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Case Report

Probable vertical transmission of severe acute respiratory syndrome coronavirus 2 infection from mother to neonate

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ABSTRACT

The pandemic spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has affected 188 countries and territories. Altered physiological status during pregnancy makes a mother vulnerable to severe SARS-CoV-2 infection. The virus may be transmitted from mother to baby during antenatal period or postnatal period. Although the primary mode of transmission of the virus is by respiratory droplets, there is emerging evidence of in utero transmission from mother to foetus. In this rare case report, we describe one such episode of probable vertical transmission. To the best of our knowledge, this is the second systematically investigated Indian case, indicating in utero transmission of SARS-CoV-2 from mother to foetus.

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Introduction

First described in December 2019, infection due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in more than 24 million cases and 0.8 million deaths globally.¹ It is a positive sense, single-stranded RNA virus that enters the human host by binding to angiotensin-converting enzyme 2 receptor (ACE-2).² The virus primarily infects the lower respiratory tract causing a spectrum of symptoms

ranging from mild fever to multiorgan dysfunction.³ The resultant disease is also called coronavirus disease 2019 or COVID-19.

Human to human transmission of SARS-CoV-2 occurs directly by respiratory droplets, whenever an infected individual coughs or sneezes. Indirectly, the disease can be transmitted by contaminated frequently touched surfaces and fomites.⁴ Although SARS-CoV-2 can infect any age group from neonates to elderly, COVID-19 in pregnancy is not much explored in Indian settings. The hormonal and physiological

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changes in pregnancy may alter the course of infection. The altered immune responses in pregnancy place the mother at risk of severe inflammation, especially during the first and third trimester.⁵ Hence, all pregnant mothers are mandatorily tested for SARS-CoV-2 infection during the third trimester as per Indian Council of Medical Research (ICMR), New Delhi, “COVID-19 testing strategy”.⁶ Transmission of SARS-CoV-2 from mother to child is also a new field of interest. It can occur during antenatal period through the placenta, during delivery or during postnatal period. Reports of COVID-19 in newborn babies of COVID-19–infected mothers raised concern over vertical transmission.⁷ Here, we describe a case report of SARS-CoV-2 infection in a newborn, possibly acquired by intrauterine route from the mother.

Case report

A 31-year-old pregnant female patient presented to obstetrics out-patient department (OPD) of a tertiary care hospital at 39 weeks period of gestation with abdominal discomfort. She was a registered case with prior antenatal check-up carried out at the same hospital. Antenatally, she was found to be hypothyroid and was initiated on tablet Eltroxin (levothyroxine) 50 µg/day. As per institutional protocol, her nasopharyngeal swab was tested for SARS-CoV-2 by real-time polymerase chain reaction (RT-PCR) at the ICMR-approved laboratory. We used National Institute of Virology (NIV)- Indian Council of Medical Research (ICMR) approved TaqMan™ RT-PCR–based diagnostic kit for qualitative detection of SARS-CoV-2. The assay includes three primers targeting envelope gene (E), Hongkong university open reading frame 1b (HKU ORF 1b) and RNA-dependent RNA polymerase (RdRp) of SARS-CoV-2. The kit was used on Quant Studio 5 (Applied Biosystem) RT-PCR instrument. Her nasopharyngeal swab was tested positive with cycle threshold (Ct value) of 30, 31 and 32 for E gene, HKU ORF 1b and RdRp, respectively.

Owing to her increasing discomfort and remote residence from the hospital, she was admitted. On admission, the patient was afebrile. She denied any history of cough and breathlessness or contact with known COVID-19 case in the family. Chest examination indicated bilateral bronchovesicular breath sounds with 98% oxygen saturation at room air. Her routine haematological and biochemical parameters were normal. She was managed conservatively in an isolation ward with routine care and foetal cardiotocographic monitoring. On the second day of admission, she developed labour

pains. She was managed with prostaglandin E2 cervical gel for ripening of the cervix and titrated dose of oxytocin intravenous infusion for augmentation of labour. Briefly, membranes were visualized directly using Sims’ speculum, while the patient was lying in the obstetric bed. Before artificial rupture of membranes, 2 ml of clear amniotic fluid was collected avoiding any contamination from vaginal secretions. The membranes were pierced with 16 G stainless steel needle with a cannula. The needle was gently removed, and 1 ml of clear amniotic fluid was aspirated with a syringe. On delivery baby weighed 2.7 kg and cried immediately after birth. The placenta weighed 0.56 kg and was grossly normal on naked eye examination.

The SARS-CoV-2 RT-PCR on the amniotic fluid sample and placental swab was positive with a Ct value (for target: HKU Orf 1b; RdRp) of 32; 33 and 34; 34, respectively. The nasopharyngeal swab of the neonate was also positive for SARS-CoV-2 RT-PCR with a Ct value of 32; 33 (for target: HKU Orf 1b; RdRp). The breast milk sample from the mother collected before initiation of feed was negative for SARS-CoV-2. The baby was initiated breastfeeding soon after the birth and managed in a COVID-19 isolation ward along with the mother. As the mother and baby were asymptomatic till the fifth day of birth, they were discharged with advice of home isolation and routine follow-up.

Discussion

The rapidly evolving COVID-19 pandemic can infect individuals of any age group and pregnant women are no exception. The causative pathogen, SARS-CoV-2, gains entry by binding to ACE-2 receptors. These receptors are predominantly expressed in the respiratory alveolar epithelium and vascular endothelium, thereby affecting lungs and other vascular organs.⁸ There is emerging evidence of presence of these ACE-2 receptors in maternal-foetal interface, raising possibility of in utero transmission of SARS-CoV-2 from pregnant mother to foetus. Based on single-cell RNA sequencing technology on placental and foetal tissues, Li et al⁹ have demonstrated high expression of ACE-2 receptors on stromal cells, cytotrophoblasts and syncytiotrophoblasts. Hence, vertical transmission needs to be explored.

