



Pregnancy Consequences and Vertical Transmission Potential of SARS-CoV-2 Infection: Seeking Answers From a Preliminary Observation

Dear Editor,

The pandemic of COVID-19 has transpired as the stiffest public health problem in 2020. For pregnant females infected with SARS-CoV-2, breach of placental barrier, *i.e.*, vertical transmission and successive fetal complications are significant concerns (1). Pregnant females are susceptible to the invasion of respiratory pathogens causing pneumonia. During this period, physiological changes in the immune and cardiopulmonary system occur (2). Maternal pneumonia is associated with adverse obstetrical outcomes such as premature rupture of membranes, preterm labor, stillbirth, and neonatal deaths (3). Since the emergence of SARS-CoV-2, which was not previously seen in humans, little knowledge about COVID-19 and its adverse maternal and fetal outcomes exists. Earlier in 2012, researchers in Taiwan, in their population-based study, showed that mothers suffering from known pneumonia (Non-COVID-19) were more likely to have low birth weight, preterm, small for gestational age, and low Apgar score babies than healthy mothers. These mothers also have more chances of caesarean section and pre-eclampsia/eclampsia (4). The objective of the present study was to assess the effect of COVID-19 on maternal and perinatal outcomes and the potential for vertical transmission of SARS-CoV-2. The present study was a cross-sectional observational study conducted between April 2020 and August 2020 period. All 28 women admitted for delivery in dedicated COVID-19 rural tertiary care hospital during the study period were included. All 29 neonates of the index pregnancy of above females (Including one stillbirth and a twin delivery) were included in the present study. Nasopharyngeal swabs were obtained for SARS-CoV-2 RT-PCR test from all pregnant females. Samples of all neonate's nasopharyngeal swabs were collected immediately after birth for the evidence of vertical transmission of COVID-19. The mean $\pm$ SD of maternal age was 27.43 $\pm$ 4.94 years (Minimum age of 20 years and maximum age of 38 years). As there was one twin pregnancy, therefore, the number of newborns that were included in the present study was 29. The mean birth weight of newborns in the present study was 2.57 $\pm$ 0.67 kgs (Minimum weight

was 700 grams, and the maximum reported weight was 4.0 kilograms). The mean period of gestation was 37.90 $\pm$ 3.75 weeks.

Maternal characteristics and outcomes: All the mothers in the study had COVID-19 (By RT-PCR test), but none of them had any COVID-19 symptoms (A pneumonia-like fever, cough, fatigue, sore throat, shortness of breath, and diarrhea). Twenty females (71.4%) out of 28 came to the hospital with no complications. One female (3.6%) came with twin pregnancy, two females (7.1%) came with the transverse lie, and two (7.1%) with leaking per vaginam. Also, one female (3.6%) presented with placenta previa, one (3.6%) with "pregnancy with an IUD" and one (3.6%) with antepartum hemorrhage. Also, there was no complication reported in any women during the delivery and after delivery.

Neonatal characteristics and outcomes: All the neonates, including stillborn and preterm, were negative cases of SARS-CoV-2 during the observation period and the rest (Excluding one stillbirth and two newborns which could not be revived probably due to pre-maturity) were normal and healthy without any COVID-19 symptoms. Out of 29 newborns, 26 (89.7%) were healthy, one (3.4%) was a stillbirth, and two newborns (6.9%) could not be revived (The premature baby of 700 grams at 27 weeks and 1000 grams baby at 28 weeks). Nasopharyngeal swabs for SARS-CoV-2 RT-PCR tests were repeated after the first sampling before the discharge of all cases. Twenty cases (69.0%) were delivered by LSCS for common obstetric factors such as the previous history of cesarean, pre-eclampsia, or fetal distress. At the same time, 9 cases (31.0%) had a vaginal delivery. The gestational age of six newborns was between "more than 28 weeks and less than 37 weeks". About 10.3% of pregnancies (3 newborns) were post-dated, *i.e.*, more than 42 completed weeks of gestational age. The birth weight in 72.4% of babies was $\geq$ 2.5 kg, six babies (20.7%) had a birth weight between "1.5 to 2.4 kg", while 6.9% of babies had a birth weight of less than 1.5 kgs. Tang et al. observed that mothers having pneumonia (Non-COVID-19) during

