

# A systemic review of vertical transmission possibility in pregnant women with coronavirus disease 2019-positive status

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## ABSTRACT

An unknown pneumonia outbreak has been reported by hospitals in Wuhan, China, in late December 2019. A public health emergency of international concern announced by the World Health Organization (WHO) on the January 31, 2020. The virus named by the WHO as coronavirus disease 2019 (COVID-19). The cases reached (266,073 cases) and deaths (11,184 deaths) globally by the end of March 21, 2020, and considered as a pandemic. By a systemic review, articles and case reports revealed 74 pregnant women for the possibility of vertical transmission of the virus from COVID-19-infected mother to infant. Review also showed that there is no difference between pregnant and nonpregnant regarding clinical manifestations. Concerning the vertical transmission, none of the positive mothers had a positive infant with COVID-19 except 1 case report that showed the infant had positive COVID-19 by the throat swab, yet negative cord blood, placenta, and mother's breast milk.

**Keywords:** 2019-nCov, coronavirus disease 2019, severe acute respiratory syndrome coronavirus 2, vertical transmission

## Introduction

In December 2019, unknown pneumonia outbreak has been reported by hospitals in Wuhan, Hubei province, China, which came into the attention of the world.<sup>[1,2]</sup> The first 42 patients who were confirmed were from China except one patient from Thailand who was linked to the seafood market in Wuhan, China, which seals fish and different live animal species including poultry, bats, snakes, and mammals.<sup>[2]</sup> A public health emergency of international concern was announced by the World Health Organization (WHO) on January 31, 2020.<sup>[3]</sup> Coronavirus disease 2019 (COVID-19) is named by the WHO on the February 11, 2020.<sup>[4]</sup> On March 7, 2020, the WHO had reported that 100,000 cases of COVID-19 confirmed globally.<sup>[5]</sup> On the latest report of WHO had revealed that the number

of COVID-19 cases is 266,073 cases globally, and the number of the deaths reached 11,184 deaths globally and increasing. Furthermore, the highest number of COVID-19 cases outside China have been reported from Italy (47,021 cases) with total deaths (4032 deaths) and Iran with (19,644 cases) with total deaths (1433 deaths). Nonetheless, WHO risk assessment considered COVID-19 as “very high” risk globally.<sup>[6]</sup> On March 11, 2020, the WHO announced COVID-19 designated as a pandemic.<sup>[7]</sup>

Coronavirus (CoV) is a single-stranded, highly diverse, enveloped, RNA virus. It hosts different animals such as bats, camels, pets, and birds. It may cause respiratory, gastrointestinal, neurological diseases which may lead to a variety of severity diseases. There were two outbreaks of severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV).<sup>[8-10]</sup> The goal of this review is to summarize the published researches regarding pregnancy and vertical transmission of COVID-19 from the

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first of January 2020 to March 20 2020, in PubMed database using keywords “COVID-19 in pregnancy, “SARS-CoV-2 in pregnancy,” “2019-nCoV in pregnancy,” “COVID-19 in vertical transmission” to answer the question. Is COVID-19 can transmit from positive COVID-19 mother to her fetus vertically? and to help to provide direction for medical staff in the clinical management and for family physicians to educate their pregnant patients of this outbreak. The summary of included clinical studies are shown in Table 1.

## Clinical Signs and Symptoms

The signs and symptoms of COVID-19 based on the recently published studies have shown that fever is a most common symptom (98.6% of 138 patients),<sup>[11]</sup> (98% of 41 patients),<sup>[12]</sup> (97% of 29 patients),<sup>[13]</sup> (96% of 51 patients),<sup>[14]</sup> and (83% of 99 patients).<sup>[15]</sup> Follow that, cough productive or dry with percent of 82%,<sup>[15]</sup> 76%,<sup>[12]</sup> 72%,<sup>[13]</sup> 59.4%,<sup>[11]</sup> and 47%<sup>[14]</sup> and myalgia (44%),<sup>[12]</sup> (41%),<sup>[13]</sup> (34.8%),<sup>[11]</sup> and (31%).<sup>[15]</sup> On X-ray and computed tomography (CT) finding which showed ground-glass appearance (100%),<sup>[11]</sup> (98%),<sup>[12]</sup> (77%),<sup>[14]</sup> and (14%).<sup>[15]</sup> On the other hand, a study conducted by Hu *et al.*<sup>[16]</sup> to asymptomatic patients ( $n = 24$ ) with nucleic acid positive revealed that 7\24 (29.2%) patients were asymptomatic during hospitalization with normal typical CT image, whereas the rest of the patients experienced low-grade fever ranged (36°–38°). The common feature between all asymptomatic patients was younger than the rest (mean age = 14.0 years). Based on their observation, they have notice that asymptomatic carriers have transmitted the virus to his cohabiting family members. Regarding pregnancy, pregnant and nonpregnant patients who were positive for COVID-19 have been reported that there was no difference regarding clinical manifestations.<sup>[12]</sup>