Owing to altered physiological and hormonal status, pregnant women are more vulnerable to develop severe COVID-19 infection.⁵ As per ICMR, New Delhi, strategy for COVID-19 testing, national guidelines necessitate testing of all

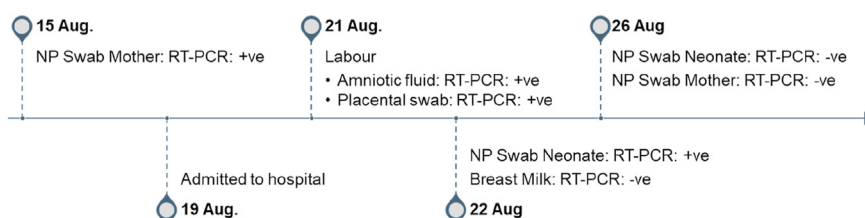


Fig. 1 – Timeline of events showing results of SARS-CoV-2 RT-PCR on various samples of the mother and child. NP, nasopharyngeal; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 1 – Salient findings of recent studies on mother-to-child transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

S.No	Reference	Place of study	Salient findings
1.	Wang et al. ¹³	China	Pharyngeal swab of a neonate was positive for SARS-CoV-2 infection by RT-PCR. The mother of this first reported case of COVID-19 in neonate used to live near Huanan Seafood Wholesale Market
2.	Alzamora et al. ¹⁴	Lima, Peru	A case of severe COVID-19 in a 41-year-old pregnant lady requiring invasive ventilation. Neonatal nasopharyngeal swab tested positive for SARS-CoV-2 by RT-PCR, 16 hours after delivery..
3.	Fenzia et al. ¹⁵	Italy	SARS-CoV-2 detected by real-time PCR in the placenta, umbilical cord blood, vaginal mucosa and breast milk of a term pregnant woman.
4.	Chen et al ¹⁶	Wuhan, China	Retrospective review of nine cases of COVID-19 pneumonia in pregnancy showed no evidence of SARS-CoV-2 infection in neonates delivered by caesarean section.
5.	Walker et al. ¹⁷	Nottingham, UK	Systematic review indicated that SARS-CoV-2 positivity rates in neonates were 2.7% and 5.3%, when delivered vaginally and by caesarean section, respectively.
6.	Kulkarni et al. ¹⁰	Pune, India	Symptomatic SARS-CoV-2 infection reported in a term neonate of a mother who was positive for anti-SARS-CoV-2 antibodies.
7.	Salvatore et al ¹⁸	New York, USA	None of the 120 neonates of SARS-CoV-2–infected mothers were positive indicating unlikely perinatal transmission

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease 2019; RT-PCR, real-time polymerase chain reaction.

pregnant women near term.⁶ Till date, our ICMR-approved COVID-19 diagnostic laboratory has tested 21,690 respiratory samples, of which 184 were from pregnant women. Only 12 (6.5%) pregnant women turned out to be positive for SARS-CoV-2 infection by RT-PCR.

In this reported COVID-19 positive pregnant woman, amniotic fluid sample was collected during labour. The SARS-CoV-2 PCR on amniotic fluid was positive, proving an important link between the mother and baby. After delivery, the placental swab collected in viral transport medium was also positive for SARS-CoV-2 by RT-PCR. Subsequently, the neonate also was detected to be positive. The timeline of events in our case is summarized in Fig. 1.

In a recent case report from Maharashtra, samples from the placenta, umbilical cord stump and neonate collected at the time of birth were positive for SARS-CoV-2 RT-PCR indicating perinatal transmission.¹⁰ In our case, we additionally tested amniotic fluid sample before rupture of membranes. The amniotic fluid sample was diligently collected to prevent contamination from genital tract secretions. The nasopharyngeal swab specimen obtained from the neonate soon after birth was also tested positive ruling out postnatal transmission. To the best of our knowledge, this is the second systematically investigated Indian case, indicating in utero transmission of SARS-CoV-2 from mother to foetus. The case study does have limitations. A positive IgM antibody test in neonatal blood subsequently would have supported our diagnosis. In addition, whole-genome sequence analysis of SARS-CoV-2 strain from the foetal and amniotic fluid would have supplemented the linkage.

Both the mother and baby remained asymptomatic during hospitalization. The neonate was afebrile, and breastfeeding was initiated soon after birth. The clinical data about COVID-19 symptomatology in neonates are scarce. Hong et al¹¹ reported only fever and mild respiratory symptoms in nine infants with COVID-19 in their study. None of these infants were put on ventilatory support. Similar to our case,

prior study has suggested that clinical characteristics of SARS-CoV-2 infection in late pregnancy is akin to that in non-pregnant individuals with no adverse pregnancy outcomes.¹² The data on risk of transmission of COVID-19 from an infected mother to her baby during antenatal period are emerging. Table 1 shows a summary of recent studies carried out in the field of mother-to-child transmission of SARS-CoV-2 infection.

To conclude, here we describe a rare case of probable vertical transmission of SARS-CoV-2 infection. SARS-CoV-2 research in obstetric cases is a relatively newer field. The proportion of pregnancies that could be affected and its significance to the neonate needs exploration. With an increase in the number of COVID-19 cases globally, pregnant mothers remain susceptible to such infection. Thus, there is a need for prospective studies to determine maternal response and foetal outcomes in SARS-CoV-2–infected mothers.

Disclosure of competing interest

The authors have none to declare.

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