**Sequential analysis of viral load in a neonate and her mother infected with SARS-CoV-2**

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**ABSTRACT**

We report changes in viral load over time in a 27-day old neonate with COVID-19 who presented with fever, cough, and vomiting. SARS-CoV-2 RNA was detected in the nasopharynx, oropharynx, stool, saliva, plasma, and urine. The highest viral RNA copies in nasopharynx decreased over time while viral load in stool remained high.

Keywords: SARS-CoV-2, COVID-19, coronavirus, neonate, viral load

## INTRODUCTION

The coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) started in China and rapidly spread worldwide, resulting in a pandemic [1]. As COVID-19 cases surge, the number of children with COVID-19 is also on the increase. Since the report of the first pediatric case in Korea, 619 cases aged <20 years (6.46% of the total cases) with COVID-19 have been reported, as of March 29, 2020 [2, 3]. Limited reports from China described the clinical manifestation of children with COVID-19 to be mild, and asymptomatic infections are not uncommon [4, 5].

However, it is difficult to infer whether neonates under 28 days of age with COVID-19 follow a similar clinical course because the immune system in early life is unique. Currently, only three descriptive studies on neonates with COVID-19 have been reported, and to our knowledge, none have investigated viral dynamics in infected neonates [6–8]. In this study, we described the clinical manifestation of COVID-19 in a neonate and her mother, and further analyzed the viral load kinetics of SARS-CoV-2 in clinical specimens from different sources.

## METHODS

### Clinical analysis

A 27-day old neonate and her mother were diagnosed with COVID-19 and hospitalized at Seoul Metropolitan Government-Seoul National University (SMG-SNU) Boramae Medical Center on March 8, 2020. Their medical records including symptoms and signs, laboratory examination, results of SARS-CoV-2 tests, radiologic findings, and management were reviewed. The exposure route to SARS-CoV-2 was described based on the report by the local government and the history taken from the mother.

### Quantitation of SARS-CoV-2

RNA of the clinical specimens was extracted by using the MagNA Pure 96 DNA and Viral NA small volume kit (Roche, Germany) according to the manufacturer's instructions. Viral RNA was detected by using the PowerChek $^{TM}$ 2019-nCoV Real-time PCR Kit (Kogene Biotech, Seoul, Korea) for amplification of the E gene and the RNA-dependent RNA polymerase region of the ORF1b gene, and quantified with a standard curve which was constructed using in vitro transcribed RNA provided from the European Virus Archive (https://www.european-virus-archive.com). This study was approved by the Institutional Review Board at SMG-SNU Boramae Medical Center and written consent was waived.

## RESULTS

### Diagnosis of COVID-19

The 27-day old baby girl was born by vaginal delivery on February 11, 2020 at 38 weeks and 6 days' gestation with a birth weight of 3.73 kg. The neonate lived at her grandparents' house with her parents and two older siblings. She was directly breastfed from birth. On March 2, 2020, both of her grandparents started to cough and noticed sputum. On March 4, 2020, her mother reported sputum production and a sore throat, followed by chills and myalgia on the next day when the neonate developed nasal stuffiness. The baby's father reported chills and a sore throat on the same day and was confirmed with COVID-19 on March 7, 2020. Accordingly, the remaining family members were all tested for COVID-19, and the neonate and her mother along with her grandparents were confirmed with the diagnosis. The two older siblings tested negative. As the neonate and her mother had not left home since her birth, SARS-CoV-2 seemed to be transmitted from one of the family members, the source of whose infection remains unknown.

### Clinical manifestation

On March 8, 2020, the neonate was hospitalized as she was too young and her mother was admitted in the same isolation room to take care of her. On admission, the neonate had mild fever of 37.6°C and nasal stuffiness. Blood pressure was 82/53 mmHg, heart rate 145/min, respiratory rate 62/min, and $SpO_2$ 95%. Whole body jaundice was observed on physical examination. Lung sounds were clear on auscultation and the abdomen was soft with normoactive bowel sound. Her jaundice was presumed to be breast milk jaundice, which spontaneously resolved within 2–3 days. The neonate developed a fever up to 38.4°C along with tachycardia from the 2$^{nd}$ hospital day and fever lasted for two days. She also had increased frequency of vomiting. From the 3$^{rd}$ hospital day, she started to have a mild cough

yet did not show any signs of respiratory difficulty and was stable without requiring oxygen. No lung lesions were observable on her chest radiographs serially taken on the 1st, 3rd, and 5th hospital days. The neonate's laboratory examination was unremarkable (see Supplementary Table). No organisms grew on blood culture and urinalysis was normal. As the neonate remained well, no antiviral or antibacterial agents were administered. She fed well and continuously gained weight. The neonate's mother remained afebrile and the only complaint she had was a sore throat with mild sputum production. Laboratory findings were normal and serial chest radiographs were unremarkable. As both the neonate and her mother's viral test results were negative from two consecutive nasopharyngeal swab specimens collected ≥24 hours apart, they were discharged home on March 26, 2020.

