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## Original Article

# Assessment of materno-foetal transmission of SARS-CoV-2: A prospective pilot study



D. Arora<sup>a</sup>, K.S. Rajmohan<sup>b</sup>, Sudhir Dubey<sup>c</sup>, Madhusudan Dey<sup>d,\*</sup>,  
Sanjay Singh<sup>e</sup>, V.G. Nair<sup>f</sup>, R.P. Tiwari<sup>f</sup>, Shyamji Tiwari<sup>g</sup>

<sup>a</sup> Consultant & Head (Obst & Gynae), Trained in Maternal-fetal Medicine, Base Hospital, Delhi Cantt, India

<sup>b</sup> Senior Advisor & Head (Pathology), Base Hospital, Delhi Cantt, India

<sup>c</sup> Classified Specialist (Pathology), Base Hospital, Delhi Cantt, India

<sup>d</sup> Senior Adviser (Obst & Gynae), Trained in Maternal-Fetal Medicine, Base Hospital, Delhi Cantt, India

<sup>e</sup> Senior Adviser (Obst & Gynae), Base Hospital, Delhi Cantt, India

<sup>f</sup> Classified Specialist (Obst & Gynae), Base Hospital, Delhi Cantt, India

<sup>g</sup> Graded Specialist (Obst & Gynae), Base Hospital, Delhi Cantt, India

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## ABSTRACT

**Background:** The issue of vertical transmission of SARS-CoV-2 infection to the foetus has not yet been resolved. Its main reason is lack of a bigger study to analyse this question. The evidence of the affection of the foetus during antenatal or intrapartum period is limited to some anecdotal reports. To look for the possibility of vertical transmission of Severe Acute Respiratory Syndrome – Corona Virus-2 (SARS-CoV-2) infection to the foetus, this prospective pilot study was conducted at a tertiary health care COVID-19 designated centre of Armed Forces.

**Methods:** This study was conducted during 01 June 2020 and 15 October 2020 and included 54 covid-positive pregnant mothers. During delivery, amniotic fluid and cord blood samples were collected in a sterile manner. Amniotic fluid samples were not collected during vaginal deliveries as chances of contamination was very high. These samples were tested for the presence of SARS-CoV-2 gene by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) test, and the results were analysed. Newborns were allowed to room in with mother, and they underwent throat and nasal swab RT-PCR testing of covid within 24–48 h of delivery.

**Results:** A total of 1520 pregnant mothers underwent RT-PCR test during the study period. Total positivity rate among our pregnant women was 2.8%. Out of 54 covid-positive women during the study period, amniotic fluid RT-PCR tests were carried out for 43 women, and cord blood was tested for 45 women.

**Conclusion:** RT-PCR test of amniotic fluid, cord blood and nasal and throat swab of all newborns delivered by SARS-CoV-2-positive pregnant women were negative. Based on our study, the possibility of intrauterine vertical transmission of SARS-CoV-2 infection appears to be unlikely.

\* Corresponding author.

E-mail address: [deym1@yahoo.com](mailto:deym1@yahoo.com) (M. Dey).

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## Introduction

The coronavirus disease 2019 (COVID-19) pandemic has rapidly spread across the world, making it a global healthcare emergency. The causative agent of Covid-19, Severe Acute Respiratory Syndrome – Corona Virus-2 (SARS-CoV-2) is an enveloped and non-segmented RNA virus, which is usually transmitted via respiratory droplets, close physical contacts and aerosols. Till date, no clear evidence has come to light regarding trans-placental or vertical transmission of SARS-CoV-2 to the foetus.<sup>1</sup> Although few publications do report about possible perinatal transmission, these are rare.<sup>2,3</sup> Vertical transmission is a common transmission route for many contagious viral diseases. Some coronaviruses, such as 229E, OC43, NL63 and HKU1, exhibit vertical transmission from mother to child.<sup>4</sup> However, it is still unclear whether SARS-CoV-2 has similar characteristics.

