsia was significant that too in the SARS-CoV-2-negative cohort. This could be explained by ours being a tertiary care center which was functional throughout the pandemic.

Medical and obstetrics complications determine the mode of delivery. Vaginal deliveries are preferred and recommended wherever possible.[31]

Earlier cesarean delivery was advocated in maternal interest to improve maternal respiratory function in severe SARS-CoV-2 infection. Elective cesarean section was done at maternal request due to fears of vertical transmission during vaginal delivery in asymptomatic women.[14] Though several authors have reported a high cesarean rate among COVID-positive pregnant women,[10,16,32,33] COVID-19 cannot be considered as an indication for cesarean section.[34] With the emergence of safe protocols, universal testing among pregnant women, and availability of personal protection equipment (PPE), cesarean sections are recommended only for obstetrical indications. We too found that the mode of delivery was dictated by obstetrical indications. There was no difference in the rates of vaginal and cesarean deliveries among SARS-CoV-2-positive and SARS-CoV-2-negative cohorts.

Early coagulopathy reflected by increased PT/INR is common in these women placing them at increased risk of PPH and blood transfusions.[2] We noted that there was no difference in PT/INR or prevalence of PPH between the two cohorts.

There were three maternal deaths during the study period in the SARS-CoV-2-negative group and one in the SARS-CoV-2-positive group—none due to severe SARS-CoV-2 infection *per se*, differing from other authors who have reported that pregnant women are at increased risk for ICU admissions, maternal morbidity, and mortality.[11,29,34,35]

Neonatal outcomes were not significantly different between the two cohorts in our study. We did not have a higher prevalence of adverse perinatal outcomes, such as LBW, low Apgar scores, or NICU admissions, in SARS-CoV-2-positive cohort, as reported by other authors.[36]

There is little evidence of vertical transmission to newborn via placenta or during vaginal or cesarean delivery or transmission of SARS-CoV-2 through breast milk.[6,8,10,37,38] Breast feeding is advocated as virus has not been isolated in breast milk, cord blood, or placenta.[8,36–38] However, long-term follow-up of these babies is recommended.[6–8] Only four (5.4%) babies tested positive for SARS-CoV-2 RT-PCR in our study.

No significant difference between the laboratory parameters was noted in the two cohorts. Thrombosis and raised D-dimers are common with COVID infection—hence the need for anticoagulants. Thromboprophylaxis in the immediate postpartum period is essential to prevent thromboembolic events.[10]

The preterm cohorts among the SARS-CoV-2-positive and SARS-CoV-2-negative groups were comparable in terms of risk factors for PTB, complications, mode of delivery, and neonatal outcomes.

The strength of the study is the prospective nature of study, conducted during the peak of the pandemic, in a tertiary care center, with SARS-CoV-2-negative cohort for comparison and the good pregnancy outcomes in SARS-CoV-2-positive cohort.

The limitations of our study are the small numbers in the preterm cohort among COVID-positive and COVID-negative pregnant women and bias due to care in a tertiary referral center. Also there is lack of information on the time point of infection during pregnancy. More research is essential to verify the consistency of our findings in the second wave of the pandemic.

Conclusion

There is no increase in incidence of preterm births in SARS-CoV-2-positive cohort compared to SARS-CoV-2-negative cohort. Risk factors for preterm births and maternal and neonatal outcomes are not different between the two cohorts. Majority of them have asymptomatic infection, and good pregnancy outcomes can be anticipated.

