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RESEARCH ARTICLE

Association of mode of delivery with maternal and perinatal outcome in SARS CoV-2 pregnancies: a retrospective observational study

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ABSTRACT

Background: The novel coronavirus pandemic has affected the pregnant women and newborns worldwide. It has become necessary to know the effect of mode of delivery on the mother and newborn in Covid-19 pregnancies as very few literature is found regarding this. **Objective:** To evaluate the association of mode of delivery with maternal and perinatal outcome in SARS CoV2 pregnancies. **Methodology**: Total 191 pregnant women who tested Covid positive and who delivered at a tertiary care hospital were included in the study, from July to December 2020. Maternal and perinatal outcomes in vaginal and caesarean delivery groups were compared. **Results**: More women delivered by caesarean section (51.3%). There is increased rate of clinical deterioration of mothers after caesarean section (p=0.03). In newborns, caesarean delivery was not found to be significantly associated with low birth weight (p=0.28) or birth asphyxia (p=0.31). 6 newborns born vaginally and 4 born by caesarean section tested positive for SARS CoV-2. Covid positive status of newborns was not significantly associated with increased risk of low birth weight (p=0.26) or neonatal sepsis (p=0.18). Statistically significant association was found between severe Covid symptoms in mothers and low birth weight of babies (p<0.0001), higher proportion of NICU admissions (p=0.0004) and early neonatal death (p=0.0005). **Conclusion**: There is increased rate of clinical deterioration of mothers after caesarean section but there is no association with increased need of NICU admissions or Covid-19 infection in newborns.

Keywords: Covid-19, pandemic, pregnancy, mode of delivery, maternal outcome, perinatal outcome.

In December 2019 some cases of pneumonia caused by infection from a newly identified coronavirus were reported in Wuhan, a city within the People's Republic of China. This newly identified coronavirus was initially termed 2019-nCoV and subsequently SARS-CoV-2[1]. Coronaviruses are spherical, enveloped, and positive stranded RNA viruses. In humans, they can cause mild illnesses like common cold, and were believed to be of modest medical importance. However, two zoonotic coronaviruses including the severe acute respiratory syndrome corona virus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are capable of causing severe lower respiratory tract infections. SARS CoV-2 has caused epidemics with significant loss of life worldwide [1]. On 30 January, WHO declared the novel coronavirus 2019 epidemica public health emergency of international concern (PHEIC) [2, 3].

The first case in India was confirmed on 30th January 2020 [4]. By 16th May 2020, the number of cases in India reached 85,940 with 2753 deaths reported by the ministry of health and family welfare [5]. The mode of transmission is by droplets, through close contact with an infected person (within 2 meters) or fomites from contaminated surfaces. The incubation period varies from 2 days to 2 weeks following exposure to the virus [6]. The period from the onset of Coronavirus disease 2019 (COVID-19) symptoms to death ranged from 6 to 41 days with a median of 14 days and

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a case fatality rate of 2.3% [7,8]. The patients can present with an array of complaints ranging from fever, cold, cough, shortness of breath, malaise, headache, itching or watering of eyes, loss of smell or taste, nausea, diarrhea to very severe diseases like pneumonia, respiratory failure, septic shock and death [9].

Pregnant women are less likely to contract the infection than the overall population. However, some factors make pregnant women more susceptible to complications of the infection [10]. Anatomical changes in pregnancy like an increased transverse diameter of the thoracic cage and an elevated level of diaphragm decrease the maternal tolerance to hypoxia [11]. Lung volume changes and vasodilatation can cause mucosal edema and increased secretions in the upper respiratory tract [12]. In fetus and newborn, the innate and adaptive immune system is immature which make them more vulnerable to infections [13]. Chinese reports found severe complications in 8% of pregnant women with COVID-19 [14]. However, limited data on the effect of mode of delivery on maternal and perinatal outcomes in COVID-19 pregnancies and its association with transmission of the virus to newborns is available. Hence, our study aims to assess the association of mode of delivery with maternal and perinatal outcomes because probably no such study has been reported in India so far.

