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RESPIRATORY CASE REPORTS

COVID-19 PCR (+) Neonatal Mortality: Case Series

COVID-19 PCR (+) Yenidoğan Mortalitesi: Olgu Serisi

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Abstract

We present here the clinical features of five infants who died in the neonatal period due to COVID-19, for which the medical records of COVID-positive pregnant women isolated in a third-level neonatal intensive care unit between December 2019 and October 2021 were evaluated retrospectively. Of the five cases, three were preterm, one had a great artery transposition and another underwent surgery for necrotizing enterocolitis. All of the cases experienced a gradual increase in respiratory distress, and none responded to remdesivir, intravenous immunoglobulin or steroid treatments. COVID-19 infection can be fatal in the neonatal period, especially in the presence of an underlying disease or comorbidities such as prematurity and congenital heart disease.

Keywords: *Covid-19, Newborn, Mortality.*

Öz

Bu çalışmanın amacı yenidoğan döneminde Covid-19 nedeniyle ölen beş bebeğin klinik özelliklerini paylaşmaktır. Aralık 2019 ve Ekim 2021 tarihleri arasında Covid-pozitif annenin bebeği olması nedeniyle üçüncü seviye yenidoğan yoğun bakım ünitesine izolasyon için kabul edilen hastaların tıbbi kayıtları retrospektif olarak incelendi. Beş olgunun üçü preterm, biri büyük arter transpozisyonu ve biri nekrotizan enterokolit nedeniyle ameliyat edilmişti. Tüm vakalarda solunum sıkıntısı giderek arttı. Hastaların hiçbiri remdesivir, intravenöz immünoglobulin ve steroidlere yanıt vermedi. Yenidoğan döneminde Covid-19 enfeksiyonu, özellikle altta yatan hastalık varlığında, prematürite ve konjenital kalp hastalığı gibi komorbiditelerde ölümcül olabilmektedir.

Anahtar Kelimeler: *Covid-19, Yenidoğan, Mortalite.*

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The novel 'severe acute respiratory syndrome coronavirus 2' (SARS-CoV-2) behind the coronavirus disease 2019 (COVID 19) pandemic resulted in severe illness in adult populations around the world. While pregnant women were considered at risk, neonatal infections have been rare. Early data indicated that older adults were at the greatest risk of severe disease and mortality, although pediatric cases (including neonates) have also been reported. That said, the number of documented cases among newborns is considerably lower than in adults (1,2). Respiratory viruses are rarely transmitted in utero, and while the vertical transmission of SARS-CoV-2 was initially considered unlikely, isolated case reports identified SARS CoV 2 RNA in amniotic fluid (3), placental tissue (4) and in the nasopharynx of neonates within 48 hours of birth, suggesting the possibility of congenital infection. The true rate of vertical transmission among infants born to SARS CoV 2–positive mothers remains unknown. In the present study we describe five cases of COVID-19-positive neonates, each of whom was born to a COVID-19-positive mother or father who died in a tertiary care pediatric hospital with a confirmed SARS-CoV-2 infection. Our article focuses on the clinical presentation, management and progression of these cases, highlighting the potential severity of COVID-19 in neonates.

CASE

Neonatal mortality among infants hospitalized at a rural tertiary referral center between December 2019 and October 2021 was reviewed, for which the institutional medical and perinatal death registries were accessed.

Inclusion Criteria:

- Live-born neonates with SARS-CoV-2 infection confirmed by PCR testing.
- Subsequent in-hospital death during the neonatal period.

Exclusion Criteria:

- Stillbirths.
- Suspected cases with negative PCR results.
- Infants who were transferred to other facilities prior to outcome ascertainment.

Clinical Management:

All infants were delivered in negative-pressure isolation rooms. The newborns were immediately separated from their mothers, all of whom had confirmed or suspected COVID 19 infection. Regardless of the neonatal symptoms, all infants underwent a SARS-CoV-2 PCR test at approximately 24 hours of life. If the initial result was negative or unavailable, a second test was conducted at 48 hours. Neonatal care was provided in accordance with institutional COVID-19 neonatal protocols, including respiratory support and pharmacologic interventions. Details of each case are presented below.