As per the available literature, there is no evidence of positive results for reverse transcriptase– polymerase chain reaction (RT-PCR) test on amniotic fluid samples of COVID-19-positive pregnant women.<sup>5</sup> However, these studies were limited due to small sample size and non-availability of umbilical cord blood sample. There is currently no direct evidence to support intrauterine vertical transmission of SARS-CoV-2. The most accurate evidence of vertical transmission would be to confirm the replication of SARS-CoV-2 in foetal lungs, which is technically not feasible.

A practical approach would be to test for the presence of the virus in the amniotic fluid, placenta or cord blood.<sup>6</sup> In this study, we have subjected amniotic fluid and umbilical cord blood samples to RT-PCR to bring out evidence regarding transplacental transmission of SARS-CoV-2.

## Materials and methods

This study was conducted for 3 months from 01 June 2020 to 15 October 2020 in a tertiary care obstetric centre, which was also a Covid-designated hospital. The study was approved by the Institute Ethics Committee. Participants of the study included all pregnant women who tested positive for COVID-19 admitted to the delivery suite. All pregnant women admitted in the delivery suite were tested for SARS-CoV-2 gene by RT-PCR test in the nasopharyngeal and oropharyngeal swabs. Those who were found positive and willing to participate were included in the study. Written informed consent was taken from all participants. All symptomatic patients were provided treatment for COVID-19 as per institutional policy and national guidelines on management of COVID-19. Maternal and foetal monitoring was done as per the protocol. Induction of labour and caesarean delivery was reserved for obstetric indications unless there was serious

jeopardy to the mother or baby where an expedited delivery was going to improve the outcome.

During the delivery, amniotic fluid and cord blood samples were collected in a sterile manner. However, amniotic fluid samples were not collected during vaginal deliveries as chances of contamination was very high. These samples were tested for the presence of SARS-CoV-2 gene by RT-PCR test, and the results were interpreted. All the newborns delivered by covid-positive mothers were allowed rooming in with mothers, and breastfeeding was allowed. Newborns underwent throat and nasal swab RT-PCR testing of covid within 24–48 h of delivery (Fig. 1). TRUPCR 3B BLACKBIO BIOTECH Kit (ICMR validated) was used for processing the samples. Exmate 32 plus Genomic Viral DNA/RNA Extraction Kits were used on Automated Nucleic Acid Extraction System that is based on magnetic bead technology. The E-gene and RdRp genes were used as targets for SARS-CoV-2 detection. The same kit was used for processing the clinical samples included in this study. Further, this kit was internally validated by our lab, prior to the commencement of study on cord blood samples. Cycle threshold values were kept at 35 as per the recommendation of the kit manufacturer.

## Statistical analysis

Results were analysed by using SPSS-23. Continuous variables were directly expressed as a range. Categorical variables were expressed as number (%).