Materials and methods

A hospital based retrospective observational analytical study was carried out in a tertiary obstetric unit attached to a medical college, located in Silchar, Assam. Pregnant women who tested positive with reverse transcriptase–polymerase chain reaction (RT-PCR) test and rapid antigen test for SARS-CoV-2 between July and December 2020, and who delivered within the subsequent 14 days were included within the study. Details about the patients like age, parity, gestational age, history of contact, any comorbid conditions, mode of delivery and outcome, baby details and treatment given were noted. All pregnant patients were tested as per ICMR guidelines recommendations that pregnant women residing in containment zones or from hotspot district presenting in labour or likely to deliver in next 5 days should be tested albeit asymptomatic.

The swabs were collected after wearing complete personal protective equipment and were transferred in viral transport medium and sent to the microbiology department for testing. All the patients were advised to wear a mask and gown. Neonatal swabs were sent within 6 hours of birth and rooming-in was recommended. Direct breastfeeding was encouraged in the mothers after wearing medical mask once they were near their baby and perform hand hygiene before close contact with the baby.

Mothers requiring advanced oxygen support or admission to the intensive care unit (ICU) or having signs of sepsis with hypoperfusion or organ dysfunction were defined as having severe symptoms. Clinical deterioration was defined by an increased need for oxygen supplementation after delivery or requiring ICU care after delivery. Neonatal outcomes included were neonatal ICU (NICU) admission and rates of SARS-CoV-2 positive RT-PCR tests.

All the maternal and neonatal parameters were analysed and percentages and proportions were calculated. Logistic regression was performed to assess the association between mode of delivery and maternal and neonatal outcomes among the patients. A 2-tailed "$p < 0.05$" was considered as statistically significant.

Result

Of 191 pregnant patients included, 93(45.7%) women delivered vaginally and 98(51.3%) delivered by caesarean section (figure 1), mainly for obstetrical indications (like previous caesarean, fetal distress, prolonged and obstructed labor, CPD, malpresentations, disorders of amniotic fluid, chorioamnionitis) (figure 2).

The mean gestational age was 40 weeks for vaginal deliveries and 39 weeks for caesarean deliveries. 11 patients presented with severe Covid-19 symptoms, amongst which 9 underwent cesarean delivery, 2 delivered vaginally and 5 required ICU care. 180 patients presented with no or mild Covid-19 symptoms, amongst whom 91 patients delivered vaginally and 89 delivered by caesarean section. 3 out of 91 patients who had vaginal delivery underwent instrumental vaginal delivery. The median age of women with vaginal delivery was 24.4 years while that of caesarean section was 25.5 years. Women with cesarean deliveries were more likely to be multiparous and have abnormal chest x-ray findings than those delivering vaginally (table 1).

2(2.1%) patients who had a vaginal delivery required ICU care due to adverse outcomes while 3(3.06%) with cesarean delivery required ICU admission. 2 patients (2.1%) with a vaginal delivery had clinical deterioration after birth versus 9(9.2%) with cesarean delivery. After adjustment for potential confounding factors, cesarean birth was significantly associated with clinical deterioration (adjusted odds ratio, 4.6; 95% CI, 0.96-21.89; $p = 0.03$) (table 2), however caesarean delivery was not significantly associated with increased need of ICU care (adjusted odds ratio 1.44;

