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CASE REPORT OPEN ACCESS

A Case Report on SARS-CoV-2 Positive Neonate with Complex Heart Disease

Jagadish C Das[1] **Mohammad Masudur Rahaman Khan**[2] **Jannatul Ferdous**[3] **Mohammed Shaheen**[2] **Syeda Humaida Hasan**[4] **Adrita Das**[5] **Kamrunnahar Bhuiyan**[6] **Arifa Akther**[7]

[1] *Professor & Head(rtd), Dept. of Neonatology & Dept. of Pediatrics, Chittagong Medical College, Chattogram, Bangladesh*
[2] *Assistant Professor, Dept. of Neonatology, Chittagong Medical College, Chattogram, Bangladesh*
[3] *Registar, Department of Neonatology, Chattogram Medical College Hospital, Chattogram, Bangladesh*
[4] *Consultant, Department of Neonatology, Chattogram Medical College hospital, Chattogram, Bangladesh*
[5] *Biotechnologist, International Centre for Diarrheal Disease Research, Bangladesh, Mohakhali, Dhaka*
[6] *Medical Officer, Department of Pediatrics, Chattogram Medical College Hospital, Chattogram, Bangladesh*
[7] *Assistant Registrar, Department of Neonatology, Chatogram Medical College Hospital, Chattogram, Bangladesh*

In pediatric patients, Coronavirus disease-19 (COVID-19) presents usually without symptoms or with mild to moderate COVID-19. However, infants may present with more severe disease, leading to even respiratory failure. It may adversely affect the course of congenital heart disease (CHD) and vice versa in neonates and small infants. There is limited data about confirmed COVID-19 with CHD in neonates and early infancy. A newborn infant with confirmed COVID-19 was admitted to the Neonatology of Chittagong Medical College Hospital. The case presented with C-Transposition of great arteries, superior-inferior ventricles, large upper muscular VSD with reverse shunt, large ASD with the left to right shunt, moderate right AV valve regurgitation (MR), and severe pulmonary hypertension. The newborn infant was isolated and was treated with antibiotics and cardiac drugs, along with supportive care. Ultimately, the infant deteriorated and expired. A newborn infant might be infected with COVID-19 even if a history of such infection in parents and caregivers is not found. Early identification of COVID-19 in neonates with CHD is essential for planning treatment, including limiting its transmission in the community.
Keywords: Newborn infant, COVID-19, SARS-CoV-2, RT-PCR assay, congenital heart disease

Introduction

Severe acute respiratory syndrome coronavirus (SARS-CoV-2), responsible for pandemic 2019 (COVID-19), goes on infecting more patients with worldwide mortality (1, 2). The virus was first identified in December 2019 in Wuhan, China. In Bangladesh, the first case of COVID-19 was detected in March 2020. Since then, cases have rapidly increased for the next six months, with a decreasing trend in a few months. The incidence has again increased rapidly recently. Although COVID-19 can affect all age groups, the disease is usually milder in children than in adults and may be accompanied by nonspecific symptoms, especially in neonates (3). Data on the neonatal COVID-19 infection are scarce and even scarcer in association with congenital heart disease.

Corresponding Author: Prof. Dr. Jagadish C Das, Professor & Head (rtd), Department of Neonatology & Pediatrics, Chittagong Medical College, Chattogram, Bangladesh
E-mail: jagadishcdas@yahoo.com
ORCID: 0000-0003-3650-5775
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PubMed search was carried out with the words 'Covid-19 with congenital heart disease in neonates', and 18 papers were identified; papers dealing with neonates alone were only 5 in number (4-9). Reports on neonatal COVID-19 are unremarkable in Bangladesh (10). It is further less remarkable in connection with complex congenital heart disease. The case is presented to orient health personnel and other biomedical researchers, particularly on the probability of occurrence of COVID-19 in neonates with congenital heart disease. This may help prevent the transmission of COVID-19 in the community from such neonates through timely measures.

