Clinical Infectious Diseases

BRIEF REPORT

Perinatal Transmission of 2019 Coronavirus Disease–Associated Severe Acute Respiratory Syndrome Coronavirus 2: Should We Worry?

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We present 2 cases of coronavirus disease 2019 (COVID-19)–associated severe respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during the third trimester of pregnancy. Both mothers and newborns had excellent outcomes. We failed to identify SARS-CoV-2 in all of the products of conception and the newborns. This report provided evidence of low risk of intrauterine infection by vertical transmission of SARS-CoV-2.

Keywords. COVID-19; SARS-CoV-2; pregnancy outcome; vertical transmission.

The 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 (Middle East respiratory syndrome). The recent viral epidemics [1] and pandemics [2] showed that pregnant women suffer worse outcomes than nonpregnant individuals. As there is increased oxygen consumption and decreased functional residual capacity during pregnancy [3], 2019 coronavirus disease (COVID-19) may impose greater risk in pregnant women compared to the nonpregnant adult population. Furthermore, pregnancy is an immunosuppressed condition, and a 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 focusing on the general population have been published [4, 5]. One report [6] reported 9 cases of pregnant women, yet they failed to collect placenta tissue and vaginal secretions, which are essential for assessment of vertical transmission.

In this article, we describe 2 physicians with COVID-19 during the third trimester of gestation and results of SARS-CoV-2 testing on their newborns.

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, placental tissue, amniotic fluid, vaginal swab, and breast milk, along with the newborns' nasopharyngeal swab, were collected at or after delivery. The sample collection, processing, and laboratory testing were based on World Health Organization 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 reverse-transcription quanitative polymerase chain reaction (qRT-PCR) kit (Bioperfectus Technologies, China) by the Quantstudio Dx Real-time PCR system (Thermo Fisher) (Supplementary Materials).

RESULTS

Case 1

A 34-year-old physician (gravida 2, para 0) presented at 37 weeks' gestation without significant medical conditions. She developed nasal congestion on 17 January 2020, the same day she performed chest auscultation for a patient with COVID-19. Investigation traced back to 10 January, when she was exposed to a patient who was eventually confirmed with COVID-19 on 23 January. She developed fever (37.3°C–37.5°C) on 20 January. She started to take Lianhua qingwen capsule (1.2 g orally [PO] every 8 hours) and cefaclor (375 mg PO twice daily [BID]). Fever diminished but returned 2 days after.

On 23 January, she also noticed a rash on her abdomen. The rash did not respond to topical beclomethasone but quickly spread to her whole body on 25 January. She was given topical calamine after intrahepatic cholestasis of pregnancy was ruled out with normal total bile acid level.

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

She was admitted on 26 January. A chest computed tomographic (CT) scan revealed no infiltrates, and laboratory results

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indicated a normal white blood cell count of 8.9×10^9 cells/L with 18.1% lymphocytes. She received azithromycin (500 mg PO daily) and oseltamivir (75 mg PO BID) and Lianhua qingwen capsule (1.2 g PO BID). Due to persistent fever, chest CT scan was repeated on 29 January, which showed patchy consolidation in both lungs (Figure 1B), and she was given 2 doses of methylprednisolone (20 mg intravenously [IV] daily) for pneumonia. Fever persisted but skin rash significantly improved.

On 31 January, she delivered a baby girl by cesarean delivery. The baby weighed 3400 g and the Apgar scores were 9 and 10 at 1 minute and 5 minutes, respectively, after birth.

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

The baby developed low-grade fever and abdominal distension with lymphopenia (16.9%) on day 3. On day 4, her chest radiograph revealed diffuse haziness in both lung fields without patchy consolidation. Her fever and lung infection responded to antibiotics. She was discharged from hospital on 8 February.

