Coronavirus Disease-19(COVID-19) infection during pregnancy: Report of two cases and review of the literature

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Abstract

In this article, we report the diagnosis and treatment of two patients with SARS-CoV-2 (severe acute respiratory syndrom coronavirus-2) infection in Hunan Province, China, and their perinatal outcomes. Two patients were admitted to the hospital due to full-term pregnancy with no fever or gastrointestinal symptoms noted during admission. However, they developed fevers and a dry cough on the day of and the third day after cesarean section; and both patients were found to be positive for SARS-CoV-2 by RT-qPCR for viral nucleic acid after symptoms appeared. After a detailed examination and history, one patient's husband proved to have had contact with whom travelled to Hubei and then this patient was found to be negative for SARS-CoV-2 and discharged after isolation and symptomatic supportive treatment. We did not detect SARS-CoV-2 in neonatal throat swabs. After isolation, the newborn recovered and was discharged.

Keywords: SARS-CoV-2, Pregnancy, infant

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Introduction

The first patient was a 26-year-old female (G3P1, 40+3weeks). On February 11, 2020, she was admitted to a hospital in Hunan due to “vaginal bleeding with irregular abdominal pain for 10 hours”. The patient’s husband had contact history in Hubei, but without any underlying symptoms, i.e., no fever, cough, or diarrhea. Her breathing was normal, and her lungs were clear by auscultation. The patient developed a fever after cesarean section on February 13 and was sent to an isolation ward soon thereafter. RT-PCR of pharyngeal fluids and saliva were negative on February 14 and February 16, and CT did not show significantly positive SARS-CoV-2 infection. The PCR test was, however, positive on February 17. Laboratory test results for liver and kidney, myocardial enzymes, and coagulation function were normal, but lactate dehydrogenase was 318.37 U/L and cardiac myocardial phosphokinase was 30.48 U/L—both slightly increased. Respiratory virus antigen, influenza virus PCR, mycoplasma antibodies, and chlamydia antibodies were negative. Subsequent conservative treatment was thus performed, and on February 15, the patient’s core body temperature returned to normal. On February 22 and 24, viral nucleic testing by RT-PCR from throat and saliva swabs were negative, and the patient was discharged on February 25. Routine blood analyses, CRP, and PCT are shown in Table 1. The neonate’s situation was as follows.: gestational age was 40+6 weeks, with the umbilical cord coiled around the neck for 1 week; the placenta was intact; amniotic fluid was clear, with a volume of approximately 1000 ml; Apgar scores were 10 and 10 at 1 and 5 min, respectively; birth weight was 3425 g; and the RT-PCT test was negative on the day when the mother spiked a fever. No related symptoms were observed [1].

***Table 1**. Patient characteristics, routine blood analyses, and CRP concentrations in two pregnancies.*

Patient	After fever	WBCs	N%	PLT	Hb	CRP
		(×109/L)	(%)	(×109/L)	(g/L)	(mg/L)
Patient 1	3rd day	14.24	11.42	294	137	314.55
	6th day	15.94	88.9	290	106	1.22
	10th day	12.33	78	237	105	7.2
	13th day	9.61	31.32	464	137	19.8
Patient 2	5th day	6.53	11	258	114	54.31
	6th day	4.59	24.4	275	113	23.87
	12th day	3.53	34.4	422	119	3.22
	17th day	4.02	35.3	374	122	0.67

The second patient was a 36-year-old female (G2P1) who was admitted to the obstetrics department of a hospital in Hunan on January 31, 2020 at 39 weeks of pregnancy. Her husband had a history of travel a half-month before delivery, but no infection-related symptoms, i.e., no fever, cough, diarrhea, or other symptoms found upon admission. Breathing was unimpaired, lung auscultation was normal, and a cesarean section was then successfully performed on the day of admission. However, the patient developed fever on February 2nd with an occasional dry cough but no headache or diarrhea. Both RT-PCR for the neocoronavirus and chest CT (Figure. 1) were performed and found to be positive on February 4th, and routine blood analyses and evaluation of C-reactive protein concentrations are shown in Table 1. No obvious abnormalities were found in procalcitonin concentrations, coagulation function, E4A, four items before blood transfusion, or liver and kidney function.

Lactate dehydrogenase (340.33 U/L) and cardiac myocardial phosphokinase (46.53 U/L) were slightly increased, but assay for respiratory pathogens and influenza A and B viruses were negative. The patient received conservative treatment, and her core body temperature was found to be normal on February 5th. On February 16th and February 18th, viral RT-PCR results were negative and chest CT improved, and she was discharged on February 19th. Newborn birth weight was 3150 g, the baby showed a good response, and her cry was loud. One-min and 5-min Apgar scores were 9 and 10 points, respectively. Amniotic fluid was clear and general conditions were normal after birth. PCR results for fetal SARS-CoV-2 were negative on February 2, and the woman's body temperature was normal, with no coughing or shortness of breath. She was quarantined at the local community hospital for 14 days without any abnormalities [2].

