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SARS-CoV-2 Real-Time PCR Analysis of Neonates Born to Mothers with Active SARS-CoV-2 Infection: A Report of Three Cases

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Abstract

The risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in neonates born to SARS-CoV-2-infected mothers is < 5%, and the number of reports on neonatal SARS-CoV-2 infection is limited. We analyzed SARS-CoV-2 polymerase chain reaction (PCR) results of tests performed on the placenta, amniotic fluid, vaginal discharge, umbilical cord blood, and breast milk of three SARS-CoV-2-infected parturient mothers, and nasopharyngeal swabs, urine, stool, and serum from their neonates. In addition, we used real-time PCR to determine the cycle threshold and quantify the viral load in maternal nasopharyngeal samples, and performed serial testing of neonatal urine, stools, and serum on days 0, 3, 7, 10, and 14 after birth.

Other than the maternal nasopharyngeal specimens and the tracheal specimens from one neonate, all PCR tests were negative. Although one mother had a high viral load and another mother had severe coronavirus disease pneumonia, none of the neonates were infected with SARS-CoV-2. Even if the mother's infection activity is high, that is, the amount of virus is large, the risk of mother-to-child transmission of SARS-CoV-2 can be minimized by taking appropriate infection control measures.

Keywords: SARS-CoV-2; COVID-19; Real-time PCR; Cycle threshold; Neonate; Vertical transmission; Placenta; Amniotic fluid; Vaginal discharge; Breast milk

Abbreviations: COVID-19: coronavirus disease; CS: cesarean section; Ct: cycle threshold; HFNC: high-flow nasal cannula; PCR: polymerase chain reaction; RDS: respiratory distress syndrome; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; TTN: transient tachypnea of the newborn.

Introduction

The risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in neonates born to SARS-CoV-2-infected mothers is 0-4 % [1-6]. There are some case reports and reviews on the possibility of vertical transmission. However, most reports focus on polymerase chain reaction (PCR) tests on nasopharyngeal samples and clinical symptoms of neonates born to mothers with coronavirus disease (COVID-19). Few studies have performed SARS-CoV-2 PCR testing of the placenta, amniotic fluid, umbilical cord blood and vaginal discharge of infected mothers, or nasopharyngeal, stool, urine, and serum samples of neonates born to SARS-CoV-2-infected mothers. We analyzed these specimens

from three SARS-CoV-2 infected parturient mothers and their neonates, including one extremely premature infant. In addition, we report the cycle threshold (Ct) of the real-time PCR, which was used to determine the viral load in the positive specimens, and the results of serial tests of neonatal urine, stools, and serum samples.

Participants

The participants were three pregnant women diagnosed with COVID-19 who were admitted to the University Hospital, Kyoto Prefectural University of Medicine and North Medical Center, Kyoto Prefectural University of Medicine, and their infants. This research was approved by the Kyoto Prefectural University of Medicine Research Ethics Committee (ERB-C-1723), and written informed consent was obtained from the mothers of each neonate.

Case Report

Table 1 shows a summary of clinical characteristics of the three mother-infant case pairs. In all three cases, the infants were delivered by cesarean section, the mother and infant were isolated immediately after birth, and the infant was placed in an incubator after resuscitation. The infants were born between April and July 2020 and underwent 14-day isolation according to recommendations during this period [7].

Table 1: Clinical characteristics of mothers infected with SARS-CoV-2 and neonates born to these mothers.Abbreviations: CS: cesarean section; HFNC: high-flow nasal cannula; RDS: respiratory distress syndrome; TTN: transient tachpnea of the newborn.

	Case 1	Case 2	Case 3
Mother			
Gestational age at COVID-19 diagnosis, wks	$37^{3/7}$	$38^{1/7}$	$25^{2/7}$
Baseline comorbidities	None	None	Asthma, gestational diabetes
Symptoms	Fever, sore throat, dysgeusia, anosmia	Fever, headache, dysgeusia, anosmia	Fever, cough, severe pneumonia
Treatment before delivery	None	None	Dexamethasone, oxygen, HFNC
Delivery mode	Elective CS	Elective CS	Emergency CS
Neonate			
Gestational age at delivery, wks	$38^{5/7}$	$38^{3/7}$	$26^{6/7}$
Birthweight, g	2558	2900	998
Apgar score 1/5min.	8/9	8/8	1/1
Complication	TTN	TTN	RDS
Treatment	Supplemental oxygen	Supplemental oxygen	Mechanical ventilation
Nutrition	Formula	Formula	Formula