Table 1: Maternal characteristics and clinical presentation

Maternal characteristics	Vaginal delivery (n=93) No (%)	Caesarean delivery (n=98) No (%)
Age		
Median age (years)	24.4 (19-45)	25.5 (18-38)
≤ 20 years	23 (24.7)	22 (22.4)
21-25 years	42 (45.2)	32 (32.6)
26-30 years	17 (18.3)	28 (28.5)
31-35 years	6 (6.4)	11 (11.2)
>35 years	5 (5.4)	5 (5.1)
Parity		
Nulliparous	46 (49.5)	39 (39.8)
Multiparous	47 (50.5)	59 (60.2)
Comorbidities		
Total	61 (65.6)	63 (64.3)
Anemia	50 (53.7)	54 (55.1)
Gestational diabetes	1 (1.07)	1 (1.02)
Gestational hypertension	4 (4.3)	2 (2.04)
Eclampsia	1 (1.07)	1 (1.02)
Hypothyroidism	2 (2.15)	4 (4.08)
Diarrhea	1 (1.07)	0
HIV	1 (1.07)	1 (1.02)
Hepatitis B	1 (1.07)	0
Covid-19 history and prepartum clinical presentation		
Signs and symptoms		
Mild/asymptomatic	91 (97.8)	89 (90.1)
Severe symptoms	2 (2.15)	9 (9.2)
Diagnostic tests		
Lymphocytosis (>11000/cu mm)	65 (69.8)	52 (53.06)
Lymphocytopenia (<20%)	73 (78.5)	76 (77.5)
Raised AST/ALT	56 (60.2)	57 (58.1)
CRP positive (>12µg/ml)	5 (5.4)	3 (3.06)
Abnormal chest X ray	2 (2.15)	9 (9.2)
Delivery management		
Gestational age at delivery		
Median (weeks)	40 (28-42)	39 (32-42)
Preterm birth		
<34 weeks	13 (13.9)	1 (1.02)
34 to < 37 weeks	10 (10.7)	14 (14.3)
Term (37 to 40 weeks)	57 (61.3)	63 (64.3)
Post term (> 40 weeks)	13 (13.9)	19 (19.4)
Premature rupture of membranes	0	3 (3.06)
Preterm premature rupture of membranes	1 (1.07)	0
Obstetrical management		
Spontaneous onset of labour	88 (94.6)	86 (87.7)
Induction of labour	5 (5.4)	12 (12.2)
Instrumental delivery	3 (3.2)	0
Prelabour caesarean delivery	0	33 (33.7)
In Labour Caesarean Delivery	0	65 (66.3)

95% CI 0.23-8.79, p = 0.63). Patients who had severe symptoms were more prone to have leucocytosis, sepsis and had raised CRP and raised liver enzymes. All patients with severe symptoms had abnormalities in their chest X ray (table 3). Statistically significant association was found between possession of severe symptoms and raised CRP levels, sepsis (odds ratio 13.1250; 95% CI 2.6574-64.8259; p=0.0016) and raised AST (aspartate aminotransferase) /ALT (alanine transaminase) levels (odds ratio 5.0753; 95% CI 1.2999-19.8153; p = 0.0194).

34 of 191(19.8%) babies in our study were born preterm, of which 14(7.3%) babies were born <34 weeks gestation earliest being at 29 weeks and 24(12.5%) were born between 34 and $36^{6/7}$ weeks of gestation. There were 8 intrauterine deaths, 3 still births and 6 early neonatal deaths. Out of 93 vaginal births, 3 newborns had early neonatal death, amongst whom 1 baby tested positive for Covid 19 by RT-PCR testing done within 6hours after birth**.** The baby delivered prematurely at 30 weeks of gestation and was admitted in NICU due to neonatal sepsis. Out of 98 caesarean births, 3 newborns died in the early neonatal period. Out of 6 early neonatal deaths, 3 babies had neonatal sepsis, 2 babies had birth weight $<10^{th}$ percentile, 2 babies had birth asphyxia, 1 had meconium aspiration syndrome, 1 had Hypoxic ischemic encephalopathy and 1 had disseminated intravascular coagulation. 22 newborns (23.6%) born vaginally and