pregnancy had more chances of preterm births and caesarean sections than the healthy mothers (5). In a retrospective study, Chen et al. investigated the probability of intrauterine vertical transmission of SARS-CoV-2 virus in pregnant women with laboratory-confirmed RT-PCR test for COVID-19 in late pregnancy; amniotic fluid, cord blood, and neonatal pharyngeal swab samples from six neonates were tested for SARS-CoV-2 using quantitative RT-PCR. All were tested negative for the virus, implying that the vertical transmission of the virus did not occur during the third trimester of pregnancy (6). There was no evidence of vertical transmission in nine pregnant women with COVID-19 in the third trimester of pregnancy, and vaginal secretion samples were also tested negative for SARS-CoV-2 RNA in a study done by Lei et al. (7). Also, Chen et al. analyzed placental tissue from three pregnant women with confirmed COVID-19 infection and neonatal pharyngeal swab samples to assess the possible risk of vertical transmission, and all were tested negative for SARS-CoV-2 RNA (8). Liu et al. conducted a study of three pregnant females who acquired SARS-CoV-2 infection in their late pregnancy. They found that two of the cases had an uneventful caesarean delivery and healthy newborns. None of the three infants became infected by vertical transmission. Li et al. published a case report of a pregnant female who was COVID-19 positive in her 35th week of pregnancy and delivered an infant by caesarean section. This infant was found negative for SARS-CoV-2 infection. Yang et al. had done a study on seven females who got infected in their late pregnancy. All the females were delivered by caesarean section. They took samples of six newborns out of seven, and all the samples were found negative for SARS-CoV-2 infection (9-11). These results are in accordance with the present research where most of the deliveries (69%) were by LSCS, and no newborn was found COVID-19 positive. Chen et al. collected data on five COVID-19 positive pregnant females between the ages of 25 and 31 years. The gestational age at delivery among them was between 38 weeks to 40 weeks. Three of them were gravida one, and two were gravida three. Four had zero parity, while one female had parity of one. Caesarean section was done among two females out of five (40%). There were no complications after delivery. All the neonates were negative for SARS-CoV-2 RT-PCR, and none of them had any symptoms of COVID-19

(12). The age group, gravida, and parity of the above study were similar to the current study and only the rate of caesarean section was slightly higher (69%) in the present study. Similarly, in the present study, there were no complications after delivery, and all the neonates (100.0%) were negative for SARS-CoV-2 RT-PCR, and none of them had any symptoms of COVID-19. Similar to the results of the present study, Lu et al. showed that there was no maternal to child vertical transmission in a 22-year-old pregnant female asymptotically infected with SARS-CoV-2 in her late pregnancy (13). In the present study, neonatal pharyngeal swabs were taken for the SARS-CoV-2 RT-PCR test, and all tested negative. Hence, our study results are consistent with the above-reported studies. In contrast, some studies showed RT-PCR positive results in neonates born to COVID-19 positive mothers. Hu et al. conducted a study on seven RT-PCR confirmed COVID-19 positive pregnant females who were between the ages of 30 to 34 years. Six out of seven females experienced caesarean section while one had vaginal delivery. One female had a liver complication, but the other six had no complications during their pregnancy. They found that one infant out of seven was positive for SARS-CoV-2 infection (14). Alzamora et al. published a study on a 41-year gravida 3 para 2 pregnant woman female (with a history of previous caesarean delivery and diabetes mellitus) who had severe symptoms of COVID-19 and required mechanical ventilation on day 5 of disease onset. Caesarean delivery was conducted, and isolation of newborn was done immediately after birth, with no delay in cord clamping or any skin-to-skin contact. The nasopharyngeal swab specimen for SARS-CoV-2 was found positive 16 hr after delivery, but immunoglobulin M (IgM) and IgG for SARS-CoV-2 were negative. The mother's IgM and IgG were found positive on day 4 postpartum (15). Nie et al. conducted research on 33 pregnant females who were positive for COVID-19. The perinatal transmission rate for COVID-19 in their study was 3.6% (16). Recently, two studies exhibited the possible risk of vertical transmission of SARS-CoV-2. Dong et al. and Zeng et al. with a combined total of seven COVID-19 infected pregnancies noted a virus-specific IgM antibody in neonatal blood tested immediately after birth, with a negative SARS-CoV-2 RT-PCR test result by nasopharyngeal swab. Cord blood and placental tissue sample testing was not done; thus, no direct evidence of

infection was found. Furthermore, these antibodies (IgM) analyses are likely to provide false-positive results (17, 18).

