



REVIEW



Vertical Transmission of Coronavirus Disease 19 (COVID-19) from Infected Pregnant Mothers to Neonates: A Review

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ABSTRACT

Background: Since early December 2019, the Coronavirus Disease 19 (COVID-19) infection has been prevalent in China and eventually spread to other countries. There are a few published cases of COVID-19 occurring during pregnancy and due the possibility of mother-fetal vertical transmission, there is a concern that the fetuses may be at risk of congenital COVID-19. **Methods:** We reviewed the risk of vertical transmission of COVID-19 to the fetus of infected mothers by using data of published articles or official websites up to March 4, 2020. **Results:** A total of 31 infected pregnant mothers with COVID-19 were reported. No COVID-19 infection was detected in their neonates or placentas. Two mothers died from COVID-19-related respiratory complications after delivery. **Conclusions:** Currently, based on limited data, there is no evidence for intrauterine transmission of COVID-19 from infected pregnant women to their fetuses. Mothers may be at increased risk for more severe respiratory complications.

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Introduction

The novel coronavirus was first detected in Wuhan City, the capital of Hubei Province, with a population of 11 million [1]. During the first weeks of January 2019, the COVID-19 virus spread rapidly to other countries including Thailand, Japan, Korea, United States, and Iran [2]. On 7 January 2020 scientists in China identified the etiological agent of the epidemic as a previously unknown coronavirus, and it was given the designation 2019-nCoV (for 2019 novel coronavirus) [3,4]. On February 11, 2020, the novel coronavirus disease received an official name by the World Health Organization (WHO), Coronavirus Disease 19 (COVID-19), [5] and the International Committee on

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Taxonomy of Viruses has proposed SARS-CoV-2 as the name of the virus that causes COVID-19 [6]. The most common manifestations of COVID-19 consist of fever, cough, and fatigue or myalgia, sputum production, and headache [4,7,8].

Viral pneumonia is an important cause of morbidity and mortality among pregnant women [9]. Maternal pneumonias are associated with several adverse obstetrical outcomes, including premature rupture of membranes (PROM) and preterm labor (PTL), intrauterine fetal demise (IUFD), intrauterine growth restriction (IUGR), and neonatal death [3]. Since the emergence of a coronavirus not previously seen in humans, there is little data on adverse pregnancy outcomes in pregnant women with COVID-19. Coronaviruses are single-stranded RNA, non-segmented, enveloped viruses, which cause illness ranging in severity from the common cold to severe and fatal illness. Limited adverse infant outcomes (e.g., miscarriage and stillbirth) have been reported among infants. However, it is not evident that these outcomes were related to maternal infection, and at this time the risk of adverse infant outcomes is not known. Data from previous coronaviruses (SARS-CoV and MERS-CoV) suggests that pregnant women may be at higher risk of severe illness, morbidity, or mortality compared with the general population. At this time, very little is known about COVID-19, particularly related to its effect on pregnant women and infants, and there currently are no recommendations specific to pregnant women regarding the evaluation or management of COVID-19. The Centers for Disease Control and Prevention (CDC) has developed Interim Guidance on Breastfeeding for a Mother Confirmed or Under Investigation for COVID-19 [10]. Currently, it is not known whether COVID-19 virus can be transmitted through breast milk, but it is well known that an infected mother can transmit the virus through respiratory droplets during breastfeeding [1].

COVID-19

As COVID-19 virus is still spreading, more infections in pregnant women are likely to be seen. Whether COVID-19 increases the risk of miscarriage, stillbirth, preterm delivery, fetal tachycardia and fetal distress is unknown. According to the official website of Ministry of Health and Medical Education (MOHME) in Mazandaran and Zanzan provinces, Iran, three infants were born from infected pregnant mothers. Among these three cases of COVID-19 infection there were two mothers who developed acute respiratory distress syndrome (ARDS) after delivery and died. According to the websites, their neonates were negative when tested for COVID-19 [11]. It seems that COVID-19 infection in pregnant patients may increase the risk of maternal mortality. Chen et al., reported the clinical characteristics and placental pathology from three women with confirmed COVID-19 infection. No COVID-19 nucleic acid was detected in the placentas or neonatal throat swabs by RT-PCR. Moreover, they found that the clinical characteristics of infected pregnant women in late pregnancy were similar to those of non-pregnant patients, and no severe adverse pregnancy outcome was found in the three cases [12]. In other study, Chen et al., evaluated clinical records, laboratory results, and chest computed tomography (CT) scans among nine pregnant women with laboratory-confirmed COVID-19 who were referred to Zhongnan Hospital of Wuhan University, Wuhan, China, between January 20 and January 31, 2020. Their results revealed that the clinical