Table 2: Maternal and neonatal outcomes

Parameters	Vaginal delivery (n=93)	Caesarean delivery (n=98)	Odds ratio	Adjusted odds ratio (95% CI)	P value
Maternal outcomes	No (%)	No (%)	No (%)	No (%)	
Total duration of hospital stay in days (median)	8 (1-21)	9 (2-19)			
Sepsis	0	1 (1.02)	NA	NA	NA
ICU admission	2 (2.1)	3 (3.06)	1.44	0.23-8.79	0.63
Deterioration of symptoms	2 (2.1)	9 (9.2)	4.6	0.96-21.89	0.03
Perinatal outcomes					
Intrauterine death	8 (8.6)	0	NA	NA	NA
Still born	3 (3.2)	0	NA	NA	NA
Early neonatal death	3 (3.2)	3 (3.06)	NA	NA	NA
NICU admission total	22 (23.6)	18 (18.4)	0.73	0.36-1.46	0.37
SARS CoV2 confirmed positive test at birth	9 (9.6)	5 (5.1)	0.57	0.18-1.81	0.33
Birth weight <10th percentile	5 (5.4)	7 (7.1)	1.97	0.57-6.8	0.28
Neonatal jaundice	0	1 (1.02)	NA	NA	NA
Birth asphyxia	5 (5.4)	10 (10.2)	1.78	0.57-5.52	0.31
Respiratory distress	2 (2.1)	1 (1.02)	0.47	0.042-5.26	0.53
Meconium aspiration syndrome	2 (2.1)	6 (6.1)	0.95	0.13-6.87	0.96
Neonatal sepsis	3 (3.2)	0	NA	NA	NA
Hypoxic ischemic encephalopathy	1(1.07)	1 (1.02)	NA	NA	NA
Myelomeningocele	1 (1.07)	0	NA	NA	NA

18(18.4%) born by cesarean section required NICU admission. Newborns born by caesarean section more likely had birth weight less than 10th percentile and had birth asphyxia (table 2). After adjusting for confounding factors, caesarean delivery was not significantly associated with low birth weight (adjusted odds ratio, 1.97; 95% CI, 0.57-6.8; p = 0.28) or birth asphyxia (adjusted odds ratio1.78; 95% CI, 0.57-5.52; p = 0.31). 6 newborns born vaginally and 4 born by caesarean section tested within 6 hours after birth had a positive SARS CoV-2 RTPCR result for their nasopharyngeal swab. 4 other newborns, 1 born by cesarean section at term and 3 by vaginal delivery, developed Covid-19 symptoms within 10 days. Though initial testing at birth was negative, repeat testing was positive. All 4 newborns were in contact with their parents immediately after birth. 1 new born died who developed Covid-19 symptoms within 10 days after birth, died within 24 hours of development of symptoms due to neonatal sepsis.

Table 3: Fetomaternal outcome in relation to severity of symptoms of women

Parameters	Mild symptoms (N=180) No (%)	Severe symptoms (N=11) No (%)	Odds ratio	Adjusted odds ratio (95% CI)	P value
Laboratory parameters of women					
Leucocytosis	97 (53.8)	7 (63.6)	1.4974	0.4235 - 5.2947	0.5309
Lymphocytopenia	81 (45)	4 (36.4)	0.6984	0.1975 - 2.4699	0.5775
Raised ALT/AST	62 (34.4)	8 (72.7)	5.0753	1.2999-19.8153	0.0194
CRP positive	5 (2.7)	3 (27.3)	13.1250	2.6574-64.8259	0.0016
Abnormal chest X ray	0	11 (100)	NA	NA	NA
Maternal outcome					
Total duration of stay (median)	9 (1-18)	9 (2-13)	NA	NA	NA
Sepsis	5 (2.7)	3 (27.3)	13.1250	2.6574-64.8259	0.0016
ICU admission	0	5 (45.4)	NA	NA	NA
Deterioration of symptoms	0	5 (45.4)	NA	NA	NA
Neonatal outcome					
NICU admission	20 (11.1)	11 (100)	180.0732	10.2248 -3171.3539	0.0004
Confirmed positive SARS CoV2 at birth	9 (5)	5 (45.4)	15.83	4.0514-61.8780	0.0001
Birth weight<10th percentile	5 (2.7)	7 (63.6)	61.25	13.4444 to 279.0427	<0.0001
IUD	8 (4.4)	0 (0)	NA	NA	NA
Still born	3 (1.7)	0 (0)	NA	NA	NA
Early neonatal death	3 (1.7)	3 (27.3)	22.125	3.8442 to 127.3377	0.0005

