



Review article

Vertical transmission of acute respiratory syndrome viruses from mother to the foetus

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ABSTRACT

Since early in month of Dec-2019, the infection of Coronavirus Disease 19 has been prevalent in Wuhan City of China and ultimately virus spread to other countries. Literature survey was carried out by using different scientific sources such as PubMed, Scopus, Google scholar etc. There is a scarcity of literature of COVID-19 happening at some stage in pregnant women and possibilities of transmission vertically are may be due to COVID-19. So, there is an alarm situation as foetus may be at risk of congenital COVID-19. Up until August 28, 2020, we investigated at the risk of COVID-19 vertical transmission to the foetus of infected women using a database of published articles and government sites. Middle East Respiratory Syndrome MERS and Severe acute Respiratory syndrome SARS were related to poor obstetrical conclusion, so there was no recognized case of 'intrauterine transmission' of either Middle East Respiratory Syndrome-coronavirus (MERS-CoV) or severe acute Respiratory syndrome-coronavirus (SARS-CoV).

Keywords: Coronavirus, COVID-19, Vertical transmission, SARS, MERS, Infected mother and foetus.

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INTRODUCTION

Initially the new corona virus was spotted in Wuhan City, the capital of Hubei Province, China with a population of 11 million [1]. The COVID-19 virus spread drastically to other countries including Thailand, Japan, Korea, United States, and Iran during initial weeks of January 2020 [2]. On January 7, 2020, scientists in China identified the etiological agent of the outbreak as a previously unknown coronavirus, and it was given the designation 2019-nCoV. (2019 novel coronavirus) [3-4]. The WHO on February 11, 2020, received an official name of novel coronavirus disease and give the name Coronavirus Disease 19 (COVID-19), [5] and the name of the virus that causes COVID-19 has proposed SARS-CoV-2" by International Committee on Taxonomy of Viruses [6]. The mainly characters of COVID-19 has cough, headache, sputum production, fever and fatigue or myalgia [4, 7-8].

On March 26th, 2020, the Journal of the American Medical Association released the primary case study of probable vertical transmission of Covid-19 illness [9]. The report suggested that neonate was born with COVID-19 and had prominent antibody levels and unusual cytokine level after two hours of birth. Neonate was infected in uterus because of the elevated IgM antibody level. The placenta

does not transfer IgM antibodies to the foetus; however, the infection may be transmitted trans placentally. On the other hand, published documents reported the nonappearance of vertical transmission before the publication of this case report [10-13] and also the scientific communities across the globe have been reacted accordingly the vertically transmitted infection possibility would have enormous scientific and clinical implications. According to Schwartz D. A. 2020; the first complete scrutiny of the existing evidences concerning the focus was executed [14].

Understanding the morbidity and mortality caused by viral pneumonia in pregnancies is critical [15]. Motherly pneumonias are related with a number of undesirable obstetrical outcomes, including preterm labour (PTL) and premature rupture of membranes (PROM), intrauterine growth restriction (IUGR), intrauterine fetal demise (IUFD), and neonatal death" [3]. There is minor data on unpleasant pregnancy conclusion with COVID-19 because appearance of a coronavirus not previously reported in individuals.

On the other hand, the possible risk on infant is not understood, and it is not evident that these outcomes were interconnected with maternal infection. According to evidence from

former corona viruses, pregnant women may be at a higher risk of severe disease, morbidity, or fatality. Also, there are no precise guidelines for pregnant women in terms of COVID-19 evaluation or care, particularly in terms of its impact on gestation. During Breastfeeding, a COVID-19 guideline has been developed by the centres for Disease Control and Prevention [16]. Currently, it was assumed that virus can be transferred through respiratory droplets, however it is unknown whether COVID-19 can be transmitted through breast secretions or not [1].

VERTICAL TRANSMISSION OF COVID-19

It is uncertain whether COVID-19 increases the risk of miscarriage, early delivery, stillbirth, foetal discomfort, or foetal tachycardia. According to the Ministry of Health and Medical Education” (MOHME) in Iran, three infants were born to infected women. Among the three cases, two mothers had acute respiratory distress syndrome” (ARDS) but their neonates tested negative [17]. Chen S et al., 2020 has been reported that three women with confirmed viral infection from the clinical character and placental pathology. On the basis of RT-PCR information there was no COVID-19 nucleic acid found in the placentas or neonatal throat swabs. Furthermore, they discovered that the medical characteristics of non-pregnant patients were identical to those of infected pregnant women in late pregnancy, and that none of the three instances had a serious poor pregnancy result [18]. Chen H et al., 2020 compared test findings, clinical records, and CT scans of nine pregnant women with laboratory-confirmed COVID-19 who were admitted to Zhongnan Hospital of Wuhan University in Wuhan, China”, between January 20 and January 31, 2020. These results were shown that the “clinical fetal and paediatric pathology” 247 characteristics of COVID-19 in infected non-pregnant women were similar to pregnant women. They reported nine neonates, however none of them showed severity and no evidence of virus was found in any of them samples. Investigators came to the conclusion that there is no evidence of vertical transmission [10].