**Analysis of SARS-CoV-2 RNA**

SARS-CoV-2 RNA was detected in the neonate's clinical specimens from several sources including the nasopharynx, oropharynx, plasma, urine, stool, and saliva specimens (Figure 1A). At the early stage of the infection, the viral load was highest in the nasopharynx ($1.2 \times 10^{10}$ copies/milliliter) followed by oropharyngeal swab ($1.3 \times 10^{8}$ copies/milliliter). The viral load in the respiratory specimens gradually decreased with time and was undetectable after 17 days from the onset of symptoms. Notably, the SARS-CoV-2 RNA in the stool sample remained high (range, $1.7 \times 10^{6} – 4.1 \times 10^{7}$ copies/milliliter) until the 18th day since the onset even though the neonate's gastrointestinal symptoms improved. The neonate also excreted the virus in urine at relatively low RNA copy numbers for more than 10 days. The viral load of the mother's respiratory and stool specimens was approximately 100-fold lower than that of the neonate's on the 10th day from symptom onset (Figure 1B). The mother's plasma and urine specimens were tested negative for SARS-CoV-2. The virus was also not detected in her breast milk.

## DISCUSSION

This study described the viral load kinetics of a neonate, the youngest COVID-19 patient in Korea as of March 29, 2020, and her mother. The neonate was febrile and SARS-CoV-2 RNA was detected in all of her clinical specimens, with high viral loads in the respiratory and stool samples. Her mother had mild symptoms with SARS-CoV-2 RNA detected in the respiratory and stool specimens at low titers. Fortunately, the neonate as well as her mother recovered well without antiviral therapies.

Limited reports on neonates with COVID-19 have been published, all from Wuhan, China [6–8]. A 17-day-old neonate had mild fever, sneezing, intermittent vomiting, and diarrhea [6]. The four other neonates were diagnosed with COVID-19 shortly after the birth from mothers confirmed with COVID-19, and it remains unclear whether the cases were from intrauterine transmission or not [7, 8]. The neonates had mild symptoms and their clinical outcomes were favorable.

An interesting finding in this study is that SARS-CoV-2 RNA was detected in all of the neonate's clinical specimens, including blood, urine, stool, and saliva along with the upper respiratory tract specimens. In comparison, although exposed to the same infection source, only the mother's respiratory and stool specimens were positive for SARS-CoV-2 and at a much lower viral load. These findings suggest that COVID-19 could be systemic in neonates, affecting multiple organs, including the kidney and the gastrointestinal tract. Only approximately 1–15% of the adult patients with COVID-19 had RNAemia, and no child with RNAemia has been reported so far [5, 9, 10]. To fight off virus infections in the absence of maternally transmitted IgG antibody, neonates must rely exclusively on their immature innate immune system and their own, also immature, T cells [11]. This makes them vulnerable to viral infections, including SARS-CoV-2. Although previously reported neonates with

COVID-19 went through favorable clinical courses, careful monitoring on this specific population at high risk is still needed until more data are available.

Recent studies have reported that SARS-CoV-2 RNA could be detected in different types of clinical specimens other than respiratory tract samples [9]. Especially, stool samples could be positive for SARS-CoV-2, irrespective of the presence of gastrointestinal symptoms, and remain positive even for one month [12]. The viral load in this neonate's stool specimen remained high even after the respiratory specimens became negative. Of note, the neonate also excreted the virus in urine at low levels. Although respiratory transmission is the primary route for SARS-CoV-2, presence of SARS-CoV-2 RNA in both urine and stool in the baby is an important finding because these specimens could serve as additional vehicles for virus transmission. Whether the virus detected in urine and stool is viable and infective needs further research. Nevertheless, caregivers need to be educated to practice proper handwashing especially when changing diapers of neonates and young infants in order to prevent the spread of SARS-CoV-2 among household contacts.

This report highlights the different clinical manifestations and viral load kinetics of a neonate and her mother with COVID-19. As neonates could have systemic complications and SARS-CoV-2 could be shed for a long time in their urine and stool, close monitoring of neonates with COVID-19 as well as good hygiene practices by caregivers are essential.

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## FIGURE LEGENDS

**Figure 1.** The RNA (E gene) copies of SARS-CoV-2 over time in different sources of clinical specimens of the neonate (A) and her mother (B) with COVID-19. The dashed line indicates the detection limit ($5.7 \times 10^3$ copies/milliliter). Specimens with undetectable viral load are presented below the dashed line.

Figure 1