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LETTER TO THE EDITOR

Intrauterine Transmission of SARS-CoV-2 (COVID-19 Virus)

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Introduction

The corona virus disease (COVID-19) caused by SARS-CoV-2—severe acute respiratory syndrome corona virus 2—first reported in Wuhan, China, in December 2019 has spread rapidly worldwide and has now become a global pandemic. The mode of transmission of the virus has been a major cause of concern. It is all the more imperative to know the mode of transmission due to unavailability of any definite treatment; hence, decreasing the transmission is the only possible way to curtail the increasing yet ever growing number of cases. Various literatures suggest that the transmission of the virus from human to human is said to occur by multiple means, namely by droplets, aerosols and fomites. However, given the presence of the virus in various body fluids and tissue specimens, the possibility of other modes of transmission should also be explored and studied.

One of the major concerns of the virus pertaining to Obstetrics is the possibility of vertical transmission of infection from mother to their foetuses, and the various effects it could possibly have on the foetus miscarriage, stillbirth, preterm delivery, IUGR, foetal distress, congenital infection and defects, etc. However, there is little data on the vertical transmission, and the adverse pregnancy outcomes it could possibly have in pregnant women with COVID-19. Few case reports have reported the possibility of perinatal transmission while few other studies have refuted the same. The reported perinatal transmission is however unclear to have occurred via the transplacental or the transcervical route or through environmental exposure [1]. Here in, we investigate the possibility of intrauterine vertical transmission of COVID-19.

A 30-year-old G2P1L1 was admitted to a tertiary care COVID-19 dedicated facility of Eastern India at 20 weeks 6 days gestation with complaints of bleeding per vagina and loss of foetal movement since one day following history of fall. Her antenatal history was otherwise uneventful with targeted anomaly scan performed at 18 weeks 2 days revealing normal study. Four days prior to her admission; she had history of mild fever, cough and sore throat. She gave history of taking two doses of 500 mg acetaminophen (analgesic), following which fever subsided and remained normal for the days that followed. Two days following her first symptoms, on her visit to a peripheral health care centre she was investigated with routine blood counts, urine culture and COVID-19 test by RT-PCR. Routine blood counts were normal, and urine culture was sterile; however, she tested positive for COVID-19 by RT-PCR. Patient was a known case of beta-thalassemia trait and had no other comorbidities.

On admission, patient was afebrile with mild cough, maintaining normal oxygen saturation on room air. Clinical examination revealed uterus of 20 weeks size, non tender with normal tone.

On per speculum examination, os was closed and mild bleeding could be seen coming through the os.

Ultrasonography on the day of admission revealed intrauterine foetus of 20 weeks 5 days with no foetal heart activity. No placental separation or retro placental clot was seen. The intrauterine death can be speculated to have occurred four days after the initial onset of symptoms, taking into account the time of diagnosis of intrauterine death to be at first sonography, that is, six hours after the admission. Her laboratory reports were as follows:

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Hb-10.7 g/dl,Platelet-164 thousand/MicroLtr, Plasma d dimer-2.90,APTT-25.4 sec, Fibrinogen-244 mg/dl, PT-20.1 s (INR-1.54), Serum ferritin-136.9 mcg/L, S.Creatinine-0.50 mg/dl, Alt-31.1U/L,AST-57.8 U/L, Alp-122.0 U/L.

The patient was given mifepristone and misoprostol for termination of pregnancy. A fresh stillborn female baby weighing 340 g was delivered. Immediately following the delivery, nasopharyngeal and oropharyngeal swab of the foetus for RT-PCR was taken by the neonatologist maintaining all aseptic precautions to prevent contamination of the swab which was tested following ICMR (Indian council of medical research) guidelines. The RT-PCR of the stillborn foetus has thus been performed six days after the initial onset of symptoms and four days after the patient tested positive for the virus. The RT-PCR of the nasopharyngeal and oropharyngeal swab of the foetus was positive for COVID-19. Since we could not prove or attribute any specific cause for the intrauterine death, placenta was sent for histopathological examination. Histopathological examination of placenta revealed hypertrophy of membrane arterioles with mixed inflammatory cell infiltrates, atherosis of maternal arterioles, deciduitis with mixed inflammatory infiltrate predominantly neutrophils, dilated foetal vessels with mural fibrin, villous oedema in many villi, with few syncytial knots with increased perivillous fibrin. All these histomorphological findings correlated with the COVID findings published and quoted till date.

Timeline Events

Initial onset of symptoms	4 days prior to her admission date, at approx gestational age—20 weeks 2 days
Date of RT-PCR	2 days after initial onset of symptoms, approx gestational age—20 weeks 4 days
Episode of bleeding per vagina following history of fall	6 h prior to time and day of admission
Date of diagnosis of IUD	Half hour after the time of admission at approx gestational 20 weeks 4 days—that is, approximately 4 days after the initial onset of symptoms
Date of delivery and date of RT-PCR of IUD foetus	The patient was induced after confirmation of IUD on the day of admission. Delivery of the IUD foetus occurred on the 2nd day of admission. RT-PCR of the dead foetus was performed immediately following delivery

Discussion

Till date very limited evidence exists on vertical transmission of COVID-19 from infected pregnant mother to their foetuses in the literature. In one such study conducted by Alexandre J Vivati et al., a proven case of transplacental transmission of SARS-CoV-2 from a pregnant woman affected by COVID-19 during late pregnancy to her offspring was reported [2]. One of the proposed mechanisms put forward by Zhao et al. by which the virus could potentially cause intrauterine infection by transplacental vertical transmission is the expression of angiotensin-converting enzyme ACE 2, as the putative surface receptor of sensitive cells for SARS-Co-2 in the human placenta [3]. Maternal hypoxemia in women with COVID-19 causes damage to the placental barrier which could potentially lead to vertical transmission of SARS-CoV-2 causing intrauterine infection. Some studies however refute the possibility of vertical transmission. A study conducted by Lei et al., demonstrated no evidence of vertical transmission in four pregnant women infected with COVID-19 in third trimester of pregnancy. Vaginal secretions of these women tested negative for the viral RNA. In a study, conducted by Chen et al., placental tissues from three pregnant women confirmed to have COVID-19, were examined histopathologically which revealed no evidence of the viral RNA. The pharyngeal swabs from the neonates tested negative for the virus [4].Till date, there is no confirmative way to ascertain the possibility of intrauterine transmission of COVID-19. Literature has suggested confirmation of replication of the virus in foetal lung tissues as probably one of the best ways of confirming intrauterine transmission; however, it is not possible in most circumstances. Alternatively, a more practical way to assess intrauterine transmission would be to test for the presence of the virus in placental, amniotic fluid, cord blood, neonatal naso and oropharyngeal swabs [5]. However, there is a challenge of the samples getting contaminated; hence, it is important that all these samples are collected immediately after delivery using aseptic technique in order to guarantee that the samples are not contaminated and that they represent intrauterine conditions. In conclusion, there is currently no concrete evidence of intrauterine vertical transmission of SARS-CoV-2, but further study is needed to confirm the same.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

Human rights The study was conducted on human participants. All procedures performed in the study involving human participants were in accordance with the ethical standards and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained for publishing.

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