

Case Report



Two Cases of SARS-CoV-2-Positive Mothers and Their Newborns in Korea

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Conflict of Interest

No conflicts of interest.

ABSTRACT

It is unclear how severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) affects pregnant women and their fetuses or newborns. We report two infants born to mothers with coronavirus disease 2019 (COVID-19) in Korea. The first case was a healthy female baby born at 39⁺³ weeks' gestation from a mother diagnosed with COVID-19. The second case was a female baby born at 38⁺⁰ weeks' gestation. The newborn in the second case had symptoms of respiratory distress immediately after birth, and nasal continuous positive airway pressure support was applied for 8 hours. Real-time polymerase chain reaction test results for SARS-CoV-2 using amniotic fluid, neonatal nasopharyngeal and oropharyngeal swabs, blood, urine, stool, and rectal swab were all negative in the 1st and 2nd days of life in both cases. Placental pathology showed acute necrotizing deciduitis and intervillous fibrin deposition with acute intervillitis. Although clinical evidence of vertical transmission was not found in our cases, with the possibility of placental inflammation, close monitoring of SARS-CoV-2 positive mothers and their newborn is required.

Keywords: COVID-19; SARS-CoV-2; Pregnancy; Placenta; Neonate

INTRODUCTION

Pregnant women become vulnerable to infection due to hormonal and immune system functional changes. Due to the high estrogen and progesterone levels, pregnant women are susceptible to respiratory pathogens, and the more severe type of the disease can occur if infected [1]. A national population cohort study in the United Kingdom reported an incidence rate of 0.49% severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in pregnancy, which is higher than that of the overall population at 0.27% [2]. Other viral infections during pregnancy can generally lead to adverse effects on fetal development and maternal mortality. However, information on the impact of coronavirus disease 2019 (COVID-19) on pregnancy, fetus, and newborns is limited. Here, we report two singleton infants born to mothers with COVID-19 in Korea.

Author Contributions

Conceptualization: SWY. Data curation: JHJ, YK, JY, EHK. Investigation: JHJ, SWY. Writing - original draft: HJJ. Writing - review and editing: SWY. Approval of the final manuscript: JHJ, YK, JY, EHK, SWY.

CASE REPORT

1. Case 1

A 38-year-old woman (gravida 1, para 0) at 36⁺⁴ weeks' gestation was referred to the National Health Insurance Service Ilsan Hospital. She was diagnosed with COVID-19 by real-time polymerase chain reaction (RT-PCR) of nasopharyngeal and oropharyngeal swabs (NP/OP swabs; E gene cycle threshold [Ct], 24.15; RdRp Ct, 25.26, STANDARD M nCoV Real-Time Detection kit, SD BIOSENSOR, Suwon, Korea). She presented no symptoms of SARS-CoV-2 infection and chest radiography findings, laboratory results were normal. The non-stress test (NST) showed no abnormal fetal heart rate pattern. She was discharged home after 11 days of conservative care in a negative-pressure isolation room. At 39⁺³ weeks' gestation, cesarean section was planned. The RT-PCR results of the NP/OP swab still remained positive (E gene Ct, 21.36; RdRp Ct, 22.01). She was transferred to a negative-pressure operating room for cesarean delivery under spinal anesthesia and all medical staff wore personal protective equipment, including powered air-purifying respirators.

She gave birth to a female baby weighing 3,220 g. Apgar scores were 8 and 9 at 1 and 5 min, respectively. The specimens from the neonatal NP/OP swab, and amniotic fluid obtained in the operating room for RT-PCR test showed negative results (Table 1). The baby was separated from the mother and closely monitored in a negative-pressure isolation room. RT-PCR test of blood, urine, stool, and rectal swab conducted at 3 hours after birth showed negative results. The baby was released from isolation after confirming that the negative PCR test results of the NP/OP and rectal swabs at 48 h after birth. The baby was discharged with a healthy caregiver on the fourth day of birth. The RT-PCR test results of the breast milk was negative. The placental pathologic results revealed acute intervillitis with increased intervillous and subchorionic fibrin deposition and acute necrotizing deciduitis (Fig. 1A).

Table 1. The real-time polymerase chain reaction for SARS-CoV-2

	Case 1		Case 2	
	At birth	48 hours	At birth	48 hours
Amniotic fluid	Negative		Negative	
Cord blood			Negative	
NP/OP swab	Negative	Negative	Negative	Negative
Blood	Negative		Negative	Negative
Urine	Negative		Negative	Negative
Stool	Negative		Negative	Negative
Rectal swab	Negative	Negative	Negative	Negative
Breast milk	Negative			

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; NP/OP, nasopharyngeal and oropharyngeal swabs.