## Vertical Transmission Regarding Middle East Respiratory Syndrome Coronavirus and Severe Acute Respiratory Syndrome Coronavirus

A large family of viruses known as CoV that cause diseases ranged from the simple common cold to severe diseases such as MERS-CoV, SARS-CoV, and a new strain of the same family which known as coronavirus disease discovered in 2019 (COVID-19).<sup>[17]</sup> regarding SARS-CoV, the possibility of vertical transmission is unlikely based on the WHO and some studies that showed pregnancy were SARS-CoV positive and delivered infants who are SARS-CoV negative (throat swab, cord blood, and placenta samples all were negative).<sup>[18-21]</sup> With respect to MERS-CoV, the vertical transmission is unlikely also, on these case reports for MERS-CoV-positive mothers showed after delivery that all their infants are negative for MERS-CoV.<sup>[22,23]</sup>

## IS Coronavirus Disease-19 Transmitting from Positive Pregnant to her Infant?

An early release research conducted by Li *et al.*<sup>[24]</sup> for one 30 years

old COVID-19 positive pregnant women in her third trimester showed that she presented on her 1<sup>st</sup> day of hospitalization with dry cough and temperature of 37.2° and scattered multiple patchy infiltrates in both lungs on CT scan image. Furthermore, her laboratory findings with a minor abnormality. Her cough resolves on the 2<sup>nd</sup> day. By a recommendation of an obstetrician to do an emergency cesarean section, she underwent a lower uterus cesarean section in a negative pressure operation room. On the delivery day, the mother was positive for COVID-19 and after the delivery, which was without complications, an oropharyngeal swab specimen obtained instantly from the baby after he was taken from the uterus which showed negative of COVID-19. Furthermore, the baby had been tested for the next 2 days for different seven times of oropharyngeal swab, blood, feces, and urine samples which all remain negative for COVID-19.

Zhu *et al.*<sup>[25]</sup> conducted a study including ten pregnant women cases from January 20 to February 5, 2020, in five different hospitals. Two of them had twins. Eight of them had a positive throat swab for COVID-19, and the rest had the typical clinical signs and symptoms. Viral interstitial pneumonia was revealed by a CT scan of her chest. Their age ranged from 25–35 years old. Only two of the patients’ symptoms started on the day of the delivery and the rest ranged from 1 to 6 days after the delivery. Eight of them had a fever as the first symptom and one only had a cough. All of the pregnant women showed ground-glass opacities on CT scan images. The prenatal complications were intrauterine fetal distress in seven of the patients, premature rupture of membrane seen in three of the patients (5–7 h before the onset of true labor). A cesarean section had done to eight of them and the rest with normal vaginal delivery including both of the twins pregnant. Six of the neonates born preterm. The most common clinical symptom observed in the neonates was shortness of breath ( $n = 6$ ). Throat swab was taken for nucleic acid testing from nine of the neonates, the samples were preformed ranging from 1 to 9 days after the delivery which all were negative for COVID-19. They have concluded their study with no evidence of COVID-19 transmitted vertically, and it may cause neonatal side effects as fetal distress, premature labor, and respiratory distress.