The mother was difiagnosed with COVID-19 based on a SARS-CoV-2 PCR test of a nasopharyngeal swab on the 3rd day of the 37th week of pregnancy. She was because a household member had been diagnosed with COVID-19. On admission, she had fever, a sore throat, dysgeusia, and dysosmia but did not develop pneumonia. The infant was delivered on the 5th day of the 38th week of pregnancy by an elective cesarean section. The infant had transient tachypnea of the newborn (TTN) and required oxygen administration for the 1st hour after birth. The infant was discharged on day 11 after birth without any respiratory problems.

Case 2

The mother was a 37-year-old woman who developed fever and fatigue on the 1st day of the 38th week of pregnancy and was diagnosed with COVID-19 based on a SARS-CoV-2 PCR test of a nasopharyngeal swab. After admission, the mother developed headache, dysgeusia, and dysosmia. The infant was delivered on the 3rd day of the 38th week of pregnancy by an elective cesarean section. The neonate had retractive breathing immediately after birth and required continuous positive airway pressure ventilation for 15 minutes and supplemental oxygen. The supplemental oxygen was discontinued on day 1 after birth and the infant subsequently had an uncomplicated clinical course, without further respiratory distress. The mother was discharged day 10 after delivery and the infant was discharged on day 17 after birth.

Case 3

The mother was a 38-year-old woman with a history of asthma and gestational diabetes. She developed a cough on the 2nd day of the 25th week of pregnancy and was diagnosed with COVID-19 based on a SARS-CoV-2 PCR test of a nasopharyngeal swab. On the 6th day of the 25th week of gestation, she developed fever and hypoxemia, and was diagnosed with pneumonia by chest computed tomography. She was treated with dexamethasone and oxygen was administered by a high-flow nasal canula (HFNC). On the 6th day of the 26th week of gestation, her respiratory distress worsened and tracheal intubation was required, so an emergency cesarean section was performed on the same day. The infant had a birth weight of 998 g and was diagnosed with respiratory distress syndrome (RDS) and required mechanical ventilation. The infant underwent patent ductus arteriosus ligation on day 31 and was extubated on day 34. The neonate required supplemental oxygen

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by HFNC at 36 weeks postmenstrual age, but was discharged on day 121 after birth (44 weeks postmenstrual age) without requiring home oxygen therapy.

Results of real-time PCR

Table 2 shows the SARS-CoV-2 real-time PCR test results of the serial maternal and infant samples. A cycle threshold (Ct) value of < 36 indicates a positive SARS-CoV-2 real-time PCR result and Ct values of ≥36 indicate a negative result. In the positive samples, the viral load level is inversely proportional to the Ct value, i.e., lower Ct values indicate higher viral load levels. All mothers were positive for SARS-CoV-2 on nasopharyngeal swabs during labor, but all placental, amniotic fluid, vaginal discharge, umbilical cord blood and breast milk samples were negative. All three neonates were negative on PCR testing of nasopharyngeal, urine, stool, and serum samples collected on the day of birth. In Case Infants 1 and 2, all serial PCR tests performed on the neonatal nasopharyngeal, serum, urine, and stool samples were negative. In Case Infant 3, strict artificial respiration management was required, so it was difficult to collect serial samples other than nasopharyngeal swabs. In Case Infant 3, an increase in tracheal secretion was observed on day 13, so a tracheal secretion sample was collected and PCR was performed, but the result was negative. Histopathological examination was performed on the placentas of Cases 2 and 3. Neither placenta showed chorioamnionitis or funisitis, and immunostaining with anti-SARS-CoV-2 antibody was negative in both cases.

Table 2: Results of real-time PCR tests in each mother with COVID-19 and neonate born to mother with COVID-19.
Numbers in parentheses show the cycle threshold (Ct) value of RT-PCR. A Ct value of < 36 indicates a positive SARS-CoV-2 result on RT-PCR.
*In Case 3 neonate, RT-PCR was performed using tracheal secretions 13 days after birth. This result was negative.
Abbreviations: Ct: cycle threshold; NA: not available; RT-PCR: real-time polymerase chain reaction; SARS-CoV-2: severe acute coronavirus coronavirus 2.