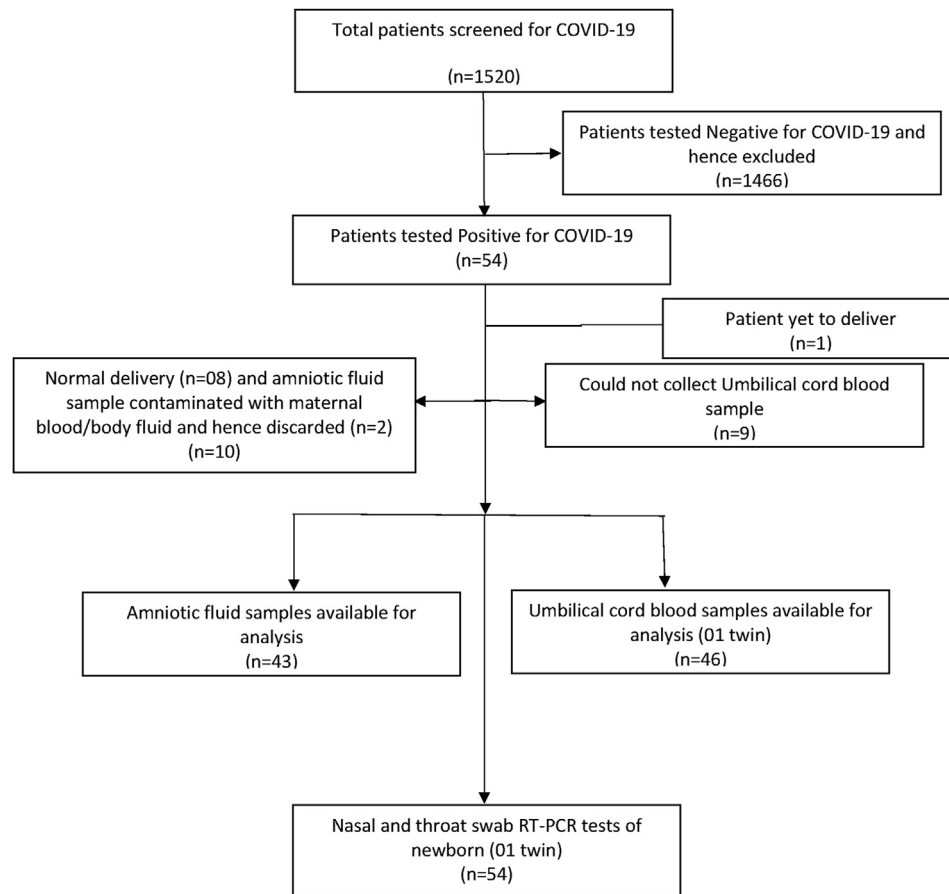
## Result

Since the start of RT-PCR tests for SARS-CoV-2, that is, from 1 April 2020, hospital has conducted 2192 tests and total positive cases were 62, and the total positivity rate among pregnant women was 2.8%. Total RT-PCR tests carried out in pregnant women at our hospital during the study period was 1520. Among 54 positive women during the study period, amniotic fluid RT-PCR tests were carried out for 43 women and cord blood tested for 45 women.

Among the antenatal co-morbid factors (Table 1), hypothyroidism, gestational diabetes mellitus along with maternal anemia (Hb < 10 gm%) constituted maximum number of cases.

Median gestational age of delivery was 264 days (Fig. 2), and about 29% of SARS-CoV-2-positive pregnant women delivered preterm (delivery before 37 weeks' period of gestation). A total of 82% of pregnant women underwent caesarean delivery in this study group (Table 2).

Forty-three amniotic fluid and forty-six cord blood RT-PCR tests for SARS-CoV-2 were negative. All 54 newborns (01 twin) were found to be SARS-CoV-2 negative in nasal and throat swab RT-PCR test.



**Fig. 1 – Flow diagram depicting patient enrolment.**

**Table 1 – Antenatal co-morbidities.**

Antenatal co-morbidity		
Co-morbidity	No. of Covid-positive	Percentage
GDM	5	11.1
Hypertension	4	8.9
Hypothyroidism	6	13.3
Post LSCS	6	13.3
Post IVF ET	4	8.9
IHCP	2	4.4
Rh-negative	1	2.2
Twin pregnancy	1	2.2
Anaemia	5	11.1

GDM, gestational diabetes mellitus; IVF ET, in vitro fertilization embryo transfer.  
IHCP, intra hepatic cholestasis of pregnancy.

## Discussion

All the pregnant women in our study group were asymptomatic for SARS-CoV-2. They went RT-PCR testing before admission and after delivery. Among them, three patients were admitted till they were tested negative for SARS-CoV-2. Two of them tested negative on the 11th day of admission,

and one of them was found negative on the 15th day as the policy for discharge was after negative RT-PCR test for SARS-CoV-2 during the first half of June 2020. The policy of discharge of dependent families that was: only after repeat Covid test became negative, was changed after mid-June 2020. The repeat test was no more mandatory, and a policy of discharge and isolation at home with due precautions after settling down of clinical and obstetric condition of the pregnant mother was adopted by hospital authorities.