References

1. Ellington S, Strid P, Tong VT, et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status—United States, January 22–June 7, 2020. Morbid Mortal Wkly Rep 2020;69(25):769. DOI: 10.15585/mmwr.mm6925a1.
2. Sentilhes L, De Marcillac F, Jouffrieau C, et al. Coronavirus disease 2019 in pregnancy was associated with maternal morbidity and preterm birth. Am J Obstet Gynecol 2020;223(6):914.e1–914.e15. DOI: 10.1016/j.ajog.2020.06.022.
3. Rasmussen SA, Smulian JC, Lednicky JA, et al. Coronavirus disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. Am J Obstet Gynecol 2020;222(5):415–426. DOI: 10.1016/j.ajog.2020.02.017.
4. Gulersen M, Blitz MJ, Rochelson B, et al. Clinical implications of SARS-CoV-2 infection in the viable preterm period. Am J Perinatol 2020;37(11):1077–1083. DOI: 10.1055/s-0040-1713851.
5. Antoun L, El Taweel N, Ahmed I, et al. Maternal COVID-19 infection, clinical characteristics, pregnancy, and neonatal outcome: a prospective cohort study. Eur J Obstet Gynecol Reprod Biol 2020;252:559–562. DOI: 10.1016/j.ejogrb.2020.07.008.
6. Li N, Han L, Peng M, et al. Maternal and neonatal outcomes of pregnant women with coronavirus disease 2019 (COVID-19) pneumonia: a case-control study. Clin Infect Dis 2020;71(16):2035–2041. DOI: 10.1093/cid/ciaa352.
7. Khoury R, Bernstein PS, Debolt C, et al. Characteristics and outcomes of 241 births to women with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection at five New York City medical centers. Obstet Gynecol 2020;136(2):273–282. DOI: 10.1097/AOG.0000000000004025.
8. Panahi L, Amiri M, Pouy S. Risks of novel coronavirus disease (COVID-19) in pregnancy; a narrative review. Arch Acad Emerg Med 2020;8(1):e34. PMID: 32232217.
9. Akhtar H, Patel C, Abuelgasim E, et al. COVID-19 (SARS-CoV-2) infection in pregnancy: a systematic review. Gynecol Obstet Investig 2020;85(4):295–306. DOI: 10.1159/000509290.
10. Ryan GA, Purandare NC, McAuliffe FM, et al. Clinical update on COVID-19 in pregnancy: a review article. J Obstet Gynaecol Res 2020;46(8):1235–1245. DOI: 10.1111/jog.14321.
11. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ 2020;370:m3320. DOI: 10.1136/bmj.m3320.
12. Delahoy MJ, Whitaker M, O'Halloran A, et al. Characteristics and maternal and birth outcomes of hospitalized pregnant women with laboratory-confirmed COVID-19—COVID-NET, 13 states, March 1–August 22, 2020. Morbid Mortal Wkly Rep 2020;69(38):1347. DOI: 10.15585/mmwr.mm6938e1.
13. Mullins E, Evans D, Viner RM, et al. Corona-virus in pregnancy and delivery: rapid review. Ultrasound Obstet Gynecol 2020;55(5):586–592. PMID: 32180292. DOI: 10.1002/uog.22014.
14. Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in the UK: a national population-based cohort study. BMJ 2020;369:m2107. DOI: 10.1136/bmj.m2107.
15. Liu H, Liu F, Li J, et al. Clinical and CT imaging features of the COVID-19 pneumonia: focus on pregnant women and children. J Infect 2020;80(5):e7–e13. DOI: 10.1016/j.jinf.2020.03.007.
16. Fan C, Lei D, Fang C, et al. Perinatal transmission of COVID-19 associated SARS-CoV-2: should we worry? Clin Infect Dis 2021;72(5):862–864. DOI: 10.1093/cid/ciaa226.
17. Sutton D, Fuchs K, D'alton M, et al. Universal screening for SARS-CoV-2 in women admitted for delivery. New Engl J Med 2020;382(22):2163–2164. DOI: 10.1056/NEJMc2009316.
18. Banerjee S, Srivastava S, Giri AK. Possible nutritional approach to cope with COVID-19 in Indian perspective. Adv Res J Med Clin Sci 2020;6(06):207–219. Published: 20th June 2020.
19. Yan J, Guo J, Fan C, et al. Coronavirus disease 2019 in pregnant women: a report based on 116 cases. Am J Obstet Gynecol 2020;223(1):111.e1–111.e14. DOI: 10.1016/j.ajog.2020.04.014.
