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CLINICAL BRIEF

Perinatal Transmission and Outcomes of SARS-CoV-2 Infection

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Abstract
Maternal SARS-CoV-2 infection can adversely affect the birth and neonatal outcomes. The authors prospectively enrolled 196 neonates born to 193 SARS-CoV-2–positive mothers to determine the rate of mother-to-baby transmission of SARS-CoV-2 and its effect on short-term neonatal outcomes in Indian population. Nineteen babies turned out to be RT-PCR–positive for SARS-CoV-2, carrying a perinatal transmission rate of 9.8%. Rates of prematurity and low birth weight were 12.8% and 18.9% in the neonatal group, respectively. On comparing SARS-CoV-2–positive ($n = 19$) and negative ($n = 177$) neonatal groups, rate of prematurity, hospital admission rate, and death rate were higher in the former group. The placental positivity rate for SARS-CoV-2 was 8.1%, but no relation was found between placental and neonatal infection.

Keywords SARS-CoV-2 · Perinatal transmission · Neonatal outcomes · Placental infection

Introduction

Maternal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection being associated with hypercoagulability and cytokine storm can adversely affect the pregnancy and birth outcomes [1]. The reported fetal complications include abortion, intrauterine growth restriction, and prematurity [2]. Besides this, maternal infection occurring within 14 d of delivery carries the theoretical risk of vertical transmission also [3]. SARS-CoV-2 infection in neonatal population can lead to hypoxia, respiratory distress, vomiting, cough, fever, disseminated intravascular coagulation, and death [4]. The Asian population, due to higher expression of ACE-2 receptors, is considered more susceptible to SARS-CoV-2 infection than European and American populations [5]. This study was conceived primarily to determine the rate of mother-to-baby transmission of SARS-CoV-2 in the Indian population and its effects on short-term neonatal outcomes.

Materials and Methods

The study was carried out at a tertiary care teaching hospital in Western Rajasthan after approval from the institutional ethics committee. All neonates with gestational age ≥ 32 wk born to SARS-CoV-2 positive mothers (maternal RT-PCR–positive for SARS-CoV-2 within 2 wk prior to delivery) underwent RT-PCR test for SARS-CoV-2 infection, and this test was repeated weekly till negative. Placentae retrieved from these women were also tested for SARS-CoV-2 infection, whenever possible. Neonatal outcomes were compared between SARS-CoV-2–positive and –negative groups. Inflammatory biomarkers such as serum ferritin, D-dimer, quantitative CRP, and interleukin-6 levels were also measured in all test positive neonates. Written informed consent was obtained from all eligible mothers.

Results

Over the 6 mo study period, 193 SARS-CoV-2–positive women delivered 196 live babies (twin births 3; vaginal delivery 84; cesarean delivery 109; male 103; female 93). The neonatal group comprised 12.8% (25/196) preterm and

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18.9% (37/196) low-birth-weight babies. All 196 neonates were tested for SARS-CoV-2 infection. The rate of perinatal transmission was 9.8% (19/193). Out of 196 neonates, 15 were tested within 24 h of life, 143 at 24–48 h of life, 32 at 48–72 h of life, and 6 were tested at 72–96 h of life. The mean (SD) age at sample collection was 2.1 (0.6) d. Maternal SARS-CoV-2 positivity did not alter the exclusive breast-feeding practices; almost all babies received exclusive breast-milk, except for 4 sick babies, who later succumbed.

Rates of prematurity, NICU admission, and death were higher and mean birth weight was lower in SARS-CoV-2–positive group as compared to –negative group (Table 1). In SARS-CoV-2–positive neonatal group, 17 babies became negative during the second test (after 1 wk); 2 babies succumbed and could not be retested. Serum ferritin levels exceeded > 400 µg/L, D-dimer levels exceeded 500 µg/L, serum CRP levels were higher than > 6 mg/L, and IL-6 levels were more than 10 nanogram/L in 21.05% (4/19), 78.94% (15/19), 63.15% (12/19), and 26.31% (5/19) SARS-CoV-2–positive babies, respectively.

