Case Series

COVID-19 in Neonates: A Case Series

Petya Angelova Radulova*, Violeta Ivanova Dimitrova, Boriana Petrova Slancheva

Abstract

Background: The WHO named the novel coronavirus infection as COVID-19 on January 7, 2020; it is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The incidence, signs, and symptoms of COVID-19 infection in children are different than those observed in adults. In children, the severity of the infection is mostly mild, but diagnosis and treatment become challenging due to unusual medical presentations and different modes of transmission (eg, vertical transmission).

Case Presentation: We analyzed the symptoms, diagnostic procedures, and challenges faced during the treatment of 3 neonates born to their respective asymptomatic mothers who tested positive in real-time polymerase chain reaction (RT-PCR) for SARS-CoV-2. Of the 3 neonates, 1 was a late preterm neonate and 2 were full-term neonates. All the 3 neonates were retained in the quarantine ward.

One of the neonates developed respiratory distress syndrome within the first 24 hours of birth and was on mechanical ventilation for 3 days. Radiography and lung ultrasound showed inflammation in the lungs. Another neonate had elevated C-reactive protein levels and hence was treated with antibiotics. In all the 3 neonates, platelet count and leukocyte count were normal but lactate dehydrogenase levels were elevated. The throat and nasopharyngeal swab samples and tracheal aspirate were tested using RT-PCR between the first and seventh day after their birth, and all 3 tested negative for SARS-CoV-2. The 3 neonates were discharged after treatment, according to specific discharge criteria.

*Correspondence

Dr Petya Angelova Radulova
Consultant
Neonatal Intensive Care Unit
Neonatology Clinic
University Hospital of Obstetrics and Gynecology "Maichin dom"
Medical University, Zdrave Street, 2
Sofia 1431, Bulgaria

E-mail: petia_radulova@abv.bg

Conclusion: Perinatal COVID-19 infection may result in adverse effects such as fetal distress, premature labor, and respiratory distress syndrome. The infection also leads to abnormal laboratory findings.

Key Words: COVID-19, coronavirus, neonate, respiratory distress syndrome, SARS-CoV-2, dyspnea

Introduction

The incidence, signs and symptoms, diagnosis, and treatment involved in the management of coronavirus disease (COVID-19) in pregnant women are well described in many studies.[1-7] In children, COVID-19 is reported to be less severe compared with that in adults. In a pediatric study conducted by Dong et al[8] in 2020, in China, it mentioned that 86 (11.8%) of 731 confirmed cases were observed in neonates aged < 1 year; of those 86 neonates, the condition was severe in 24% (21) and critical in 5.9%. Fortunately, no deaths were reported among these neonates. A few other studies reported that neonates as young as 2 days old were also affected with COVID-19.[9,10]

It is still not clear whether severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has the potential for vertical transmission. Studies conducted in China did not report detection of the virus in maternal serum, whole blood, amniotic fluid, vaginal mucus, and/or breast milk; but the virus was detected only in the maternal nasopharyngeal specimens.[6,7] However, studies that detected SARS-CoV-2–specific IgM and IgG immunoglobulins in newborns of infected women suggest that transplacental or vertical transmission is possible. The presence of SARS-CoV-2–specific IgM in a neonate indicates that the fetus was infected because IgM antibodies cannot pass the placenta.[11,12] The interpretation of these results is rather limited because of the false-positive IgM results in TORCH infections; hence, further studies are required to assess the potential for vertical transmission of COVID-19.[13]

In this case series, we discuss case reports of 3 neonates, whose mothers were positive for COVID-19 infection, with a different clinical course of the disease. The case reports were prepared according to the CAse REport (CARE) Guidelines.[14]

Case Presentations

The first neonate was born from a fourth pathological pregnancy, with cerclage in the 14th week of gestation. During pregnancy, the mother had infections (rhinoviral infection and vaginal *Escherichia coli* infection) along with elevated levels of WBC and C-reactive protein (CRP), which were treated with multiple courses of antibiotics.

The second neonate was born from a first pregnancy, which was complicated because of a *Staphylococcus aureus* infection during the first trimester. But blood test results were normal before delivery.

The third neonate was born from a third uncomplicated pregnancy.

All the 3 pregnant women were positive for SARS-CoV-2, as confirmed through real-time polymerase chain reaction (RT-PCR), and were asymptomatic before delivery.

Neonate 1

The first neonate was born at 34 weeks of gestation (late preterm). Within the first 24 hours of birth, the neonate progressively developed signs of acute respiratory distress syndrome (ARDS) with shortness of breath, intercostal and xiphoid retractions, expiratory grunting, and decreased oxygen level. As the condition of the neonate rapidly deteriorated, invasive respiratory support was started at 19 hours of postnatal life and IV ampicillin–gentamycin treatment was started. The chest X-ray showed patchy shadows of different sizes and

interlobar pleural effusions. The lung ultrasound (LUS) revealed consolidations in the right lung (Figure 1). As the neonate's condition improved and the subsequent LUS showed reduced lung consolidations, the mechanical ventilation was discontinued after 3 days.

