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## Perinatal Transmission of COVID-19 Associated SARS-CoV-2: Should We Worry?

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**Abstract**

We presented two cases of COVID-19 associated SARS-CoV-2 infection during third trimester of pregnancy. Both mothers and newborns had excellent outcomes. We failed to identify SARS-CoV-2 in all the products of conception and the newborns. This report provided evidence of low risk of intrauterine infection by vertical transmission of SARS-CoV-2.

**Keyword:** COVID-19, SARS-CoV-2, pregnancy outcome, vertical transmission

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## Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is one of the family members including viruses that cause diseases ranging from the common cold to SARS (Severe Acute Respiratory Syndrome) and MERS (the Middle East Respiratory Syndrome). The recent viral epidemics [1] and pandemics [2] showed that pregnant women suffer worse outcomes than non-pregnant individuals. Since there is increased oxygen consumption and decreased functional residual capacity during pregnancy [3], COVID-19 may impose greater risk in pregnant women compared to non-pregnant adult population. Furthermore, pregnancy is an immune suppressed condition, and compromised immune system renders the women more susceptible to complicated infections. Finally, SARS-CoV-2 might be transmitted vertically from mother to fetus and cause clinically significant infection.

Several reports regarding clinical, laboratory, radiological, and treatment data focus on general population were published [4, 5]. One [6] reported 9 cases of pregnant women, yet they failed to collect placenta tissue and vaginal secretion which are essential for assessment of vertical transmission.

In this article, we described two physicians with COVID-19 during the third trimester of gestation but their newborns showed no abnormalities at birth.

## Methods

This study was approved by the Research Ethics Committee of Renmin Hospital of Wuhan University (approval number WDRY2020-K016). Written informed consent was obtained from both patients. Maternal nasopharyngeal swabs were collected after admission.

Specimens of maternal serum, cord blood, placenta tissue, amniotic fluid, vaginal swab, breast milk, and newborn's nasopharyngeal swab were collected at or after delivery. The sample collection, processing and laboratory testing were based on WHO guidelines. Three target genes of SARS-CoV-2, including open reading frame 1ab (*ORF1ab*), nucleocapsid protein (N), and Envelope protein (E) were identified with the qRT-PCR kit (Bioperfectus Technologies, China) by Quantstudio Dx Real-time PCR system (Thermo Fisher, USA, **Supplemental material**).

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## Results

### Case 1

34-year-old physician (gravida 2, para 0) at 37 weeks' gestation without significant medical conditions. She developed nasal congestion on January 17, 2020 the same day she performed chest auscultation for a COVID-19 patient. Investigation traced down to January 10, when she was exposed to a patient who was eventually confirmed with COVID-19 on January 23. She developed fever (37.3°C-37.5°C) on January 20. She started to take Lianhua qingwen capsule (1.2gm PO Q8hrs) and Cefaclor (375mg PO BID). Fever went down but it came back two days after.

On January 23, she also noticed rash on her abdomen, Rash did not respond to topic Beclomethasone but quickly spread to whole body on Jan 25, She was given Calamine Topical after intrahepatic cholestasis of pregnancy was ruled out with normal total bile acid level.

On January 24, SARS-CoV-2 was identified on her nasopharyngeal swab, it was confirmed by a second specimen on January 25.

She was admitted on January 26, CT chest scan revealed no infiltrates, laboratory results indicated a normal white blood cells of  $8.9 \times 10^9/L$  with 18.1% of lymphocyte. She received Azithromycin (500 mg PO daily) and Oseltamivir (75 mg, PO BID) and Lianhua qingwen capsule (1.2 gm PO BID). Due to persisted fever, CT chest scan was repeated on January 29 which showed patchy consolidation in both lungs (**Figure1B**), and she was given two doses of methylprednisolone (20 mg IV daily) for pneumonia. Fever persisted but skin rash significantly improved.

On January 31, She delivered a baby girl with C-section. The baby weighs 3400gm and the Apgar scores were 9 and 10 at 1 and 5 minutes after birth.

The baby was separate from her mother immediately after birth without skin-to-skin contact. Serial qRT-PCR assays failed to detect the SARS-CoV-2 in any of the specimens including newborn's nasopharyngeal swab, maternal serum, placenta tissues, umbilical cord blood, amniotic fluid, vaginal swabs and mother's breast milk.

The baby developed low-grade fever and abdominal distension with lymphopenia (16.87%) on day 3. On day 4, her chest radiograph revealed diffuse haziness in both lung fields

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without patchy consolidation. Her fever and lung infection responded to antibiotics. She was discharged from hospital on Feb 8.

The mother received Cefotiam hydrochloride (2.0g, IV BID), Ornidazole (0.5g, IV BID), and methylprednisolone (20mg, IV daily) within 72 hours of delivery. SARS-CoV-2 was still positive on Feb 3, but the viral load decreased (Ct value of 22, 17 vs 32, 33 for N, O genes). On Feb 8, total white blood cell and lymphocyte counts returned to normal levels. Computed tomography of the thorax showed resolution of the right lower zone infiltrates (**Figure 1C**). She was transferred to isolation ward. After two consecutive negative samples (Feb 10, Feb 13), her nasopharyngeal swab was positive (Ct of 34, NA for N, O genes) again on Feb 17, with high level of IgG antibody (178Au/ml) to SARS-CoV-2.