Case-1: A female newborn was delivered via cesarean section at 30 weeks' gestation weighing 1450 g. The mother had not received antenatal steroid treatment prior to delivery. The neonate developed respiratory distress, polycythemia and perinatal asphyxia immediately after birth. A cord blood gas analysis revealed a pH of 7.04, base excess of -19.7, lactate 16.6 mmol/L and bicarbonate 10.4 mmol/L. Chest X-ray revealed diffuse ground-glass opacities in the left lung (Figure 1).

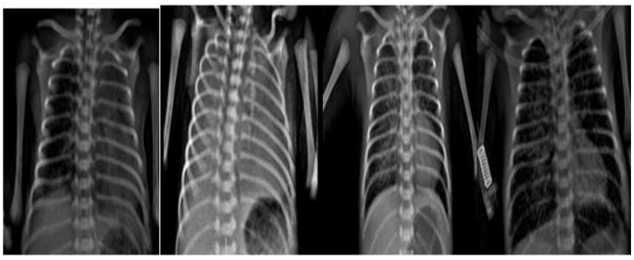

Figure 1: *Case 1 PA Chest X-ray*

The mother delivered at 30 weeks of gestation, and provided a positive nasopharyngeal PCR test at the time of delivery. The neonate's PCR test was positive on day 5. Initial management included partial blood exchange transfusion, the administration of three doses of exogenous surfactant and invasive mechanical ventilation. The infant's hematocrit was 74% at the time of birth, with increased plasma viscosity and thrombocytopenia. Clinical signs included slowed blood flow, features of polycythemia, respiratory distress and need for mechanical ventilation. An 80 ml/kg partial blood exchange was performed to alleviate symptoms, but the infant's condition deteriorated with worsening renal and hepatic function and the progression of radiographic findings to bilateral opacities. Echocardiography (ECHO) detected a hemodynamically significant large patent ductus arteriosus (PDA), alongside poor thermal regulation, increased ventilatory requirements and decreased urine output. After failure of conservative management, two courses of ibuprofen were administered to close the PDA. The infant's escalating respiratory failure prompted the administration of broad-spectrum antibiotics (meropenem, vancomycin, amikacin) and inotropic support (dopamine), and the initiation of high-frequency oscillatory ventilation (HFOV). Pulmonary hypertension was observed, and sildenafil therapy was started. The infant's first two SARS-CoV-2 PCR tests (taken 48 hours apart) were negative but turned positive on day 5. Therapeutic interventions included remdesivir (loading dose 5 mg/kg followed by 2.5 mg/kg/day for 5 days), methylprednisolone (2 mg/kg/day) and intravenous immunoglobulin (IVIG) at 0.4 g/kg/day for 5 days. Despite aggressive treatment, the infant died on day 24 of life due to acute respiratory distress syndrome (ARDS) and multiple organ failure.

Case-2: A male neonate born via cesarean section at 34 weeks' gestation weighing 2400 g presented with cyanosis, respiratory insufficiency, tachycardia and low oxygen saturation. A cord blood gas analysis revealed pH 7.10, base excess -14.5, lactate 6.5 mmol/L and bicarbonate 15.1 mmol/L. Chest X-ray revealed bilateral opacification with pleural effusions, consistent with acute respiratory distress (Figure 2).