	Days after birth				
	0	**3**	**7**	**10**	**14**
Case 1					
Mother					
Nasopharyngeal swab	+				
Placenta	–				
Amniotic fluid	–				
Vaginal discharge	–				
Umbilical cord blood	–				
Breast milk	–				
Neonate					
Nasopharyngeal swab	–	–	–	–	–
Serum	–	–	–		–
Urine	–	–	–		–
Stools	–	–	–		–
Case 2					
Mother					
Nasopharyngeal swab	+ (14.6)	+ (16.0)	+ (25.0)	– (38.1)	– (37.0)
Placenta	–				
Amniotic fluid	–				
Vaginal discharge	–				
Umbilical cord blood	–				
Breast milk	–				
Neonate					
Nasopharyngeal swab	–	–	–	–	–
Serum	–	–	–	–	–
Urine	–	–	–	–	–

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Stools	–	–	–	–	–
Case 3					
Mother					
Nasopharyngeal swab	+ (29.7)	+ (35.9)	+ (32.0)	+ (33.5)	+ (27.0)
Tracheal secretion	+ (26.7)		+ (22.0)	+ (23.2)	
Placenta	– (41.0)				
Amniotic fluid	–				
Vaginal discharge	–				
Umbilical cord blood	–				
Breast milk	NA				
Neonate					
Nasopharyngeal swab	–	–	–	–	–*
Serum	–				
Urine	–				
Stools	–				

Discussion

We conducted a virological study of two term infants born to mothers with COVID-19 and one extremely premature infant born to a mother with severe COVID-19 pneumonia. In all three mothers, PCR tests performed with maternal vaginal secretions, amniotic fluid, placenta, umbilical cord blood, and neonatal nasopharyngeal swab, blood, urine, and stools gave negative results. Mother-to-infant transmission of SARS-CoV-2 around the time of birth, may occur via vertical transmission or via horizontal transmission including droplet infection. We were able to significantly limit the risk of horizontal transmission by isolating the mothers and infants immediately after birth. The results confirm that there was no vertical transmission in these three mother-infant pairs.

In past reports, positive SARS-CoV-2 PCR test results have been reported in placental [8,9], amniotic fluid [10], and breast milk [8] specimens of parturient mothers infected with SARS-CoV-2. Although these cases raise the possibility of vertical transmission in one case in which the placenta was positive [8], the neonate was not infected. Therefore, it is not clear whether the neonatal infection can be acquired by vertical transmission in utero. Previous reports analyzing PCR of SARS-CoV-2 in maternal placenta, amniotic fluid, and vaginal discharge are limited, and this report could provide useful information.

Furthermore, in this study, the viral load was evaluated with real-time PCR in two cases. Although the mother in Case 2 had mild symptoms, her viral load was very high, and the mother in Case 3 had severe COVID-19 pneumonia, yet neither of their infants became infected. The relationship between maternal clinical disease severity and risk of transmission to neonates is unclear [5]. Furthermore, the risk factors mother-to-child transmission, such as delivery patterns, breastfeeding, and mother-infant contact, have been investigated but remain unclear [1]. Although our study is limited by the small number of cases, we demonstrated a high level of viral shedding by mothers even in mild illness. Appropriate infection control measures at birth and post-partum, even if infants born to mothers with a high viral load, including severe pneumonia, could significantly reduce the risk of mother-to-neonate transmission.

Conclusion

We performed real-time PCR on placenta, amniotic fluid, and vaginal discharge in three SARS-CoV-2 infected mothers and confirmed that they were all negative. In addition, we performed serial real-time PCR testing of nasopharyngeal, serum, urine, and stool samples of their three infants, including an infant with extreme prematurity, and did not detect SARS-CoV-2 infection in any of the infants. Even if the mother's infection activity is high, and the maternal viral load is large in respiratory samples, it is likely that the risk of infection between mother and child can be minimized by taking appropriate infection control measures.

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Conflicts of Interest

The authors declare no conflict of interest.

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