STRONG PROOF OF COVID-19

Vertical transmission of virus through the transplacental” way confirmed recently published in “Nature Communications” involving one mother–newborn pair gave burly support. “Daniele De Luca of Paris Saclay University, France” reported that the virus primarily seen in mother's blood and afterwards and infecting placenta and further inflammations to foetus and infant suffered clinical manifestations of COVID-19. Similarly, 23-year-old woman (35 weeks of pregnancy) admitted with signs of coronavirus infection. The RTPCR was carried out for presence of two viral genes (E and S). The researchers also collected clear amniotic fluid to screen for vertical transmission. The positives results were observed for amniotic fluid. The infant was delivered via c-section to avoid

normal birth infection [19].

CONFIRMING INFECTION OF COVID-19

Here, researchers took blood and bronchoalveolar lavage samples of newborn and tested for virus but unfortunately both samples were found positive. Also, Swabs of nasopharyngeal and rectal samples were taken at three different times: one hour, three hours and 18 days following birth and found positive for the same. Both the mother and the infant have variable amounts of virus in different tissues. “The viral load in placental tissue was much higher than in maternal or newborn blood and amniotic fluid.” While the virus was found in the least quantity in the newborn's blood, but the viral load in the nasopharyngeal sample collected three days after birth was elevated. The findings demonstrate that transplacental transmission is indeed conceivable in the latter weeks of pregnancy, while we cannot exclude out transmission and foetal repercussions earlier in the pregnancy [19].

The India’s first case of “vertical transmission” has reported in the Sassoon General Hospital of Pune Maharashtra. Dr. Aarti Kinikar reported that, mother infects the infant via nursing and other exposures. In this case, woman had signs for a week before delivery but she tested negative. However, after the birth, swabs from nose, umbilical cord, and placenta were found positive and two to three days later the infant experienced severe symptoms such as fever and cytokine storm, indicating serious inflammation and that foetus was shifted to intensive care, where she was settled down and recovered. It was proven throughout the examination, that it was a case of vertical transmission. She waited three weeks for retesting of mother's and child's blood samples for antibody response. Doctor stated that both had acquired antibodies, but that the mothers were higher and the babies were lower level of antibodies. The baby contracted a severe coronavirus illness, which necessitated a great deal of attention and effort to successfully treat. This is the first incidence of “vertical transmission” in India, according to Dr Murlidhar Tambe, Dean-Sassoon General Hospital [20].

As per Chen et al, nine women who were pregnant in their third trimester underwent caesarean delivery. All had an account of epidemiological observation to virus, and their ages ranged from 26 to 40 years. At the time of admission, these patients' gestational weeks ranged from 36 to 39 weeks plus 4 days. Diabetes, chronic hypertension, and cardiovascular problems have not been documented in any of these patients. Nevertheless, one patient had symptoms such as “gestational hypertension” since the 27th week also another patient had pre-eclampsia at 31 weeks of pregnancy. Both of these women were found to be in good health during their pregnancies. Furthermore, an influenza virus infection was discovered in one of the patients while admitting. Here, 7 of the 9 patients had fever (not high fever, body temperature >39°C) without

chills, and their temperatures ranged from 36.5 to 38.8°C. Before the caesarean section, both patients had postpartum fever (range 378–393°C) with a normal body temperature. These patients were also reported to have upper respiratory tract infections. Aside from them, four patients complained of a cough, two of a sore throat, three of muscular ache, and two of malaise. Also, one patient has observed gastrointestinal symptoms. Another patient has preeclampsia and breathlessness. However, as of February 4, 2020, none of the 9 deaths occurred from COVID-19 caused by severe pneumonia, and they do not need mechanical ventilation. Pregnancy complications encountered included foetal distress (in 2 of 9 patients) and premature membrane rupture, and these problems are analysed after the commencement of COVID-19 infection. All were undergone for therapy of antibiotics with oxygen support, and six patients were given antiviral medication. As according laboratory results, 5 of the 9 women who are pregnant with COVID-19 pneumonia had lymphopenia. Six had elevated C-reactive protein concentrations (>10 mg/L). Three had elevated levels of ALT and AST, with one having ALT at 2093 U/L and AST at 1263 U/L. In addition, 7 patients had a normal WBC count. All 9 patients underwent a chest CT scan, and 8 of them had typical chest CT findings-“multiple patchy ground-glass shadows” in the lungs. The all nine births were safe but four patients experienced preterm labour, but all were more than 36 weeks pregnant. After 36 gestational weeks plus 2 days, two of the four premature neonates had birth weights less than 2500 g. According to the data, neonate seven had a birth weight of 2460 g and neonate 4 had a birth weight of 1880 g due to a pre-eclampsia problem during pregnancy. All 9 live births had an APGAR score of 8–9 at 1 minute and APGAR score of 9–10 at 5 minutes. Neonate 1 has a mild increase in myocardial enzymes on the day of birth with no clinical symptoms. Here, SARS-CoV-2 observed in amniotic fluid, cord blood, neonatal throat swab, and breast milk samples from 6 patients^[10].