The medical staff in contact with the two patients during hospital maternity admission were medically isolated for 14 days, and none became ill. The contacts were found to be negative by viral nucleic acid testing.

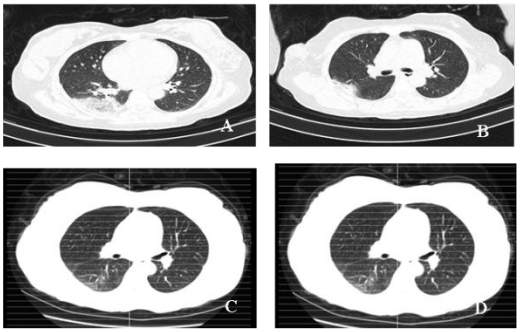

Figure 1. *CT scan of patient 2's chest. A and B show the increased thickness of both lungs in a sheet-like, ground-glass-like density. C, D show a slightly thickened bronchovascular bundle in both lungs, with an increase in the scattered sheet-like, ground-glass-like opacities, principally under the pleurae, which significantly improved compared to initial evaluation. Local small panel shows interstitial thickening.*

Discussion

The first case of coronavirus disease 2019 (COVID-19) was uncovered in Wuhan City, Hubei Province, in December 2019. The viral infection produced a large-scale outbreak in a short period of time, and it quickly gets the global reach of the virus including Japan, South Korea, Southeast Asia, the United States, and European countries, posing a huge threat to global public health.COVID-19 was declared a global pandemic. Based upon current epidemiologic investigations, the incubation period for COVID-19 is 1-14 days—and more narrowly, 3-7 days. The longest current incubation period for patients has reached 24 days; and and other retrospective analysis of 1099 cases of COVID-19 before January 29 found that the median incubation period was 3.0 days. The most common symptoms were fever (87.9%), cough (67.7%), diarrhea (3.7%), and vomiting (5.0%); pneumonia was present in 76.4% of cases, with 25.2% of patients manifesting at least one underlying disease (including hypertension and chronic obstructive pulmonary disease). Over 1 in 7 cases (15.7%) were severe, with only 0.9% under 15 years of age. The case fatality rate was 2.7%, and most of the patients were middle-aged and elderly individuals. SARS-CoV-2 is more infectious than ordinary influenza viruses, but far weaker than the human severe acute respiratory syndrome (SARS) coronavirus, Ebola virus, or the H7N9 influenza virus. In laboratory tests, the numbers of lymphocytes (prevalence, 82.1%), thrombocytes (36.2%), and leukocytes (33.7%) decreased, as well as levels of C-reactive protein. However, elevations in alanine aminotransferase, aspartate aminotransferase, creatine kinase, and the fibrin degradation product D-dimer levels were rare, except for critically ill patients [3].

At present, there are few research data regarding neocoronavirus infections during pregnancy and the perinatal period. Chen reported that clinical data from nine confirmed pregnant women with COVID-19 showed that their body temperatures fluctuated between 36.5°C and 38.8°C, and that there was no case of high fever (body temperature>39°C).The disease in these women was manifested as coughs, myalgia, and sore throat, with a few women exhibiting gastrointestinal symptoms, shortness of breath, and preeclampsia. Laboratory results showed a normal white blood cell count, decreased lymphocyte number, and increased C-reactive protein concentrations. In some patients, the concentrations of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were elevated. There were no cases of pneumonia that required mechanical ventilation, and no deaths have yet been reported. It was suggested that the characteristics of COVID-19 during pregnancy were similar to those of the infected adult population, and that the prognosis for women in the third trimester was better. Both patients in our article showed infection after delivery, and their primary symptoms were fever and dry cough; neither showed any other clinical manifestations such as dyspnea, fatigue, or myalgia. Body temperature soon turned to normal, C-reactive protein levels increased, and lymphocyte count decreased. Through supportive treatment, their symptoms improved, and they were discharged. By comparison, it was found that patients with COVID-19 in the third trimester had milder symptoms, faster recovery, and less-severe illness. The results of our study were consistent with those of COVID-19 is a β-coronavirus, and epidemiologic investigations have shown that the nucleotide sequence identity among SARS-CoV-2, SARS-CoV, and Middle East respiratory syndrome (MERS)-CoV is as high as 85%. Wongreported that about 50% of pregnant women with SARS in 2003 were admitted to the intensive care unit, 33% needed mechanical ventilation, and the maternal mortality rate was as high as 25%. Alfaraj reported that 11 cases of pregnant women with MERS in 2012 (54%) were admitted to the intensive care unit, and 3 (27%) died. The marked differences in results may be related to differences in viral pathogenicity and virulence that effect infection during pregnancy. The present and related articles show that newly pregnant women were primarily infected during the third trimester, while Alfaraj

reported that their pregnant women were infected during the first or second trimester, or had complications during pregnancy. Therefore, understanding the impact of COVID-19 infections on pregnant women and fetuses/newborns requires further study.