The mother received cefotiam hydrochloride (2.0 g IV BID), ornidazole (0.5 g IV BID), and methylprednisolone (20 m IV daily) within 72 hours of delivery. SARS-CoV-2 was still positive on 3 February, but the viral load decreased (cylce threshold [CT] value of N and O genes was 22, 17 on 24 January and 32, 33 on 3 February, respectively). On 8 February, total white blood cell and lymphocyte counts returned to normal levels. CT of the thorax showed resolution of the right lower zone infiltrates (Figure 1C). She was transferred to an isolation ward. After 2 consecutive negative samples (on 10 and 13 February), her nasopharyngeal swab was positive (Ct of 34 and NA for the N and O genes) again on 17 February, with high levels of immunoglobulin G (IgG) antibody (178 AU/mL) to SARS-CoV-2.

Case 2

A 29-year-old primigravida physician (gravida 1, para 0) presented at 36 weeks' gestation with no past medical history. She developed chill, fever (37.6°C–38.5°C), nasal congestion, and

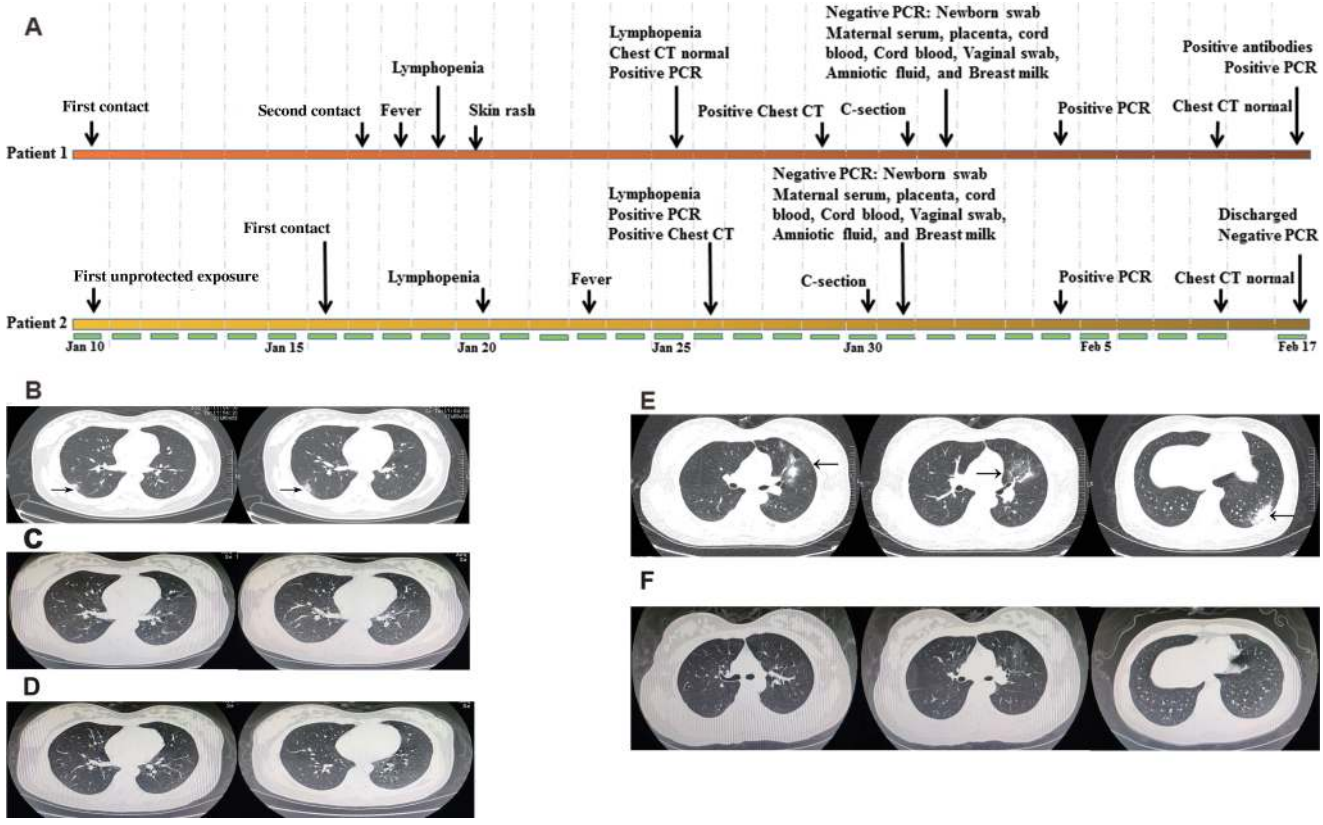

Figure 1. Epidemiological and clinical features in 2 pregnant physicians with 2019 coronavirus disease (COVID-19). *A,* Timeline of epidemiologic data and clinical events. Adapted from [7]. *B–D,* Transverse chest computed tomographic (CT) images from case 1 showing patchy consolidation of right lower lobe with fuzzy margin (arrows) on day 6 after symptom onset (*B*) and absorption of right lower-lung infection on day 12 after symptom onset (*C* and *D*). *E* and *F,* Transverse chest CT images from case 2 showing patchy ground glass shadow and consolidation in the left lung (arrows) on day 8 after symptom onset (*E*) and complete absorption of lung infection on day 17 after symptom onset (*F*). First or second contact indicates contact with a COVID-19 patient. C-section indicates cesarean delivery. Positive or negative polymerase chain reaction (PCR) indicates that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was present or absent on nasopharyngeal swab unless otherwise specified. Positive chest CT indicates that chest CT was confirmed with COVID-19. Positive antibodies indicate specific antibody to SARS-CoV-2.

sore throat on 23 January 2020, the same day she was discharged from hospital for vaginal bleeding. Despite the use of diclofenac sodium suppositories, fever persisted. On 25 January, she was admitted to hospital again due to unprotected exposure to her husband, who had close contact with a COVID-19 patient. Complete blood count with differential suggested lymphopenia (14.4%). Her nasopharyngeal swab turned out to be positive for SARS-CoV-2 on 26 January. She received ceftazidime (2 g PO daily), oseltamivir (75 mg PO daily), and Lianhua qingwen capsules (1.4 g PO every 8 hours). Chest CT on 28 January showed multiple patchy infiltrates on the left side of the lung (Figure 1D). Methylprednisolone (20 mg IV daily) was added.