Compared with general population, hospital admission of pregnant women was more during the pandemic of H1N1 2009 influenza virus infection.<sup>7</sup> Immunosuppressive state and physiological changes during pregnancy like elevation of diaphragm due to gravid uterus, and increased consumption of oxygen can render the pregnant lady intolerant to hypoxia. SARS infection during pregnancy was severe requiring mechanical ventilation in 33% patients, and mortality rate was as high as 25% with various adverse pregnancy outcomes like spontaneous abortion, intrauterine growth restriction and premature deliveries,<sup>8,9</sup> and SARS-CoV-2 has up to 85% sequence similarity with SARS.<sup>8</sup> In our study we did not find such association with SARS-CoV-2-positive patients, and none of our patients required any specific treatment for the disease itself, although zinc and vitamin C were given to all patients. Twenty-nine percent of SARS-CoV-2-positive

Period of gestation at delivery for COVID 19 positive patients delivered from 1 June 2020 to 15 October 2020

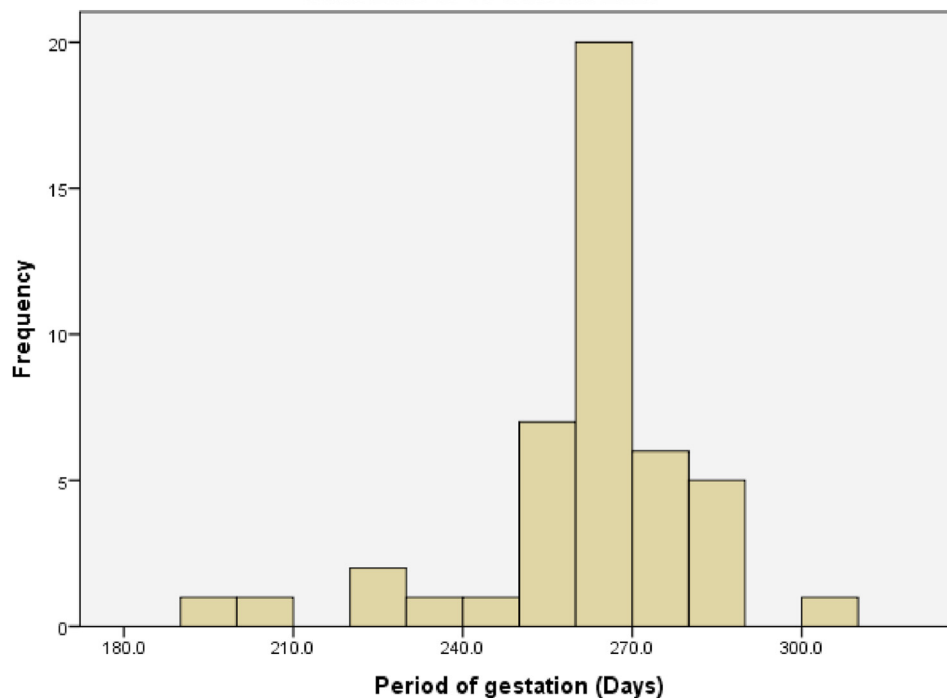


Fig. 2 – Gestational age at delivery.

Table 2 – Labour and delivery outcomes.

Mode of delivery		
Mode of delivery	No. of Covid-positive	Percentage
Emergency LSCS	11	24.4
Elective LSCS	26	57.8
Normal vaginal delivery	8	17.8
Period of gestation at delivery		
Period of gestation	No. of Covid-positive	Percentage
<37 weeks (preterm)	13	28.9
>37 weeks (term)	32	71.1
Labour and intra-/postpartum complications		
Complications	No. of Covid-positive	Percentage
Abruption	1	2.2
Foetal distress	7	15.6
PPH	1	2.2
PROM/PPROM	10	22.2
NPOL/arrest of labour	2	4.4
MSL	2	4.4
NICU admission	4	8.9
Neonatal death	—	—
PPH, postpartum haemorrhage; PPROM, preterm premature rupture of membrane.		
NPOL, non-progress of labour; MSL, meconium-stained liquor;		
NICU, neonatal intensive care unit.		