A case report was done by Wang *et al.*<sup>[26]</sup> on February 1, 2020, for a 40-week gestation pregnant who lived near to Huanan Seafood Wholesale Market, Wuhan, China. Presented as pre vaginal bleeding and lower abdominal pain, who also developed fever (37.8°) 2 h later. CT scan was done and revealed ground-glass opacities in the left upper and lower lobes and abnormalities in laboratory findings. Therefore, they admitted the patient for suspicion of viral pneumonia. An emergency cesarean section was done, and the mother was wearing an N95 mask throughout the surgery and there was no contact between the mother and the baby. Throat swab for COVID-19 done after the cesarean section for the mother and reported positive. Thirty 6 h later after birth, neonatal pharyngeal swab obtained and reported positive for COVID-19. To exclude the vertical transmission of COVID-19, they have obtained cord blood, placenta specimens,

**Table 1: Pregnant patients and neonates who is positive for coronavirus disease 2019**

	Li <i>et al.</i> <sup>[24]</sup>	Zhu <i>et al.</i> <sup>[25]</sup>	Wang <i>et al.</i> <sup>[26]</sup>	Chen <i>et al.</i> <sup>[27]</sup>	Wang <i>et al.</i> <sup>[28]</sup>	Liu <i>et al.</i> <sup>[29]</sup>	Chen <i>et al.</i> <sup>[30]</sup>	Chen <i>et al.</i> <sup>[31]</sup>	Zhang <i>et al.</i> <sup>[32]</sup>
Maternal RT-PCR positive for COVID-19	1\1	8\10	1\1	17\17	1\1	15\15	9\9	4\4	16\16
Neonates RT-PCR positive for COVID-19	Negative	Negative	Positive RT-PCR Negative cord blood, placenta, and breast milk	Negative	Negative	Negative	6 of 9 who was tested, and they were negative	3\4 tested negative. 1 refused to be teste by the parents	10 out of 16 who were tested and all were negative
Maternal trimester	3 <sup>rd</sup> trimester	All in the 3 <sup>rd</sup> trimester, except case 1 in 2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester	3 <sup>rd</sup> trimester	3 <sup>rd</sup> trimester	All in their 3 <sup>rd</sup> trimester except 3 on their 2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester	3 <sup>rd</sup> trimester	All were in their 3 <sup>rd</sup> trimester
CT findings	Ground-glass opacities	Viral interstitial pneumonia	Ground-glass opacities in the left upper and lower lobes	Ground-glass opacities	Right-sided ground-glass opacities and left-sided subpleural patchy consolidations	Ground-glass opacities and consolidations	8 out of 9 had multiple patchy ground-glass opacities	Multiple patchy ground-glass opacities	Not stated

RT-PCR: Real-time polymerase chain reaction, CT: Computed tomography, COVID-19: Coronavirus disease 2019

and mother’s breast milk for nucleic acid testing and all revealed negative results. No special treatment was given to the fetus. On the 14<sup>th</sup> day from delivery, both nucleic acids of the pharyngeal swab and anal swab were negative and discharged. They have concluded their case report with no evidence of intrauterine transmission, even though they could not rule it out because of some limitations they have had.

Chen *et al.*<sup>[27]</sup> conducted a case series for 17 pregnant patients published on the March 1, 2020, they all have been positive for COVID-19 and ground-glass opacities on CT scan images. All of the 17 cases underwent cesarean delivery, three of them were emergency cesarean delivery under general anesthesia due to fetal distress, and the rest were elective cesarean delivery under epidural anesthesia. In regard to the neonates, no intrapartum death, serious neonatal asphyxia, or neonatal death was noted. Three born prematurely and all admitted to the neonatal intensive care unit and tested negative for COVID-19. Eventually, all 17 neonates were healthy and discharged from the hospital.

Another case report conducted in China,<sup>[28]</sup> for 28 years old pregnant, who was on her 30-week gestation had a history of visiting Wuhan 3 weeks before the time of presentation. She presented on the February 2, 2020, with intermittent fever for 1 week. A two-throat swab had been collected and tested negative for COVID-19. On the February 4, a CT scan was done and showed right-sided ground-glass opacities and left-sided subpleural patchy consolidations. On the February 6, a positive result reverse transcription polymerase chain reaction (RT-PCR) of her sputum for COVID-19. On the February 8, the patient had no fetal movement, and the fetal heart rate was not viable, so an emergency cesarean section had done and delivered a

preterm male infant. Samples of amniotic fluid, placenta, cord blood, gastric juice, and throat swab had obtained and tested by RT-PCR for the susceptibility of COVID-19, and all the results were negative. On the February 15–17, throat swab RT-PCR tests for both the mother and the infant were negative.