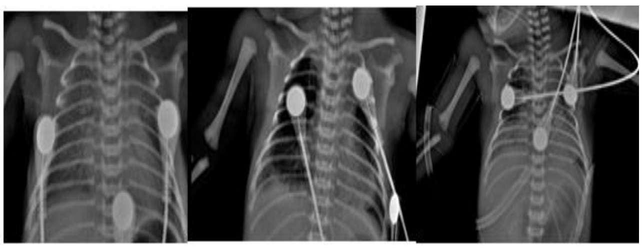

Figure 2: *Case 2 PA Chest X-ray*

The mother's PCR test was positive at the time of delivery, and the neonate's PCR test was also positive on day 0. Echocardiography confirmed the transposition of the great arteries (TGA). Invasive mechanical ventilation was initiated due to progressive hypoxia. An alprostadil (prostaglandin E1 at 0.1 μg/kg/min) infusion was given and an urgent balloon atrial septostomy was performed to improve systemic oxygenation. Additional management included surfactant therapy, cardiovascular support with milrinone and noradrenaline, and inhaled nitric oxide for pulmonary hypertension. Despite the interventions, the infant developed oliguria, hyperammonemia and acute renal failure, necessitating peritoneal dialysis, and his clinical condition had deteriorated further by day 3, complicated by massive pulmonary hemorrhage, ARDS and multi-organ failure. A SARS-CoV-2 PCR test was positive at this time. Despite maximal supportive care, the infant died on day 3 of life.

Case-3: A male neonate was born vaginally at 41 weeks' gestation weighing 3050 g, and developed respiratory distress, low oxygen saturation, shortness of breath and bilateral patchy infiltrates shortly after birth. Chest X-ray revealed diffuse ground-glass opacities in both lungs (Figure 3).

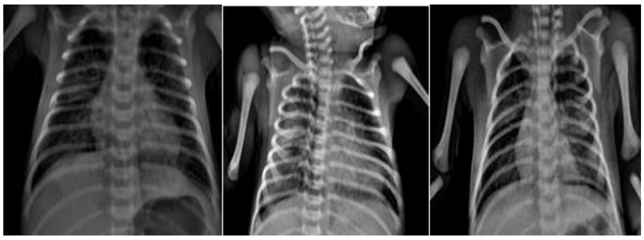

Figure 3: *Case 3 PA Chest X-ray*

PCR tests of the mother and father were negative and positive, respectively, while the neonate provided a positive PCR test 8 days after birth. Initial management included non-invasive respiratory support via CPAP and empirical antibiotics (ampicillin and amikacin). Despite treatment, his respiratory status worsened, and SARS-CoV-2 PCR testing returned positive. Treatment was escalated to invasive mechanical ventilation, with the addition of cefotaxime and the initiation of antiviral and immunomodulatory therapies including remdesivir, methylprednisolone and IVIG. Despite intensive care, the infant developed progressive ARDS, complicated by pulmonary hemorrhage and multi-organ failure, and died on day 13 postnatally.

Case-4: A 19-day-old male neonate, born vaginally at 38 weeks' gestation with an uneventful perinatal course, presented with stage 3A necrotizing enterocolitis (NEC) requiring surgical intervention. The infant had significant perinatal asphyxia (Apgar scores 3, 5, and 6; pH 6.8; base excess –23.1 mEq/L), which likely contributed to intestinal ischemia and NEC. Histopathological examination of the resected bowel revealed transmural necrosis, inflammatory cell infiltration and bacterial colonization. The mother provided a positive PCR test at delivery, while the neonate's PCR test was positive on day 3. Preoperative SARS-CoV-2 PCR testing was positive. Post-surgery, the neonate was intubated and transferred to our tertiary neonatal intensive care unit (NICU) for ongoing management. Upon admission, portal venous thrombosis was detected on Doppler ultrasonography, leading to the initiation of low-molecular-weight heparin (LMHW) therapy. Broad-spectrum antibiotics (meropenem, vancomycin and amikacin), antiviral therapy (remdesivir), methylprednisolone and IVIG were also administered. Although the infant's SARS-CoV-2 PCR tests were initially negative at birth, subsequent tests during hospitalization were positive. Over the following days, liver function and coagulation parameters deteriorated, and thrombocytopenia developed. Platelet transfusions and fresh frozen plasma were provided as needed. Despite aggressive management, the patient suffered massive pulmonary and gastrointestinal hemorrhages on day 25 of life (NICU day 6) as well as acute respiratory distress syndrome (ARDS) and multiorgan failure, leading ultimately to death (Figure 4).