patients had preterm delivery, and 8.9% (04 newborns) neonates had NICU admissions. Among the four newborns, one set of twins delivered at 33 weeks of gestation, and the other two newborns delivered at 34 weeks of gestation. We had

favourable neonatal outcome, and it was comparable with the study carried out by Prabhu et al.<sup>10</sup> In this study, 82% SARS-CoV-2-positive pregnant women underwent caesarean section, and these high rates were due to anticipated high-risk cases who during labour would have required emergency caesarean in covid OT that takes atleast 45 min of time to get prepared for surgery and were electively operated in covid OT for the safety of the mother and the baby. This as well as the thought process that prolonged labour exposes the health care worker to covid infection would have also significantly played a role in the high caesarean rate. A recent systematic review from Bologna Italy by Della et al<sup>11</sup> found that of the 51 women diagnosed with COVID-19, 46 (90.2%) women underwent cesarean delivery, and the authors from Wuhan China<sup>12</sup> also reported that 93% of women underwent cesarean section during initial reports of pregnancy outcome in SARS-CoV-2-positive pregnant women. None of the caesarean patients in our study had surgical site infection, possibly implying that the virus does not alter the surgical site healing process.

Obstetrician and mother are always concerned about the possibility of vertical transmission from mother to the foetus. Vertical transmission in cases of viral infection is a known fact, and various adverse perinatal outcomes like abortion, intrauterine growth restriction and premature deliveries were observed in viral infections.<sup>13,14</sup> Two cases of neonatal SARS-CoV-19 infection were reported in the early parts of Covid epidemic. One was a 17-day-old neonate who had close contact with two persons positive for SARS-CoV-2, and another neonate was found to be SARS-CoV-2-positive after 36 h of delivery. In the latter case, there was however no clear

evidence of vertical transmission.<sup>15,16</sup> In a recent study published by Zeng et al,<sup>17</sup> three cases of SARS-CoV-2-positive neonates were confirmed. According to the researchers, three infants had early-onset covid infection. The sources of SARS-CoV-2 infection in these neonates were from maternal origin as firm infection control and prevention procedures were followed in all cases of deliveries.

In a systemic review by Yang et al,<sup>18</sup> this comprised of 22 studies and included 83 newborns delivered by SARS-CoV-2-positive women, the review concluded that they did not find any direct evidence to support vertical transmission of SARS-CoV-2. In one of the published case reports, Vivanti et al<sup>2</sup> described placental infection demonstrated by histological examination and immunohistochemistry. In our study also amniotic fluid and cord blood RT-PCR was negative for all the newborns delivered. RT-PCR testing of nasal and throat swab of all newborns taken within 24–48 h post delivery was also found negative for SARS-CoV-2. As per Dumitriu et al,<sup>19</sup> no clinical evidence of vertical transmission was identified in 101 newborns of mothers positive for or with suspected SARS-CoV-2 infection, despite most newborns rooming-in and direct breastfeeding practices, and this study supports our finding as all our newborns were roomed in with mothers after birth and direct breastfeeding was allowed. The latest research carried out by Zheng et al suggested that the interface between maternal and foetal cells has low levels of expression of angiotensin-converting enzyme 2 (ACE2), and ACE2 is important for cell entry of SARS-CoV-2.<sup>20</sup> It was also reported that histopathological examination of placenta in cases of SARS-CoV-2-positive patients did not reveal any morphological changes.<sup>21</sup> These evidences did not support possible intrauterine transmission of SARS-CoV-2, and it supports our findings in the present study.

The fact that it was a prospective study and it included 54 newborns with 46 cord blood and 43 amniotic fluid RT-PCR tests to find out the possibility of vertical transmission. Is probably the strong point of our study. Possibly, it may be one of the largest prospective studies as on date conducted to know the mother-to-child transmission of SARS-CoV-2. This finding will help effective planning for the maternal and foetal care protocol for the covid-positive cases.

## Conclusion

RT-PCR test of amniotic fluid, cord blood and nasal and throat swab of all newborns delivered by SARS-CoV-2-positive pregnant women were negative. It was a pilot study, and based on this finding, it is highly unlikely that there is a possibility of intrauterine vertical transmission of SARS-CoV-2. Larger studies need to be undertaken to confirm the findings of our study.

## Disclosure of competing interest

The authors have none to declare

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