A 15 pregnant woman was included in a study conducted by Liu *et al.*<sup>[29]</sup> on February 5, 2020 to 10, 2020, that showed that all were positive RT-PCR for COVID-19. All of the patients had mild symptoms and two of them had no clinical symptoms of COVID-19. CT findings revealed typical findings (ground-glass opacities and consolidations). Eleven of them delivered at the study period, ten of them delivered by cesarean section, and one by normal vaginal delivery. No neonatal death or neonatal asphyxia was reported. Fourteen out of fifteen of the patients had negative COVID-19 on RT-PCR after the treatment. In regard to the four pregnant who did not deliver in the study period, they had not taken any antiviral; they received empirical antibiotics to prevent bacterial infection and general supportive treatment. However, they had done the test again at the end of the study period for COVID-19 and all were negative.

Chen *et al.*<sup>[30]</sup> conducted this report released on February 12, 2020, revealed nine pregnant ladies with positive COVID-19. They were all healthy with no chronic comorbidities. One had gestational hypertension since 27 weeks of gestation, another one had preeclampsia at 31 weeks, both were stable. Seven out of nine presented with low fever (<39°C), four patients had a cough, three patients had experienced myalgia, and only with shortness of breath. None of them have developed severe pneumonia or required mechanical ventilation. Two had fatal distress and two underwent PROM (premature rupture of membrane). Regarding

CT scan, eight of nine patients revealed typical CT scan findings of COVID-19 (multiple patchy ground-glass opacities). All nine pregnant have labored nine live births with no fatal death or neonatal asphyxia. Four had preterm labor, yet tests were obtained from six patients using amniotic fluid, cord blood, neonatal throat swab, and breastmilk samples and all of them were negative. The remaining three infants who had not tested for COVID-19 were not mentioned.

This study was published on the March 16, 2020, by Chen *et al.*,<sup>[31]</sup> conducted where the outbreak takes place in Wuhan city, China. Four Pregnant ladies were positive of COVID-19 confirmed by RT-PCR after throat swab with typical CT findings (multiple patchy ground-glass opacities), all of them were in their third trimester. Three of them presented with fever, two had a cough, two myalgia, two complained of headache, and one experienced dyspnea with a history of anemia. In the acute phase of the disease, three underwent cesarean section to prevent the transmission while one of them had placenta previa. The remaining underwent normal spontaneous vaginal delivery because of the onset of labor. Four infants were immediately isolated and three were tested, the latter parents did not provide consent. All tests were negative of COVID-19. However, two of the infants had rashes (differed from each) and one suffered transient tachypnea and required continuous positive airway pressure. Another infant developed lateral edema of the thigh with 26 mg/dL of albumin. None of them showed any symptoms of COVID-19.

Sixteen pregnant women have been studied by Zhang *et al.*<sup>[32]</sup> that revealed their age ranged from 24 to 34 years old. Their gestational age varies from 35 to 41 weeks, and all tested positive for COVID-19. They have some comorbidities during their pregnancy, three had premature rupture of membrane, three had gestational diabetes, three had a preterm delivery, two had scarred uterus, and two required B-Lynch suture. They all delivered by cesarean section. Regarding neonates, 10\16 who were tested for COVID-19 were negative.

## Conclusion

In conclusion, a total of 74 pregnant patients have been reviewed in this article for COVID-19. Seventy-two patients were tested positive of COVID-19, and the remaining two had the typical symptoms and viral interstitial pneumonia shown by the chest CT scan with negative nucleic acid for COVID-19. Pregnant and nonpregnant patients who were positive for COVID-19 had no difference regarding clinical manifestations. Concerning neonates, 75 neonates have been reviewed (one set of twins), and they all born from a positive mother of COVID-19 except the twins. Answering our question, all the neonates who had tested after the delivery was negative for COVID-19 except one baby who born from a positive mother and tested positive for throat swab, yet tested negative for cord blood, placenta, and mother's breastmilk. The cause remains unknown until this moment. Based on this review family and women's health physicians are able to

clarify the possibilities of vertical transmission of COVID-19 in pregnant woman in collaboration with obstetrics.

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## Conflicts of interest

There are no conflicts of interest.

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