The possibility of postpartum neonatal infection cannot be completely excluded because of many factors such as the delay in testing and high viral load of severely symptomatic mothers. The present results showed no evidence of vertical transmission of SARS-CoV-2 in pregnant females suggesting the function of placenta as a barrier to this viral disease. There was no complication encountered during the delivery of any females in this study.

Conflict of Interest

Authors declare no conflict of interest.

References

1. Sutton D, Bertozzi-Villa C, Lasky J, Fuchs K, Friedman A. Outcomes and epidemiology of COVID-19 infection in the obstetric population. *Semin Perinatol.* 2020;44(7):151283.
2. Dashraath P, Wong JLJ, Lim MXK, Lim LM, Li S, Biswas A, et al. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. *Am J Obstet Gynecol.* 2020;222(6):521-31.
3. Schwartz DA, Graham AL. Potential maternal and infant outcomes from coronavirus 2019-nCoV (SARS-CoV-2) infecting pregnant women: lessons from SARS, MERS, and other human coronavirus infections. *Viruses.* 2020;12(2):194.
4. Chen YH, Keller J, Wang IT, Lin CC, Lin HC. Pneumonia and pregnancy outcomes: a nationwide population-based study. *Am J Obstet Gynecol.* 2012;207(4):288.e1-7.
5. Tang P, Wang J, Song Y. Characteristics and pregnancy outcomes of patients with severe pneumonia complicating pregnancy: a retrospective study of 12 cases and a literature review. *BMC Pregnancy Childbirth.* 2018;18(1):434.
6. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet.* 2020;395(10226):809-15.
7. Lei D, Wang C, Li C, Fang C, Yang W, Chen B, et al. Clinical characteristics of COVID-19 in pregnancy: analysis of nine cases. *Chinese J Perinatal Med.* 2020;23(3).
8. Chen S, Huang B, Luo DJ, Li X, Yang F, Zhao Y, et al. [Pregnancy with new coronavirus infection: clinical characteristics and placental pathological analysis of three cases]. *Zhonghua Bing Li Xue Za Zhi.* 2020;49(5):418-23. Chinese.
9. Liu W, Wang Q, Zhang Q, Chen L, Chen J, Zhang B, et al. Coronavirus disease 2019 (COVID-19) during pregnancy: a case series. *Preprints* 2020, 2020020373.
10. Li Y, Zhao R, Zheng S, Chen X, Wang J, Sheng X, et al. Lack of vertical transmission of severe acute respiratory syndrome Coronavirus 2, China. *Emerg Infect Dis.* 2020;26(6):1335-6.
11. Yang P, Wang X, Liu P, Wei C, He B, Zheng J, et al. Clinical characteristics and risk assessment of new-borns born to mothers with COVID-19. *J Clin Virol.* 2020;127:104356.
12. Chen S, Liao E, Cao D, Gao Y, Sun G, Shao Y. Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia. *J Med Virol.* 2020; 92(9):1556-61.
13. Lu D, Sang L, Du S, Li T, Chang Y, Yang XA. Asymptomatic COVID-19 infection in late pregnancy indicated no vertical transmission. *J Med Virol.* 2020;92(9):1660-4.
14. Hu X, Gao J, Luo X, Feng L, Liu W, Chen J, et al. Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) vertical transmission in neonates born to mothers with Coronavirus disease 2019 (COVID-19) Pneumonia. *Obstet Gynecol.* 2020; 136(1):65-7.
15. Alzamora MC, Paredes T, Caceres D, Webb CM, Valdez LM, Rosa ML. Severe COVID-19 during pregnancy and possible vertical transmission. *Am J Perinatol.* 2020;37(8):861-5.
16. Nie R, Wang SS, Yang Q, Fan CF, Liu YL, He WC, et al. Clinical features and the maternal and neonatal outcomes of pregnant women with coronavirus disease 2019. 2020. *MedRxiv.* 2020 Jan 1.
17. Zeng H, Xu C, Fan J, Tang Y, Deng Q, Zhang W, et al. Antibodies in infants born to mothers with COVID-19 Pneumonia. *JAMA.* 2020;323(18): 1848-9.
18. Dong L, Tian J, He S, Zhu C, Wang J, Liu C, et al. Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn. *JAMA.* 323(18):1846-8.

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