In survived ($n = 17$) and expired ($n = 2$) groups, mean serum ferritin, D-dimer, CRP, and interleukin levels were 308.59 ± 190.55 vs. 675.00 ± 592.55 µg/L, $p = 0.051$; 980.75 ± 620.09 vs. 1798.00 ± 285.67 µg/L, $p = 0.088$; 6.23 ± 3.48 vs. 12.55 ± 0.77 mg/L, $p = 0.023$; 7.14 ± 4.77 vs. 10.61 ± 7.62 nanogram/L, $p = 0.364$, respectively. Total 62 samples of placental tissue (vaginal 23, cesarean 39) could be tested for SARS-CoV-2; out of these, 5 were positive (vaginal 3, cesarean 2), carrying a SARS-CoV-2 placental positivity rate of 8.1% (5/62). No relation was found between neonatal and placental infections (Fisher exact test, $p = 0.058$).

Discussion

Perinatal acquisition of infection by the baby from its mother is conventionally termed as vertical transmission. However, some authors differ and consider only intrauterine transmission as vertical transmission. The presence of SARS-CoV-2 or its RNA in placental membrane in a few case reports raised the possibility of its intrauterine transmission. However, this phenomenon could not be confirmed [6, 7]. In the present study, the rate of perinatal transmission of SARS-CoV-2 was 9.8%, which is slightly higher than the previously reported—3%–6.9% [8]. In the present study, all neonates tested within 24 h of life were negative, and early skin-to-skin contact between mother and baby was practiced, so postnatal acquisition of infection could not be excluded.

Among neonates born to SARS-CoV-2–positive mothers, rates of prematurity and low birth weight in the present study were 12.8% and 18.9%, respectively, which fluctuated widely from 4.4% to 31.8% and from 4.4% to 33.3%, respectively in the past studies [9, 10]. Variability in the characteristics of the study population and diagnostic methods of SARS-CoV-2 may explain these wide fluctuations in results.

Biochemical markers of inflammation were raised in majority of SARS-CoV-2–positive neonates. There is a paucity of data on the levels of inflammatory markers in SARS-CoV-2–positive neonates. In the present study, the placental positivity rate for SARS-CoV-2 was 8.1%, but no relation was found between placental and neonatal infection. Previous studies have also documented the presence of SARS-CoV-2 in placental tissue. However, as the virus has been detected in urine and fecal material also, contamination at

Table 1 Comparison of clinicodemographic characteristics between SARS-CoV-2–positive and –negative neonates

Characteristics	SARS-CoV-2–positive neonates ($n = 19$)	SARS-CoV-2–negative neonates ($n = 177$)	p value
Gestational maturity, *n* (%)			
Term	13 (68.4)	158 (89.3)	0.01*
Preterm	6 (31.6)	19 (10.7)	
Birth weight, grams, mean (SD)	2470 (703)	2814 (452)	0.0034**
Low birth weight, *n* (%)			
Birth weight babies < 2500 g	8 (42.1)	29 (16.4)	0.006*
Birth weight ≥ 2500 g	11 (57.9)	148 (83.6)	
NICU admission, *n* (%)			
NICU admitted	5 (26.3)	3 (1.7)	0.0002***
Not admitted	14 (73.7)	174 (98.3)	
Final outcome, *n* (%)			
Expired	2 (10.5)	2 (1.1)	0.047***
Survived	17 (89.5)	175 (98.9)	

*Chi square test, **Student *t* test, ***Fisher exact test

No significant effect on mode of delivery (vaginal vs. cesarean), twinning (singleton vs. twin births), sex ratio (male vs. female), and need of resuscitation at birth

n Numbers, *SD* Standard deviation

the time of delivery could not be excluded [8]. Exclusion of SARS-CoV-2–positive pregnant women with gestational age less than 32 wk is the major limitation of the present study.

Conclusion

The perinatal transmission rate of SARS CoV-2 in Indian population was 9.8%. Rates of prematurity, NICU admission and death were higher and mean birth weight was lower in SARS CoV-2 positive as compared to negative neonatal group. No relation was found between placental and neonatal infection.

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Declarations

Conflict of Interest None.

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