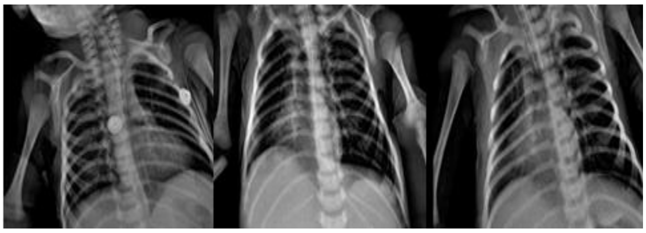

Figure 4: *Case 4 PA Chest X-ray*

Case-5: A male neonate born vaginally at 28 weeks' gestation weighing 1150 g presented immediately after delivery with respiratory distress, complications related to prematurity, perinatal asphyxia and a small patent ductus arteriosus (PDA). The mother provided a positive PCR test at delivery, while the neonate's PCR test was positive on day 0. On day 6, the infant developed life-threatening complications, including massive pulmonary hemorrhage, metabolic acidosis, anemia and thrombocytopenia. Endotracheal intubation was performed, and blood cultures revealed Acinetobacter baumannii bacteremia. The SARS-CoV-2 PCR tests remained positive throughout hospitalization. The infant was treated with broad-spectrum antibiotics, including meropenem, vancomycin and amikacin, as well as inhaled colistimethate (colimycin). Supportive care included transfusions of platelets and red blood cells, as well as fresh frozen plasma. Despite intensive management, the infant succumbed to massive pulmonary hemorrhage on day 10 of life, complicated by ARDS and multiple organ failure secondary to COVID-19 (Figure 5). Table 1 presents a summary of the demographic and clinical characteristics of the five cases, while Table 2 presents the key laboratory findings.

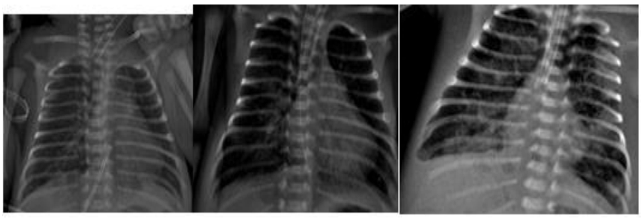

Figure 5: *Case 5 PA Chest X-ray*

Table 1: *Clinical Characteristics and Outcomes of Neonatal COVID-19 Cases*

	Case 1 BY	Case 2 BK	Case 3 BO	Case 4 EK	Case 5 BT
Maternal age(years)	34	26	24	17	22
Gestational age at delivery (weeks)	30	34	41	38	28
Comormidities (GDM, HPD, PE, Hypothyroidism)	NR	NR	NR	NR	NR
Maternal nazopharingeal PCR	Positive	Positive	Negative (father's positive)	Positive	Positive
Mode of delivery	Cesarean	Cesarean	Vaginal	Vaginal	Vaginal
Birth weight (g)	1450	2400	3050	3070	1100
Apgar score (1'/5')	3/5	3/7	8/8	3/5	5/7
Resuscitation requirement (yes/no)	Yes	Yes	No	No	Yes
Neonatal nasopharyngeal PCR	Positive	Positive	Positive	Positive	Positive
Sex	Female	Male	Male	Female	Male