Case Presentation

A 12-day-old female baby patient presented to the Special Care Newborn Unit (SCANU) of Chittagong Medical College Hospital (CMCH) on 4th October 2020 with a history of respiratory distress and bluish discoloration of the body since birth. The newborn infant was delivered by lower uterine caesarean section at 38^{+} weeks of gestation with a birth weight of 2600 g in a maternity center. She breathed spontaneously, and resuscitation was not needed. However, as she had respiratory difficulty and cyanosis since birth, she required hospitalization. She was diagnosed with a case of complex congenital heart disease and was treated with oxygen support, intravenous fluid, and antibiotics. On the ninth day, she was shifted from Chattogram to Dhaka in a private health facility where a nasopharyngeal swab specimen for COVID-19 was collected from the newborn infant. The RT-PCR report of the specimen was positive, and she was referred back to CMCH. Her mother's antenatal period was uneventful. A history of risk factors of previous infection and contact with known COVID-19 patients was not found. Other family members were in good health. She had no history of fever, rhinorrhoea, and gastrointestinal symptoms.

On admission, the infant was cyanosed, icteric up to the thigh, dyspnoeic with respiratory rate 70/min, heart rate 184/min, and SPO^{2} 80%. Temperature and capillary refill time were within normal limits, but she was lethargic. There was a murmur on the precordium. Other physical findings were normal. Her total count of WBC was 15500/mm^{3} with neutrophil-66%, lymphocytes-30%, and platelet count was 70000/mm^{3}. Other laboratory findings included: hemoglobin-15.3 mg/dl, CRP-14.3 mg/L, serum ferritin-380 ng/ml, serum bilirubin-14.9 mg/dl (direct-0.6 mg/dl, indirect-14.3 mg/dl). Serum calcium, serum electrolytes, and blood glucose were normal. Chest x-ray showed ill-defined opacity in the right mid and lower lung zone.

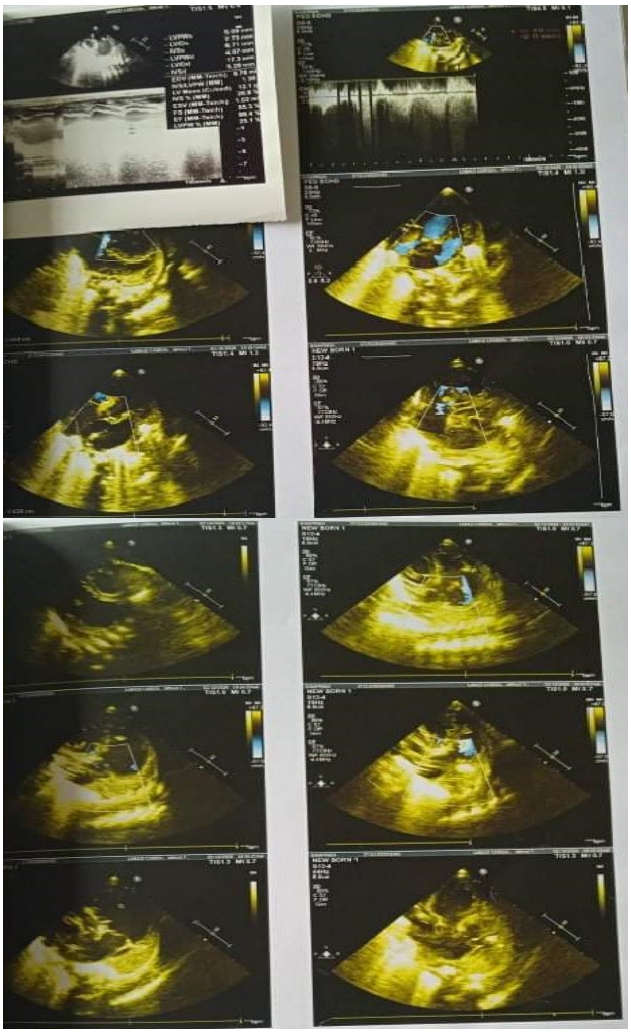


Figure-1. Echocardiographic findings of neonate showing complex CHD

Colour Doppler echocardiography revealed C-Transposition of great arteries, superior-inferior ventricle, large (10 mm size) upper muscular VSD with reverse shunt, large ASD with left to right shunt, moderate right AV regurgitation (MR) and severe pulmonary hypertension (Table-1). The second nasopharyngeal swab sample for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by RT-PCR on the 14th postnatal day was also positive, but both parents were found to be COVID-19 negative. The newborn infant was kept in an isolated room by the side of SCANU in the Department of Neonatology with facilities for essential care. Separate service providers were allocated, and visitors were restricted. Treatment was given with antimicrobials-Meropenam and Linezolid being the last 2, along with general measures. Oxygen was given with a nasal cannula and a head box. Injectable frusemide, digoxin, and oral sildenafil were continued, starting from the 10th postnatal day. After 96 hours of admission in CMCH, the neonate deteriorated and expired at 16 days of her postnatal age.