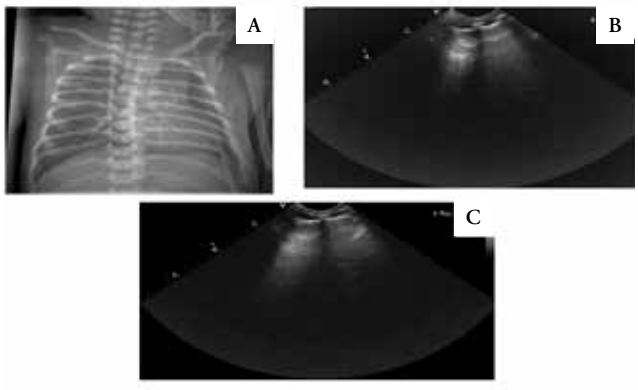

Figure 1. The Chest X-Ray (**A**) and Lung Ultrasound (**B**, Right Lung and **C**, Left Lung) of Neonate 1

Table 1. Clinical Features of the Neonates

	Neonate 1	Neonate 2	Neonate 3
Sex	Female	Female	Male
Gestational Age, wk	34^{+6}	39^{+0}	38^{+0}
Birth Weight, g	2110	2750	2920
APGAR Score in the First Minute	6	7	7
APGAR Score in the Fifth Minute	7	9	9
Clinical Symptoms	Shortness of breath, retractions, reduced oxygen level	No	No
Blood Sample for Neonatal Infection	Normal	Normal	Positive (CRP)
Treatment	Ampicillin–gentamycin IV	No	Ampicillin and Sulbactam
Complications	No	No	No
Outcome	Cured	Healthy	Cured
RT-PCR for SARS-CoV-2 (Tracheal Aspirate and Throat Swab Sample)	Negative (after 36 h and 7 d)	Negative (after 4 d)	Negative (after 4 d)

CRP, C-reactive protein; MV, mechanical ventilation; NICU, neonatal intensive care unit; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

As the clinical examination and LUS were normal and the neonate recovered eventually, the neonate was discharged after 8 days. Table 1 depicts the early postnatal period of the 3 neonates.

Neonate 2

The second (term) neonate had normal postnatal adaptation at birth and tested negative (on day 4) for SARS-CoV-2. The neonate was discharged after 6 days as per our protocol for neonates born of cesarean delivery.

Neonate 3

The third (term) neonate had normal postnatal adaptation. However, the CRP level was elevated (6.3 mg/L; reference range: < 5 mg/L), and treatment with ampicillin and sulbactam was given for 5 days.

Table 2. Laboratory Findings and Imaging Reports of the Neonates

Parameter	Neonate 1	Neonate 2	Neonate 3
Hemoglobin, g/L	165–166	155	174
WBC, $\times 10^9$/L	20.7–13.3	16.2	15.6
Platelet Count, $\times 10^9$/L	261–330	401	206
Lymphocyte, %	17	15	32
CRP, mg/L	2.48–0.24	2.66	6.31
LDH, U/L	965.4	—	797.1
AST, U/L	26.0	—	—
ALT, U/L/	6.1	—	—
Blood Culture	Negative	Negative	Negative
Chest X-Ray	Patchy shadows of different sizes and interlobar pleural effusions	—	—
LUS	Consolidations in the right lung and AIS in the left lung	Normal A pattern	AIS in the right lung and normal A pattern in the left lung
Cranial Ultrasound	IVH grade 2 bilaterally	Normal	Normal

AIS, alveolar interstitial syndrome; ALT, alanine transaminase; AST, aspartate transaminase; CRP, C-reactive protein; IVH, intraventricular hemorrhage; LDH, lactate dehydrogenase; LUS, lung ultrasound; WBC, white blood cell.

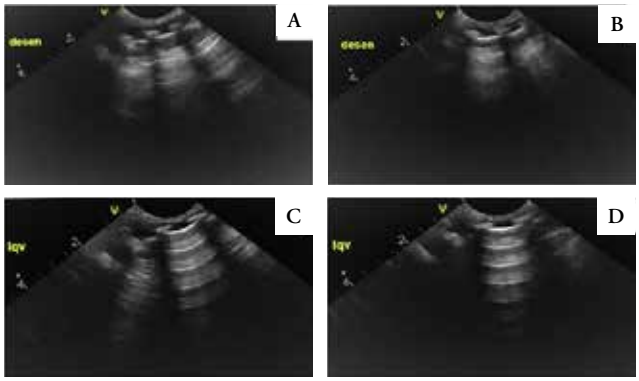

Figure 2. The Lung Ultrasound of Neonate 2 (**A** and **C**, right and left lungs, respectively) and Neonate 3 (**B** and **D**, right and left lungs, respectively)

The neonate was discharged after 7 days after clinical examination, and blood test results were normal as per our protocol for neonates born by cesarean delivery. Table 2 summarizes the laboratory and radiologic evaluations of all the 3 neonates.