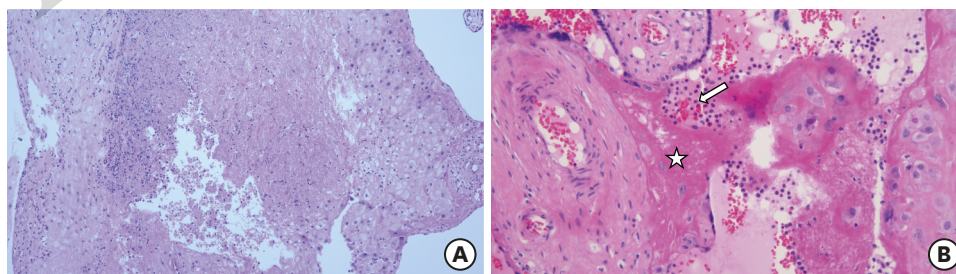


Figure 1. Histopathology of the placenta of mothers with coronavirus disease (COVID-19). (A) Acute necrotizing deciduitis (hematoxylin-eosin, original magnification x100) in case 1. (B) Perivillous fibrin deposition (star) with acute intervillitis showing infiltration of inflammatory cells (arrow) in case 2 (hematoxylin-eosin, original magnification x200).

Her mother was discharged home 6 days after giving birth, but the RT-PCR test result still remained positive (E gene Ct, 35.29; RdRp Ct, 33.45). At the 1-month follow-up visit with the mother, the baby was breast feeding and thriving well without any symptoms.

2. Case 2

A 19-year-old woman (gravida 1, para 0) at 34⁺⁶ weeks' gestation was admitted to Ilsan Hospital, diagnosed with COVID-19 due to positive RT-PCR results of NP/OP swab (E gene Ct, 14.708; RdRp Ct, 14.553). She had headache, fever, dyspnea, and loss of smell and taste. Initial laboratory tests revealed decreased hemoglobin (9.6 g/dL) and elevated CRP (1.55 mg/dL) levels. Chest radiography findings were normal, and oxygen treatment was not required. The fetus had normal NST results. Despite the repeated positive RT-PCR test results (E gene Ct, 34.29; RdRp Ct, 35.49), all symptoms resolved, and she was discharged home after 12 days. At 38⁺⁰ weeks' gestation, she was readmitted with symptoms of regular uterine contractions and the RT-PCR was still positive (E gene Ct, 28.16; RdRp Ct, 28.02).

A 3,130 g female baby was delivered at 38⁺⁰ weeks' gestation by cesarean section in a separate negative-pressure operating room. Apgar scores were 8 at 1 min and 9 at 5 min. She presented with labored breathing signs, including chest retractions and moaning sounds. The baby was transferred to a negative-pressure isolation room and nasal continuous positive pressure (nCPAP, FiO₂ 0.21, 5 cm H₂O) was applied. The vital signs were stable, and oxygen saturation was maintained at 98 - 100%. Chest radiography showed a mild bilateral minimal ground-glass pattern, which resolved after 4 hours. RT-PCR results at birth for amniotic fluid, cord blood, NP/OP swabs, blood, urine, rectal swab, and stool were all negative (Table 1). Respiratory symptoms improved after 8 hours of birth, and nCPAP was discontinued. Results of RT-PCR test of the neonatal NP/OP swab, blood, urine, stool, and rectal swab conducted at 48 h after birth were negative. The baby was fed infant formula because the mother refused to breastfeed. Pathology revealed intervillous fibrin deposition with calcification and acute intervillitis in the placental parenchyma (Fig. 1B). On the fifth day of life, the baby was discharged with a healthy caregiver, and the mother was discharged home with contact precautions.

3. Ethics statement

This study was approved by the Institutional Review Board of the National Health Insurance Service Ilsan Hospital (IRB NO. 2020-12-007). Informed consent was obtained from the patients' legal guardians.

DISCUSSION

We reported two cases of neonates born from mothers with COVID-19. Both newborns were generally healthy without vertical transmission or perinatal infection of SARS-CoV-2. The second case showed brief respiratory distress, probably due to transient tachypnea of the newborn. Previous study reported that the majority of neonates born to SARS-CoV-2-positive mothers had a favorable clinical course [3]. Dani et al. reported that 81.2% of newborns born to mothers positive for or with suspected COVID-19 were healthy and admitted to a well-baby nursery [4]. Yoon et al. summarized that 93.2% of 201 infants born to COVID-19 confirmed mothers were asymptomatic [3]. The other coronaviruses, SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), are associated with severe adverse pregnancy outcomes, such as high incidences of spontaneous miscarriage, preterm delivery, and intrauterine growth restriction [5, 6]. To date, fetal complications of SARS-CoV-2 are

relatively lower than those of SARS and MERS. However, the adverse outcomes of pregnant women and their fetuses and newborns were continuously reported. Dashraath et al. estimated a miscarriage rate of 2%, intrauterine growth restriction rate of 10%, and preterm birth rate of 39% [7]. Therefore, an intensive check-up for pregnant women with COVID-19 and their fetus and newborns should be performed.