Discussion

The SARS-CoV-2, belonging to the genus Beta coronavirus, is a single-stranded ribonucleic acid (RNA) virus. The virus is transmitted across humans, primarily through respiratory droplets and contact. Infants and children are affected by this virus, usually with a history of exposure to COVID-19. The median incubation period is five days, ranging from 2 to 14 days (11). Despite COVID-19 being the cause of the pandemic in 2020 and thus affecting a large population worldwide, very few studies were published on neonates to understand its pathophysiology, management, and outcome (11-18).

Children are described to assume a less severe clinical course when infected with SARS-CoV-2 (14). The immature immune system in children may respond to the SARS-CoV-2 differently than adults. This may be responsible for less damaging cytokine reactions. To gain entry, the SARS-CoV-2 binds to angiotensin converting enzyme-II (ACE-2) receptors on type II alveolar epithelial cells in the lower respiratory tract. Although the potential harm of the disease remains largely unknown in neonates, they tend to have more severe disease than older children. There are some prognostic differences within the paediatric population. Neonate is associated with an increased likelihood of admission to the intensive care unit (19, 20). Children may present with COVID-19-related severe cardiovascular complications (21, 22). A few reports showed that these viruses cause direct myocardial injury mediated via angio tensin-converting enzyme-2 (ACE-2) (23, 24). Severe hypoxia from acute respiratory damage caused by the virus may result in oxidative stress and cardiac injury from increased myocardial oxygen demand (25). Congenital heart disease (CHD) is the most common congenital anomaly in neonates, accounting for around 30% of all congenital defects (26). Underlying diseases are likely to predispose to severe manifestation of another disease and have a higher mortality rate. However, evidence of outcomes of COVID-19 in children, especially in neonates with congenital heart disease (CHD), is scarce.

A COVID-19 patient with CHD, especially of cyanotic verity, is more likely to require ICU support with assisted ventilation. COVID-19 may interact with the cardiovascular system differently, increasing morbidity and mortality in patients with CHD (23,24,27-30). COVID-19 may lead to more pronounced hypoxemia and worsened tissue perfusion (21,22). Additionally, patients with complex CHD complicated by depressed myocardial contractility, pulmonary hypertension, and immunodeficiencies (i.e., DiGeorge syndrome) may develop severe and critical COVID-19 (22,31). As per the British Congenital Cardiac Association (BCCA), CHD patients, particularly those with complex diseases, are considered at-risk patients prone to developing severe COVID-19(31). The severity of CHD is an essential factor in predicting the

COVID-19 outcome. Immune dysregulation during the severe phase of COVID-19 following inflammatory cascade and cytokine production may result in an increased risk of vascular permeability and multi-organ failure (32). Septal defects, such as VSD and PDA, are generally considered mild and simple cardiac defects, and aortic/mitral valve diseases are considered of moderate complexity. Based on classification by Alsaied et al., these are considered less vulnerable to COVID-19, whereas those with cyanotic CHD, cardiomyopathy, or depressed cardiac function may be at increased risk for COVID-19 (22). The present COVID-19 neonate with cyanotic complex CHD is categorized into the third category with a worse prognosis.

Again, the fact is that cardiac diseases have been associated with high mortality in low and middle-income countries (33). Hereby, it is difficult to predict the role of SARS-CoV-2 in mortality in this respect. In a study of 26 neonates with confirmed COVID-19 conducted in Bangladesh, two neonates were reported to have congenital heart disease, and both of them eventually died (34). Presentation of COVID-19 in children and neonates can range from asymptomatic infection to severe respiratory distress (3). History and symptoms associated with neonatal population include prematurity, known contacts with sick patients, temperature instability, respiratory symptoms (congestion, tachypnoea, grunting, respiratory distress, apnea), lethargy, vomiting, poor feeding and diarrhoea (35). Fever and gastro intestinal symptoms appear to be the leading presenting symptoms of COVID-19 in most neonates (12,15,16,18), but the present case was afebrile throughout hospitalization.