In our study, mothers and neonates were kept separately after birth. The mothers were shifted to another facility meant exclusively for treating patients with COVID-19, and the neonates were retained in a separate, isolated department where only neonates born to COVID-19–positive mothers were taken care. The neonates were given formula milk till the mothers were discharged. Although neonates 2 and 3 had no symptoms of respiratory distress syndrome during the hospital stay, we analyzed their lungs with LUS (Figure 2). In neonate 3, normal aeration (A pattern) with only discrete alveolar interstitial syndrome in the right lung was observed, which is a normal finding during the first few days in healthy neonates. All the 3 neonates were followed up with either in-person assessments or on telephone for at least 14 days after discharge.

Discussion

Although the guidelines from international associations are being updated continuously, all aspects of care to be provided to neonates born to women with confirmed or suspected COVID-19 infection continue to be center specific. The treatment to be provided depends on different factors such as availability of protective equipment, diagnostic equipment, building infrastructure constraints, and local guidelines for neonates.

Regarding the perinatal and early neonatal care, some regular practices of care (ie, delayed cord clamping [DCC], mother and newborn contact, and breastfeeding guidelines) were not followed for these 3 neonates because of the COVID-19 restrictions. To reduce the risk of secondary transmission of the coronavirus infection, some experts recommend not to perform DCC in neonates born to mothers with confirmed or suspected SARS-CoV-2 infection.[15] In contrast, because of lack of evidence for the increased risk of secondary transmission, the Royal College of Obstetricians and Gynecologists still recommends to continue DCC according to the standard guidelines.[16] Nevertheless, DCC was not performed in all the 3 neonates presented in this case series. As these neonates were term and late preterm neonates and did not require extensive resuscitation, only a neonatologist with a PPE kit and other safety equipment entered the labor room immediately after the birth and evaluated color, muscular tone, gestational age, heart rate, and respiratory rate and wrapped the neonates in warm blankets and shifted them to prewarmed transport incubators. The neonates were kept away from their mothers, and both the neonates and mothers were admitted to the quarantine wards separately. In contrast to the routine practice, the neonates were not breastfed, which could have negative effects on the long-term outcomes of these neonates. However, almost all international associations highly recommend breastfeeding even if the mother is a suspected or confirmed COVID-19–positive patient.[17,18]

It is also interesting to note that the clinical course and the early neonatal period in neonates born to COVID-19–positive mothers were different. Only the condition of neonate 1 deteriorated with rapidly progressive ARDS and reduced oxygen level; therefore, invasive respiratory support was started. As the RT-PCR test for SARS-CoV-2 from tracheal aspirate of neonate 1 was negative, it is not clear whether this clinical course is more likely connected with the premature birth and the typical problems of late preterm neonates, rather than the COVID-19 infection in the mother. Because of the

PPE kit used by the neonatologist, the vocal cords could not be clearly visualized; as video laryngoscope facility was unavailable in the study center, the intubation procedure was to be followed, which was a new challenge for us.

The nasopharyngeal swab and tracheal aspirate samples were collected from the intubated neonate 1 for initial diagnosis using RT-PCR, which is the only recommended method for qualitative detection of SARS-CoV-2 nucleic acid in respiratory tract specimens.[19] The late preterm neonate 1 was tested twice because of the presence of COVID-19 symptoms. In addition, the early results could be negative because of the incubation period of the virus.

Based on the literature on prior epidemics and recent case series, we decided to use LUS over chest radiography in the diagnosis and monitoring of these 3 neonates. The LUS was mostly preferred because it is easy to use at bedside, economical, and the chances of spread of infection are also less.[20] The radiographic findings were nonspecific, whereas the LUS showed differential lung inflammation (with lung consolidations) and transient tachypnea (with B lines and alveolar interstitial syndrome) in neonate 1. Moreover, we performed serial LUSs to assess the improvement in the condition and the proper time to withdraw the respiratory support. Similarly, neonates 2 and 3 were also analyzed using LUS.

Conclusion

These case reports highlighted the possible effects of maternal COVID-19 infection on neonatal health and possible clinical outcomes that can be expected in such neonates. The COVID-19 pandemic has changed the routine care, as the neonate and the mother had to be separated, and breastfeeding was not possible. Health care workers should come up with innovative treatment strategies to address the challenges they face due to COVID-19. The LUS has the advantage over other imaging techniques in the diagnosis of COVID-19. Based on our results, although mothers test positive for COVID-19 before delivery, the neonates born to infected women may not contract the infection. Further studies are required to prove or confirm the vertical transmission of COVID-19.

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Authors' Affiliations

Dr Petya Angelova Radulova, Neonatologist and Pediatrician; **Dr Violeta Ivanova Dimitrova**, Neonatologist; **Dr Boriana Petrova Slancheva**, Professor, Head of Department, NICU, Neonatology Clinic, University Hospital of Obstetrics and Gynecology "Maichin dom", Medical University, Sofia 1431, Bulgaria