Table 4: Neonatal outcomes in respect to SARS CoV-2 test result

Neonatal outcome	Covid positive (N=14) No (%)	Covid negative (N=177) No (%)	Odds ratio	Adjusted odds ratio (95% CI)	P Value
Birth weight <10th percentile	2 (14.3)	10 (5.6)	2.78	0.54-14.16	0.26
Neonatal sepsis	1 (7.1)	2 (1.1)	6.73	0.57-79.23	0.18
Meconium aspiration	0	8 (4.5)	NA	NA	NA
Respiratory distress	0	3 (1.7)	NA	NA	NA
Hypoxic ischemic encephalopathy	0	2(1.1)	NA	NA	NA
Neonatal jaundice	0	1(0.05)	NA	NA	NA

The neonates of patients with severe symptoms had higher proportion of NICU admissions 11(100%), covid positive status 5(45.4%), low birth weight 7(63.6%) and early neonatal death 3(27.3%) (table 3) and all the associations were statistically significant. 2 newborns who tested positive for SARS CoV2 had birth weight <10th percentile and 1 had neonatal sepsis (table 4). However, Covid positive status was not significantly associated with increased risk of low birth weight (adjusted odds ratio, 2.78; 95% CI, 0.54-14.16; p = 0.26) or neonatal sepsis (adjusted odds ratio, 6.73; 95% CI, 0.57-79.23; p = 0.18).

Discussion

SARS-Cov 2 is a highly infectious disease which has spread across the world at quite an alarming rate. Men have been found to have a higher incidence and severity when compared to women worldwide. Elderly patients (≥65 years old), were more likely to develop severe form of the disease and mortality was also higher in the elderly.

Pneumonia arising from any infectious etiology is a crucial explanation for morbidity and mortality among pregnant women. It is the most prevalent non-obstetric infectious condition that occurs during pregnancy [1]. WHO reported that the adverse pregnancy outcomes were high in Covid pregnancies especially among those women with associated comorbidities [15]. In our study, patients had presented with a number of comorbidities in their pregnancy such as anaemia, gestational diabetes mellitus (GDM), gestational hypertension and hypothyroidism. Studies by Liu et al [15] and Fan et al [16] reported that most pregnant women acquired the infection in the third trimester of pregnancy. Our study also reported that most patients presented in third trimester, the median gestational age being 40 weeks for vaginal deliveries and 39 weeks for caesarean deliveries.

A study by Mertinez Perez O et al [17] in Spain found that patients with mild symptoms at presentation, who delivered vaginally, had excellent outcomes. In contrast, 13.5% of women undergoing cesarean delivery had severe maternal outcomes and 21.6% had clinical deterioration. Cesarean birth was an independent risk factor for clinical deterioration. The stress imposed by surgery leads to postpartum maternal complications. Our study had reported a similar finding. 9.2% of patients with caesarean delivery had deterioration of symptoms in contrast to 2.1% patients who had vaginal delivery and the association was statistically significant (p value = 0.03). Our study reported that Covid patients with severe symptoms had higher levels of WBC counts, CRP and AST/ALT. However, Na Li et al [18] in their study found that Covid patients had lower WBC counts but raised CRP and ALT. Recent literatures found more incidence of LSCS in covid pregnancies. There are reports of a concerning high rate of cesarean deliveries (>90%) in Chinese literature [19]. Rates of caesarean births as reported by Elshafeey F et al [20] and Debrabandere ML [21] were 69.4% and 68.9% respectively. In our study, more number of patients was delivered by LSCS (51.3%), the indications mainly being obstetrical and not just because the pregnant woman had Covid 19 infection. 19.8% babies in our study were born preterm, of which 7.3% babies were born <34 weeks gestation and 12.5% were born between 34 and 36$^{6/7}$ weeks of gestation. Study by Debrabandere ML et al [21] reported that 30.1% births in Covid positive pregnant women were preterm. Preterm birth before 34 weeks of gestation was observed in 9.2% neonate and preterm birth between 34 and 36$^{6/7}$ weeks of gestational age occurred in 20.9% neonates. It was observed that several of these preterm deliveries were the result of a cesarean intervention for a positive Covid-19 status. The rates were nearly similar in this study.