On February 1st, 2020, a pregnant woman in her 40th week of pregnancy experienced minor vaginal discharge and discomfort. After two hours, she was admitted to the “Wuhan Women and Children's Medical Care Center” with suspected viral pneumonia and a fever (37.8°C). She was referred to “Wuhan Tongji Hospital's fever clinic” the next morning. Thoracic CT scan revealed ground-glass opacities in the left upper and lower lobes, which could indicate viral pneumonia. In addition, blood tests revealed neutrophilia, lymphopenia, and an elevated high-sensitivity C-reactive protein level. COVID-19 infectious diseases in newborns are still extremely rare due to a lack of clinical data. It is still unknown whether SARS-CoV-2 can transmit vertically through the placenta and cause short- and long-term harm to offspring. As a result, all SARSCoV-2

infected and suspected pregnant women and their newborns' specimens, including pharyngeal swabs, peripheral blood, placenta tissue after delivery, amniotic fluid, cord blood, newborn pharyngeal swabs, and breast milk, must be kept for in-depth study and continuous follow-up assessment^[21].

Furthermore, no cases of SARS have been observed of vertical transmission in pregnant women. From March to May 2003, data from the “Princess Margaret Hospital, Hong Kong” SAR demonstrate that of 10 healthy women aged 27-44 years who developed SARS during pregnancy, six admitted to ICU, 4 were ventilated, and three died. There was no virus observed in either the cord blood or the liquor, and there was only one death among the five first-trimester pregnancies and four unprompted abortions. Although all five infants endured and no spread found. As per a study, SARS in pregnancy necessitates increasing the sample size of case series^[22].

Anker has reported world - wide SARS cases, with an estimated 100 pregnant women among the more than 8000 cases. It is unlikely that any single country will have a large enough sample of pregnant women among its probable SARS instances to definitively respond to questions about the course and outcome of SARS in pregnant and lactating women, such as whether pregnancy results are impacted by gestational age at infection. WHO will facilitate a collaborative international study on SARS in pregnancy, the impact of pregnancy on the clinical course, outcome and impact of SARS on pregnancy outcomes for both to understand the role of vertical transmission, if any^{[22]?}

According to a recent review, there is no confirmed episode of transmission during prior SARS and MERS. During the SARS pandemic in 2002-2003, 12 women were reported to have been infected during pregnancy. SARS-CoV infection led to severe clinical outcomes in this cohort, with 4 of 7 women having miscarriages in the first trimester and 2 of 5 women having a neonate with “intrauterine growth restriction” (IUGR) in second and third trimesters. Preterm birth occurred in four of five pregnancies, with one spontaneous and three induced deliveries made due to maternal circumstances. Consequently, despite the fact that both SARS and MERS have been linked to poor obstetrical outcomes, no cases of SARS-CoV or MERS-CoV transmission identified^[22].

The dissimilarity in clinical course between pregnant patients infected with SARS-CoV-2 and those suffering with SARS-CoV are an intriguing problem to investigate. Certain studies have shown that the virus caused various unfavourable outcomes in pregnant women^[24]. The most recent data on foetal problems associated with SARS-CoV-2 maternal infection are available; however the rates are low, with an estimated rate of miscarriage of 2% and restricted intrauterine growth of 10%^[25]. The viruses were

not discovered in any of the patients' amniotic fluid samples, infant blood cultures, or endotracheal aspirates. At birth, the neonates were not shown to have dimorphisms. In addition, all of the neonates

exhibited a clinical course alike other neonates under the equivalent medical circumstance [24, 26, 27, 28].