Cesarean delivery was performed at 37 weeks gestation on 30 January due to persistent fever (38.5°C). The newborn weighed 2890 g with Apgar scores of 9 and 10 at 1 minute and 5 minutes, respectively. SARS-CoV-2 was not detected in any of the products of conception or the infant. The newborn developed mild neonatal pneumonia and lymphopenia (10.5%); she was treated with antibiotics, resulting in good hematological response and clinical response in 2 days. The mother was also discharged from hospital on 19 February after negative chest CT (Figure 1E and 1F) and nasopharyngeal samples (17 and 19 February).

DISCUSSION

We reported 2 physicians with COVID-19 during the third trimester of pregnancy. Both mothers and newborns had excellent outcomes. This suggests low risk 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 [8].

In our cases, both patients revealed a mild disease course, with patient 1 exhibiting a more severe condition, probably due to a high viral load–associated placental proinflammatory cytokine release (Supplementary Table).

Human-to-human transmission of SARS-CoV-2 via direct contact, fomites, and potential aerosol routes is recognized [4, 5]. Vertical transmission after maternal primary infection usually occurs during intrauterine life via the transplacental route, during delivery, or through ingestion or aspiration of cervicovaginal secretions, and postpartum via breastfeeding [9]. However, the risk of vertical transmission of SARS-CoV-2 was low, as we did not detect the virus in any of the products of conception or the infants. Previous studies showed that influenza, SARS [10], and MERS [11], similar to the characteristics of COVID-19, have resulted in miscarriage, abortion, and more severe outcomes in pregnant women compared with nonpregnant 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 was discouraged even though we did not detect SARS-CoV-2 in consecutive breast-milk samples during follow-up. First, person-to-person transmission occurs by contact with infected body fluids, so unprotected exposure to mothers with COVID-19 may put infants at great risk of perinatal infection. Second, our first patient had a positive nasopharyngeal swab on 17 February after 2 consecutive negative samples, even with substantially increased IgG to SARS-CoV-2. Therefore, pregnant women should take efforts to minimize risk exposure whenever possible.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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