Normal or reduced white blood cell count, with decreased lymphocyte normal or increased C-reactive protein (CRP), is an essential finding in COVID-19 patients. Procalcitonin (PCT) is standard in most cases. The level of PCT> 0.5 ng/mL indicates the co-infection with bacteria. Elevation of liver enzymes, muscle enzymes, myoglobin, and increased levels of D-Dimer might be seen in severe cases (36). Chest x-ray findings are variable and nonspecific, including unilateral/bilateral ground-glass opacity, lobar or sub-segmental areas of lung consolidation, and pneumothorax, and they are sometimes expected (36). The neonate shows average total and differential white blood cell count with raised CRP (24 mg/L), normal procalcitonin, and normal chest x-ray. These findings are consistent with many of the published case reports where acute phase reactants show a raised level (37). In contrast, some case reports like Aghdam et al. show completely normal laboratory findings (15).

No specific drug treatment for SARS-CoV-2 is similar to MERS-CoV and SARS-CoV (3). Symptomatic and supportive treatment and supplemental oxygen are mainstay of therapy for COVID-19. Maintaining body temperature, water-electrolyte, acid-base balance, and nutrition is essential. Supplementing water and electrolytes should be appropriate to avoid pulmonary edema and hypoxia (3). Data on the application of effective antiviral drugs (i.e., remdesivir or lopinavir/ ritonavir) and anti-cytokine storm (i.e., tocilizumab) for children, including infants with COVID-19 is lacking. Routine use of corticosteroids (dexamethasone, prednisolone) is not indicated. It suggests that low-dose corticosteroids are helpful for patients with severe symptoms, as well as oxygen supplementation and ventilation (38).

The management strategy in the present case is customized according to the neonate's condition and the known effect of COVID-19. Recommendations on management strategies for pediatric patients with CHD might be considered. The general consideration of mild COVID-19 in children does not include patients with CHD. It is necessary to pay greater attention to formulating guidelines for treating pediatric patients, especially neonates with

COVID-19 and CHD (39). A notable aspect of the present case is that though the parents of the neonate were not affected by COVID-19, a history of contact with COVID-19 was also not found, and the newborn infant was COVID-19 positive. Here, the possibility of nosocomial transmission of COVID-19 or transmission from caregivers to the neonate could not be ruled out.

Conclusion

The present case is one of the first few reported neonatal cases of COVID-19 with complex congenital heart disease in Bangladesh. Much is yet to be known about SARS-CoV-2 infection in CHD patients, especially infants. However, it is now considered that severe consequences of COVID-19 may develop in infants with CHD. As COVID-19 goes on, further trials involving CHD infants are required to assess the clinical effect of COVID-19 in these patients. Suspicion of the occurrence of COVID-19 in newborn infants with prompt identification along with appropriate measures is essential to limit transmission of such conditions.

Conflict of Interest

The authors declare no conflict of interest.

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Contact Details

Jagadish C Das
Professor & Head (rtd), Dept. of Neonatology & Dept. of Pediatrics, Chittagong Medical College (CMC), Chattogram, Bangladesh
E-Mail: jagadishcdas@yahoo.com
ORCID: 0000-0003-3650-5775

Mohammad Masudur Rahaman Khan
Assistant Professor, Dept. of Neonatology, Chittagong Medical College, Chattogram, Bangladesh
E-Mail: drmasudrgt@gmail.com
ORCID: 0000-0002-2103-7086

Jannatul Ferdous
Registar, Department of Neonatology, Chattogram Medical College Hospital, Chattogram, Bangladesh
E-Mail: jferdousdr@gmail.com
ORCID: 0000-0003-2997-475X

Mohammed Shaheen
Assistant Professor, Dept. of Neonatology, Chittagong Medical College, Chattogram, Bangladesh
E-Mail: shaheen3388@gmail.com
ORCID: 0000-0002-7578-4482

Syeda Humaida Hasan
Consultant, Department of Neonatology, Chattogram Medical College Hospital, Chattogram, Bangladesh
E-Mail: humaidahaan@yahoo.com
ORCID: 0000-0003-3818-5963

Adrita Das
Biotechnologist, International Centre for Diarrheal Disease Research, Bangladesh (icddr,b), Mohakhali, Dhaka
E-Mail: adritadas03@gmail.com
ORCID: 0000-0002-3171-8352

Arifa Akther
Medical Officer, Department of Pediatrics, Chattogram Medical College Hospital, Chattogram, Bangladesh
E-Mail: arifa.akhee@gmail.com
ORCID: 0000-0006-9391-9930

Kamrunnahar Bhuiyan
Assistant Registrar, Department of Neonatology, Chatogram Medical College Hospital, Chattogram, Bangladesh
E-Mail: kamrunnaharmukta2014@gmail.com
ORCID: 0009-0004-9657-753X

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