Table 1: Vertical transmission of SARS/COVID-19 in various groups of pregnant women

Patients Infected with SARS-CoV-2/ COVID19	Samples	Result
02 Pregnant women in third trimester.	Neonates nasopharyngeal swab sample at birth, in placenta, umbilical cord, amniotic fluid, breast milk, and maternal vaginal swab [29].	Virus was not detected.
09 Pregnant women in third trimester.	Neonates nasopharyngeal swab sample at birth, in umbilical cord, amniotic fluid, breast milk [30].	Virus was not detected.
03 Pregnant women in third trimester.	Neonates nasopharyngeal swab sample at birth, in placenta [31]	Virus was not detected.
03 Pregnant women in third trimester.	Neonates nasopharyngeal swab sample at birth, in placenta, umbilical cord, amniotic fluid, breast milk, and maternal vaginal swab [32].	Virus was not detected.
Neonate infected with SARS-CoV-2	Neonates pharynx swab sample at 36 h of age, in placenta, umbilical cord, and breast milk [33].	Virus was not detected.
06 Pregnant women in third trimester.	Neonate's nasopharyngeal swab/serum sample at birth. But two newborns had elevated level of IgM for SARS-CoV-2. In addition, all 6 newborn elevated level of IL-6 [34].	Virus was not detected.
Neonate infected with SARS-CoV-2	Neonates nasopharyngeal swab sample at birth. But elevated level of IgM, IL-6, and IL-10 in serum sample at 2 h of age [35]	Virus was not detected.
01 Pregnant woman in third trimester.	Neonates nasopharyngeal swab sample at birth, umbilical cord, amniotic fluid, and breast milk [36]	Virus was not detected.
10 Neonate born to mother infected with SARS-CoV-2 in third trimester.	Neonates' nasopharyngeal swabs 01 to 09 days after birth [37]	Virus was not detected.
04 Neonate born to mother infected with COVID19.	03 Neonates nasopharyngeal swabs sample at birth but one neonate not performed the test [38]	Negative result.
18 Neonate born to mother infected with SARS-CoV-2.	Neonates' nasopharyngeal swabs samples at birth or at one to two days of life [39]	Negative result.
33 Neonate born to mother infected with SARS-CoV-2.	Neonates' nasopharyngeal swabs samples at birth or at two to four days of life [40]	Positive result in 03 neonates for SARS-CoV-2

Table 2: Vertical transmission in different age of Pregnant Woman

Patient Age (Years)	Complications	Signs and symptoms	Epidemiological history	Gestational age on admission	Delivery
33	Influenza	Post-partum fever and Cough	Yes (exposure to relevant environment)	37 weeks	C-section due to Severely elevated ALT or AST; COVID-19 pneumonia [41]
27	None	Fever on admission, Post-partum fever, Myalgia, and Cough	Yes (contact with infected person)	38 weeks	C-section due to Mature; COVID-19 pneumonia [42]
40	Gestational Hypertension	Post-partum fever, and Cough	Yes (contact with infected person)	36 weeks	C-section due to History of C-section (× 2); COVID-19 pneumonia [43]
26	Pre-eclampsia	Fever on admission, Post-partum fever Dyspnoea, Diarrhoea	Yes (exposure to relevant environment)	36 weeks	C-section due to Pre-eclampsia; COVID-19 pneumonia [44]
26	Fetal distress	Fever on admission, Post-partum fever, Myalgia, Malaise	Yes (exposure to relevant environment)	38 weeks	C-section due to Fetal distress; COVID-19 pneumonia [45]
26	None	Fever on admission, Myalgia, Malaise, Cough, and Sore throat	Yes (contact with infected person)	36 weeks	C-section due to History of stillbirth (× 2); COVID-19 pneumonia [46]
29	Premature rupture of membrane (PROM)	Fever on admission and Sore throat	Yes (contact with infected person)	36 weeks	C-section due to PROM; COVID-19 pneumonia [47]
28	Fetal distress	Fever on admission	Yes (contact with infected person)	38 weeks	C-section due to Fetal distress; COVID-19 pneumonia [48]
34	Premature rupture of membrane (PROM)	Fever on admission and Post-partum fever	Yes (exposure to relevant environment)	39 weeks	C-section due to PROM; COVID-19 pneumonia [49]
34	Vaginal bleeding and lower abdominal pain	Fever on admission, Post-partum fever	Yes (exposure to relevant environment)	40 weeks	C-section due to throat swab positive, COVID-19 pneumonia [49]

CONCLUSION

According to the reports, Covid-19 is likely to spread vertically. Mothers may also be at a higher risk of developing more serious respiratory issues. Unlike pregnant women infected with other corona viruses (SARS-CoV or MERS-CoV), those infected with SARS-CoV-2 are not prone to unfavourable pregnancy outcomes. Additional research is needed to determine whether the virus is spread vertically or not.

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