20. Gao YJ, Ye L, Zhang JS, et al. Clinical features and outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. BMC Infect Dis 2020;20(1):1-1. DOI: 10.1186/s12879-020-05274-2.
21. Picchianti Diamanti A, Rosado MM, Pioli C, et al. Cytokine release syndrome in COVID-19 patients, a new scenario for an old concern: the fragile balance between infections and autoimmunity. Int J Mol Sci 2020;21(9):3330. DOI: 10.3390/ijms21093330.
22. Perez OM, Rodriguez PP, Hernandez MM, et al. The association between COVID-19 and preterm delivery: a cohort study with a multivariate analysis. medRxiv 2020. DOI: 10.1101/2020.09.05.20188458.
23. Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet 2012;379(9832):2162–2172. DOI: 10.1016/S0140-6736(12)60820-4.
24. Kasuga Y, Tanaka M, Ochiai D. Preterm delivery and hypertensive disorder of pregnancy were reduced during the COVID-19 pandemic: a single hospital-based study. J Obstet Gynaecol Res 2020. DOI: 10.1111/jog.14518.
25. Been JV, Ochoa LB, Bertens LC, et al. Impact of COVID-19 mitigation measures on the incidence of preterm birth: a national quasi-experimental study. Lancet Public Health 2020;5(11):e604–e611. DOI: 10.1016/S2468-2667(20)30223-1.
26. Philip RK, Purtill H, Reidy E, et al. Reduction in preterm births during the COVID-19 lockdown in Ireland: a natural experiment allowing analysis of data from the prior two decades. MedRxiv 2020. DOI: 10.1101/2020.06.03.20121442.
27. Wei SQ, Bilodeau-Bertrand M, Liu S, et al. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. CMAJ 2021;193(16):E540–E548. DOI: 10.1503/cmaj.202604.
28. Adhikari EH, Moreno W, Zofkie AC, et al. Pregnancy outcomes among women with and without severe acute respiratory syndrome coronavirus 2 infection. JAMA Netw Open 2020;3(11):e2029256. DOI: 10.1001/jamanetworkopen.2020.29256.
29. Villar J, Ariff S, Gunier RB, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID multinational cohort study. JAMA Pediatr 2021;175(8):817–826. DOI: 10.1001/jamapediatrics.2021.1050.
30. Nayak AH, Kapote DS, Fonseca M, et al. Impact of the coronavirus infection in pregnancy: a preliminary study of 141 patients. J Obstet Gynecol India 2020;70(4):256–261. DOI: 10.1007/s13224-020-01335-3.
31. Di Toro F, Gjoka M, Di Lorenzo G, et al. Impact of COVID-19 on maternal and neonatal outcomes: a systematic review and meta-analysis. Clin Microbiol Infect 2021;27(1):36–46. DOI: 10.1016/j.cmi.2020.10.007.
32. Yu N, Li W, Kang Q, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. Lancet Infect Dis 2020;20(5):559–564. DOI: 10.1016/S1473-3099(20)30176-6.
33. Zhang I, Jiang Y, Wei M, et al. Analysis of pregnancy outcomes of pregnant women during the epidemic of new coronavirus pneumonia in Hubei. Zhonghua Fu Chan Ke Za Zhi 2020;55(3):166–171. DOI: 10.3760/cma.j.cn112141-20200218-00111.
34. Karimi L, Makvandi S, Vahedian-Azimi A, et al. Effect of COVID-19 on mortality of pregnant and postpartum women: a systematic review and meta-analysis. J Pregnancy 2021;2021:8870129. DOI: 10.1155/2021/8870129.

35. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, et al. Maternal death due to COVID-19 disease. Am J Obstet Gynecol 2020;223(1):109.e1–109.e16. S0002-9378(20)30516-0. DOI: 10.1016/j.ajog.2020.04.030.
36. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. Transl Pediatr 2020;9(1):51. DOI: 10.21037/tp.2020.02.06.
37. Wastnedge EAN, Reynolds RM, van Boeckel SR, et al. Pregnancy and COVID-19. Physiol Rev 2021;101(1):303–318. DOI: 10.1152/physrev.00024.2020.
38. Rodrigues C, Baía I, Domingues R, et al. Pregnancy and breastfeeding during COVID-19 pandemic: a systematic review of published pregnancy cases. Frontiers in public health 2020;23(8):806.