characteristics of COVID-19 in pregnant women were similar to infected non-pregnant women. They reported nine livebirths and none of the patients developed severe COVID-19 or died, and all samples tested negative for the virus in neonates. Their findings supported that there is currently no evidence for vertical transmission in infected mothers in late pregnancy [13]. In a retrospective study, Zhang et al., evaluated the effect of COVID-19 on pregnancy outcomes and neonatal prognosis between 16 infected women with COVID-19 and 45 women without COVID-19 women undergoing cesarean section (CS) in Hubei Province. There were no significant differences in fetal distress, meconium-stained amniotic fluid, preterm delivery, and neonatal asphyxia between the two groups. They did not find 2019-nCoV infection in neonates delivered from pregnant mothers with COVID-19. In the treatment of uterine contraction fatigue, carbetocin or carboprost tromethamine was used more in CS for infected pregnant mothers compared to healthy mothers. They observed that timely termination of pregnancy after 32–34 weeks of pregnancy by CS was not associated with an increased risk of maternal complications in pregnant women with indications for obstetric surgery or critical illness of COVID-19, but it was beneficial for the treatment and rehabilitation of maternal pneumonia [14].

MERS-CoV or SARS-CoV

Studies have not yet reported ongoing transmission of MERS-CoV or SARS-CoV within communities outside of health care settings. In 2004, Lam et al., in a case-control study including 10 pregnant mothers infected by SARS-CoV and 40 non-pregnant women with SARS evaluated the clinical course and outcomes of pregnancy in women with severe acute respiratory syndrome. Their results revealed that pregnancy appeared to have no effect on clinical symptoms or time to presentation after symptom onset. However, complications and adverse outcomes including longer hospital stay, renal failure, sepsis, and disseminated intravascular coagulopathy (DIC) in pregnant women were statistically significantly increased. They reported the need for mechanical ventilation and rate of mortality among them were more frequent than non-pregnant women [15]. Other studies in the USA, Canada and Hong Kong reported that these pregnant women required mechanical ventilation, hemodialysis due to acute renal failure, developed seizures and positive cerebrospinal fluid for SARS-CoV more frequently [16,17]. Those studies did not report any stillbirths among the infected mothers. According to those studies all mothers recovered and their neonate's tests for SARS-CoV RNA were negative. In another study, Maxwell et al., reported that of seven pregnant mothers infected with SARS-CoV at a designated SARS unit, two mothers died and four mothers required intensive care unit (ICU) hospitalization and mechanical ventilation. Two infected mothers recovered and maintained their pregnancy but had infants with intra-uterine growth restriction (IUGR). Among the live newborn infants, none had clinical or laboratory evidence for SARS-CoV infection [18]. Ng et al., in a study evaluated the placental pathology in seven pregnant women infected with SARS-CoV. In two women who were convalescing from SARS-CoV infection during the 1st trimester of pregnancy, the placentas were normal. In three mothers, the placentas demonstrated increased

subchorionic and intervillous fibrin, which could be associated with abnormal maternal blood flow to the placenta [19].

Conclusions

Limited evidence exists on vertical transmission, prevalence and clinical features of COVID-19 during pregnancy, birth, and the postnatal period. Currently there was no evidence for intrauterine vertical transmission of COVID-19 from infected pregnant mothers to their fetuses. However, infected mothers may be at increased risk for more severe respiratory complications. It is well known that an infected mother can transmit the COVID-19 virus through respiratory droplets during breastfeeding. Thus, the mothers with known or suspected COVID-19 should adhere to standard and contact precautions during breastfeeding.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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