Studies have shown high proportion low birth weight in covid patients [22, 23] and our study too found similar findings, especially in women with severe symptoms. This can be implicated to the pre-placental hypoxia which can occur as a result of maternal respiratory compromise in patients with severe Covid symptoms. Also we found that all newborns of patients with severe symptoms (n=11) required NICU admissions. A study by Zhu et al (n = 10) [24] showed that 60% of the neonates required NICU support.

There were four cases of intrauterine fetal death and three cases of neonatal death, including one set of twins as reported by Liu Y et al [25]. Intrauterine fetal death was reported only with critical maternal Covid -19, including a patient with ARDS and multiple organ dysfunction syndrome requiring extracorporeal membrane oxygenation support. Our study also found higher proportion of neonatal deaths in patients with severe Covid symptoms.

Hantoushzadeh et al [26] reported neonatal death on day 3 of life in a set of twins due to complications relating to preterm delivery at 28$^{0/7}$ weeks of gestational age. These two infants were negative for SARS CoV-2. In our study, there were 8 intrauterine deaths and 3 still births. 6 out of the rest 180(3.3%) newborns had early neonatal death, amongst whom 1 baby was positive for SARS-CoV-2**.** This baby died due to complications of prematurity and neonatal sepsis. Other 5 babies were SARS CoV-2 negative. This was in concordance with a study by Zeng et al [27] who reported 1 case of seriously ill neonate with SARS Cov-2 infection,

however the symptoms might have been due to prematurity, asphyxia, and sepsis, rather than SARS-CoV-2 infection.

Lastly, the data for Covid-19 vertical transmission is limited. A study by Chen et al [28] reported the maternal–neonatal outcomes and vertical transmission potential of Covid-19 infection in pregnant women who delivered by LSCS, and no case for normal vaginal delivery was reported. Intrauterine vertical transmission was assessed by testing cord blood, amniotic fluid and neonatal throat swab samples for the presence of SARS-CoV-2 and all were tested negative. Hence there was no evidence of intrauterine and vertical transmission of disease in Covid-19 positive pregnant women. Ferrazzi E et al [29] reported that 1 out of 24 newborns born vaginally was infected with SARS CoV-2 but the infection was probably due to postpartum contamination. In a second case after vaginal delivery a potential intrapartum infection may have occurred, but it was not possible to exclude other sources of infection in the immediate post-partum. We found that the rate of positive tests for SARS CoV-2 in the nasopharyngeal swabs of newborns were more in case of vaginal deliveries than caesarean births (6 versus 4). This might have been a result of contamination from maternal genital secretions or stool during vaginal births. Limitations of the study include a lack of sufficient information on newborns to determine vertical transmission.

Conclusion

Literature of the effect of mode of delivery on maternal and perinatal outcome in Covid 19 infected pregnancies is limited. In our study we have tried to determine the association of mode of delivery with maternal and perinatal outcome. The result of the study suggest that there is increased rate of clinical deterioration of mothers after caesarean section but there is no association of caesarean delivery with increased need of NICU admissions. Also, we found no association of mode of delivery with Covid-19 infection in newborns. As most literatures suggest that there is very less chance of vertical transmission of Covid-19 infection, further studies to assess the effect of mode of delivery on the rate of Covid-19 infection in newborns is needed so that infection in newborns can be curtailed.

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