Vertical transmission refers to the transmission of pathogens from mother to fetus/baby before and after birth. This includes transmission through the gametes or placental blood during pregnancy, or transmission through the birth canal during reproductive intervals or postpartum breastfeeding. The two patients we described in this article both underwent laparotomies at the stage of latent infection without symptoms such as intrapartum asphyxia and dyspnea, such that the possibility of vertical transmission in the first or second trimester of pregnancy could not be determined. Because these pregnancies ended in cesarean sections, no exfoliated vaginal cells or vaginal secretion samples were collected for testing, and it was not possible to analyze whether SARS-CoV-2 was transmitted during vaginal delivery. In the present case, the neonatal RT-PCR results from pharyngeal secretions were negative after the mother got fever. At the same time, became febrile, and the patient was not find any uncomfortable during the isolation. We therefore observed no evidence of vertical transmission of SARS-CoV-2, and this is corroborated by also did not report any neonatal asphyxia or dyspnea in their cohort of nine pregnant women with SARS-CoV-2 infection. Four infants were born preterm but none before 36 weeks' gestation. Two of them weighed less than 2500 g, while one had a birth weight of 1880 g; the 1-min and 5-min Apgar scores of the nine infants were not lower than eight, and only one newborn exhibited slightly elevated myocardial enzymes on the day of birth but without any clinical symptoms. The amniotic fluid, umbilical cord blood, neonatal throat swabs, and breast milk collected from the six patients were all negative for SARS-CoV-2, suggesting that patients with neocoronavirus pneumonia in late pregnancy did not manifest vertical intrauterine transmission resulting in adverse neonatal outcomes—which is consistent with the findings for SARS and MERS pregnancies . Zhang reported a positive case of a newborn whose mother tested positive for SARS-CoV-2, but it was a specimen taken 30 hours after the birth of the newborn. There is currently no test for the mother's amniotic fluid, cord blood, placenta, or for neonatal venous blood or feces. The data are thus insufficient to confirm or disprove vertical transmission. At the same time, the newborn's immune system is not well developed, the clinical manifestations of newborns after infection are generally non-specific, and studies on newborns are limited. In the future, antibody testing or more sensitive detection methods for mother-to-child transmission.

Previous studies have shown that fever and viral infection during pregnancy can cause abnormal fetal brain and lung development reported that pharyngeal fluids from nine neonates (10 neonates born from nine pregnant women) tested for SARS-CoV-2 were negative, with the babies showing abnormal clinical manifestations (such as shortness of breath, rapid heart rate, vomiting, and fever). However, due to the sample conditions, RT-PCR was not performed on amniotic fluid, umbilical cord blood, or gastric secretions. Therefore, vertical transmission in utero was not supported, but the data suggested that maternal infection might cause adverse outcomes to the newborn. Even if the fetus was not infected through vertical transmission, viral infection in early pregnancy could still be manifest as fever, and persistent high fever and increased oxygen consumption could affect the development of embryonic tissues and thus require special attention [4].

The two patients in this communication demonstrated no clinical symptoms when they were first admitted to the hospital; none of the medical staff with whom they were in contact wore any special protection, but rather had general protection according to standard precautionary guidelines. It is intriguing that RT-PCR for SARS-CoV-2 was negative, and yet the individuals were still isolated for 14 days despite no abnormalities being found. By referring back to MERS in 2015, we have identified a study where the investigators reported a case of asymptomatic or mild MERS-CoV infection that was tracked to the outbreak in Korea, and 82 medical staff with whom the patient was in contact were classified as making first-level (with a contact range of less than 2 m and no protective equipment), second-level (contact range greater than 2 m without protective equipment), or tertiary-level contacts (people who have stayed in the same space without protective equipment) and were quarantined for 14 days. Interestingly, viral detection of MERS by RT-PCR was found to be negative for these staff members. The aforementioned study showed that the infection rate for patients upon contact during the incubation period was low after general protection of medical staff. However, due to the lack of such studies, antibody testing and expansion of the sample size are still needed to determine the infection rate for medical staff who make contact with an infected individual during the incubation period [5].

In summary, currently reported cases and the present case study do not support the possibility of vertical transmission. Compared with SARS and MERS, pregnant women infected with SARS-CoV-2 exhibited milder symptoms, a faster recovery, and fewer patients underwent severe illness—which may be related to differences in pathogenesis. However, additional studies concerning biologic characteristics and pathogenic mechanisms underlying any potential vertical transmission of SARS-CoV-2 are still needed with respect to both mothers and infants.

Conflict of interest

All authors declare that they have no conflict of interest.

The present study is 1) an analysis of the examination of symptoms of neocoronavirus infection in addition to other investigators' previous research, 2) an analysis of vertical transmission and the status of neonatal infection, and 3) a recommendation to foster continued study of this area in the future.

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