The clinical criteria for releasing COVID-19 patients from isolation in Korea is 10 days after confirmation if symptoms are negative [8]. Both mothers were asymptomatic at first discharge and met the clinical criteria for release. However, as per our hospital's policy, both mothers used a negative-pressure isolation room at readmission for delivery because the repeated PCR test remained positive with Ct value less than 30. Previous study reported that vaginal delivery in COVID-19 infected women does not increase the risk of neonatal COVID-19 infection [9]. In our cases cesarean sections were performed and neonates were separated from the mothers after birth, due to our hospital's negative pressure isolation room for vaginal delivery and rooming-in care was not available. The newborn of the Case 2 had symptoms of respiratory difficulty and required intensive monitoring care. World Health Organization recommends that mother with COVID-19 should be encouraged to initiate or continue to breastfeed [10]. In Case 1, the breast milk PCR results were negative. Although there have been a few reports of detection of SARS-CoV-2 RNA in breast milk, it is not clear whether SARS-CoV-2 could be transmitted through breast milk [11]. Mother with confirmed COVID-19 can try breastfeeding carefully after taking strict viral precautions of washing hands or wearing a mask [10].

For SARS-CoV-2, vertical transmission remains controversial. There are several neonatal cases with laboratory-confirmed SARS-CoV-2 infection after being born from mothers with COVID-19. According to a systemic review, 8 neonates (2%) out of 397 born to mothers with COVID-19 in China had a positive RT-PCR test result for SARS-CoV-2 from NP swab [12]. Since the timing of RT-PCR tests is heterogeneous among studies, intrauterine transmission and intrapartum or early postnatal infection could not be differentiated by the positive RT-PCR test results. Blumberg et al. proposed the definitions of vertical SARS-CoV-2 transmission considering the characteristics of modes of transmission and laboratory tests [13]. Based on the RT-PCR results of the respiratory tract secretions, amniotic fluid, umbilical cord blood, and neonatal blood performed within 24 hours after birth and whether these results persisted after 24 hours, the authors distinguished intrauterine transmission from intrapartum or early postnatal transmission. In the present cases, we conducted RT-PCR tests of neonatal NP/OP swabs, neonatal blood, urine, stool, amniotic fluid, and cord blood to confirm intrauterine transmission. To confirm intrapartum or early postnatal transmission, RT-PCR tests were performed again at 48 h after birth in neonatal NP/OP swabs, blood, urine, and stool. Because all RT-PCR test results were negative, we concluded that any type of vertical transmission and perinatal infection was absent in our cases.

The placental pathologic findings of our cases were acute intervillitis and intervillous fibrin deposition, which is consistent with a previous studies on placental pathology of COVID-19 mothers [14-16]. Vivanti et al reported increased perivillous fibrin deposition and acute and chronic intervillitis in a 35⁺ week placenta of a PCR-positive woman [14]. Results of RT-PCR tests for SARS-CoV-2 of neonatal blood, bronchoalveolar lavage fluid, NP and rectal swabs were all positive and transplacental transmission was proved. Patane et al. reported that two neonates born from SARS-CoV-2-positive mothers were COVID-19 positive [15]. The placentas of these two mothers showed chronic intervillitis with macrophages. A systemic

review summarized that histopathological abnormalities including maternal/fetal vascular malperfusion and signs of inflammation were reported [16]. However, in several other studies reported that there were no specific pathologic findings in the placenta of SARS-CoV-2 positive women [17, 18]. The placenta acts as a good barrier against infection, but several viruses, such as cytomegalovirus and rubella virus, can infect the placenta and cause vertical transmission to the fetus [19]. The angiotensin-converting enzyme 2 (ACE2), which is the key protein for host cell entry of SARS-CoV-2, is observed diffusely in the placenta, including cytotrophoblasts, syncytiotrophoblasts, and extra-villous trophoblasts [1, 19, 20]. The mechanism cannot be clarified pathologically, but if pregnant women has viraemia due to SARS-CoV-2, it can transmit the virus to fetus through the placenta. The studies with larger sample size including women infected at first or second trimester and excluding variables that may affect placental pathologic findings should be needed to establish the association between placental pathology and vertical transmission of COVID-19.

This is the case study that describes the two SARS-CoV-2-positive mothers and their newborns. The newborns were generally healthy, and PCR tests of samples were all negative. Although clinical evidence of vertical transmission was not found in our cases, possibility of placental inflammation is described. As RT-PCR on the placental tissue and viral immunohistochemistry or in-situ hybridization was not available, we were not able to evaluate further. But our cases showed histopathology of intervillitis with intervillous fibrin deposition which is consistent with findings of inflammation in the proven cases of transplacental transmission of SARS-CoV-2 positive mothers. Further investigation on mechanism of vertical transmission and barrier function of placenta is needed, and close monitoring of COVID-19 confirmed mothers and their newborns is required.

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