## Case 2

29-year-old primigravida physician (gravida 1, para 0) at 36 weeks' gestation with no past medical history. She developed chill, fever (37.6~38.5°C), nasal congestion, and sore throat on January 23, 2020, the same day she was discharged from hospital for vaginal bleeding. Despite the use of diclofenac sodium suppositories, fever persisted. On January 25, She was admitted to hospital again due to unprotected exposure to her husband who had close contact with a COVID-19 patient. CBC with differential suggested lymphopenia (14.4%). Her Nasopharyngeal swab turned out to be positive for SARS-CoV-2 on January 26. She received Ceftazidime (2g, PO daily), Oseltamivir (75 mg, PO daily), and Lianhua Qingwen capsules (1.4g, PO Q8hrs). CT chest on January 28 showed multiple patchy infiltrates on left side of the lung (**Figure 1D**). Methylprednisolone (20mg, IV daily) was added.

Caesarean section was performed at 36 weeks and 5 days pregnant on January 30 due to persistent fever (38.5 °C). The newborn weighed 2,890 grams with Apgar scores were 9-10 at 1 and 5 minutes. SARS-CoV-2 was not detected in all the products of conception and the infants. The newborn developed mild neonatal pneumonia and lymphopenia (10.5%), she was treated with antibiotics resulted in good hematological response and clinic response in two days. The mother also discharged from hospital on Feb 19 after negative chest CT (**Figure 1E&F**) and nasopharyngeal samples (Feb 17, Feb 19).

## Discussion

We reported two physicians with COVID-19 during the third trimester of pregnancy. Both mothers and newborns were with excellent outcomes. This will provide evidence of low risk

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of intrauterine infection by vertical transmission of SARS-CoV-2.

Currently, we have very limited knowledge regarding the clinical impact of COVID-19 on maternal, fetal, and placental aspects of pregnancy. Previous studies found that pregnant women are at increased risk for severe complications, and are more likely to develop cardiopulmonary events during seasonal influenza compared with postpartum women [7].

In our cases, both patients revealed a mild disease course, with patient one exhibited more severe condition probably due to a high viral load associated placental proinflammatory cytokine release. (**Supplemental table**).

Human-to-human transmission of SARS-CoV-2 via direct contact, fomites, and potential aerosol routes are recognized [4, 5]. Vertical transmission after maternal primary infection usually occur during intrauterine life via trans-placenta, delivery via ingestion or aspiration of cervicovaginal secretions, and postpartum via breastfeeding [8]. However, the risk of vertical transmission of SARS-CoV-2 was low, as we did not detect the virus in all the products of conception and the infants. Previous studies showed that influenza, SARS [9], and MERS [10], similar to the characteristics of COVID-19, have resulted in miscarriage, abortion, and more severe outcomes in pregnant women, when compared with non-pregnant individuals. The viral infection of the above mentioned cases during pregnancy was also suspected to be the cause of poor fetal outcomes.

Due to immune response to SARS-CoV-2 infection, it is possible that the mother produces sufficient neutralizing antibodies without developing serious conditions. These passive antibodies may have a protective effect on the infants via breastfeeding. In our cases, breastfeeding is discouraged even we did not detect SARS-CoV-2 in consecutive breastmilk samples during follow-up. First, person-to-person transmission occurs by contact with infected body fluids, unprotected exposure to the COVID-19 mother may put infants at great risk of perinatal infection. Second, patient one had positive nasopharyngeal swab on Feb 17 after two consecutive negative samples, even with substantially increased IgG to SARS-CoV-2. Therefore, the pregnant women should take efforts to minimize risk exposure whenever possible.

#### **Declaration of interests**

We declare no competing interests

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**Figure legend:**

**Figure 1.** Epidemiological and clinical features in two pregnant physicians with COVID-19. Timeline of epidemiologic data and clinical events (**A**). Transverse chest CT images from case one showing patchy consolidation of right lower lobe with fuzzy margin (Red arrows) on day 6 after symptom onset (**B**), absorption of right lower lung infection on day 12 after symptom onset (**C&D**). Transverse chest CT images from case two showing patchy ground glass shadow and consolidation in the left lung (Red arrows) on day 8 after symptom onset (**E** Red arrows), complete absorption of lung infection on day 17 after symptom onset (**F**).

Abbreviation: First or Second contact: Contacted with a COVID-19 patient. C-section: Cesarean section. Positive PCR or Negative PCR: SARS-CoV-2 present or absent on nasopharyngeal swab unless otherwise specified. Positive chest CT: Chest CT confirmed COVID-19. Positive antibodies: specific antibody to SARS-CoV-2.