Table 1: *Continued*

Time to positive PCR (days from delivery)	0	0	8	3	0
Maternal mortality	NR	Yes	NR	NR	NR
Clinical signs and symptoms	Severe polycythemia, thrombocytopenia, inflammation (elevated CRP, PCT, ferritin, LDH), metabolic acidosis, bleeding risk (prolonged PT/INR, elevated D-dimer), severe azotemia, severe hypoxemia, pulmonary hemorrhage; liver dysfunction (elevated AST, ALT, bilirubin, hypoalbuminemia)	Severe mixed acidosis, respiratory failure, cyanosis, massive pulmonary hemorrhage, renal failure, perinatal asphyxia, mild anemia and thrombocytopenia, high bleeding risk, liver dysfunction, and hyperammonemia.	Shortness of Breath, Decreased Oxygen Saturation, Dyspnea, Congenital Pneumonia	Severe anemia, thrombocytopenia, coagulopathy, severe renal and liver failure, respiratory failure, metabolic acidosis, NEC stage 3a, portal vein thrombosis, and massive pulmonary and gastrointestinal hemorrhage.	Severe anemia, critical thrombocytopenia, metabolic acidosis, multiorgan failure with severe renal and liver dysfunction, respiratory failure with possible pulmonary and GI hemorrhage, suspected NEC, and hyperkalemia.
Administered drugs and treatment	Surfactant (3 courses), Allopurinol Parsiyel Exchange transfusion, İbuprophen, Meropenem, Vancomycin, Amikacin, Dopamin, Sildenafil	Alprostadil Surfactant, Milrinone, Dopamine, Noradrenalin, inhale Nitric Oksit, Carnitine, Coenzim Q Sodyum Benzoat Peritoneal Dialise, Atrial Septostomi	Ampisilin, Amicasin Sefotaksim,	Meropenem, Vancomycin, Amikacin	Meropenem, Vankomisin, Amikasin, Colimycin
Antiviral therapy, remdesivir	+	-	+	+	-
Ritonavir	-	-	--	-	-
HFOV ventilation	+	-	+	+	+
IVIG treatment	+	-	+	+	-
Corticosteroids (methylprednisolone)	+	-	+	+	-
Respiratory support (HFOV/MV)	HFOV	MV	HFOV	HFOV	HFOV
Main findings of Echocardiography	Large PDA, pulmonary hypertension	c-TGA, perimembranous VSD(3 mm) restrictive PFO	PFO	PFO	Small PDA
Hospital stay(days)	29	3	13	25	10
Day 1, neonatal SARS-CoV-2 RNA (RT-PCR) nasopharyngeal swab	Negative	Positive	NR	Negative	Positive
Day 2-5, neonatal SARS-CoV-2 RNA (RT-PCR) nasopharyngeal swab	Negative	NR	NR	Negative	Positive
Day >5 , neonatal SARS-CoV-2 RNA (RT-PCR) nasopharyngeal swab	Positive	NR	Positive	Positive	Positive
Time of neonatal SARS-CoV-2 RNA (RT-PCR) nasopharyngeal swab positivity, day	14	1	11	19	1
Additional complications or comorbidities	Neonatal asphyxia, prematurity, Grede1 germinal matrix hemoragy	Trasposition of great arteries (ballon atrial septostomy), prematurity	Neonatal pneumonia,	Nekrotizan enterokolitis with colostomy	Neonatal asphyxia, prematurity, periventricular leukomalacia
Neonatal outcomes	Death	Death	Death	Death	Death

Abbreviations: GDM (Gestational Diabetes Mellitus), HFOV (High-Frequency Oscillatory Ventilation), HPD (Hypertensive Disorders in Pregnancy), IVIG (Intravenous Immunoglobulin), MV (Mechanical Ventilation), NEC (Necrotizing Enterocolitis), NR (Not Reported), PE (Preeclampsia), PDA (Patent Ductus Arteriosus), PM (Prematurity), PFO (Patent Foramen Ovale), TGA (Transposition of the Great Arteries), VSD (Ventricular Septal Defect).

DISCUSSION

The clinical course of neonates infected with SARS-CoV-2 remains an area of active investigation, given the severe outcomes and high mortality observed in some cases. In the present study we describe five COVID-19-positive neonates, each born to a COVID-19-positive mother or father, who died while hospitalized in a pediatric tertiary care hospital. This case series highlights the compounded risks associated with prematurity, congenital heart disease (CHD) and immune immaturity in the presence of neonatal COVID-19 infection. Most neonates with SARS-CoV-2 infection are either asymptomatic or present with mild symptoms, and generally result in favorable outcomes (5). That said, severe manifestations can occur, especially in neonates with underlying comorbidities such as prematurity, CHD and immune dysregulation. The mortality rate observed in the presented series is alarmingly high. In a study by Oncel et al. (6) of 120 neonates born to COVID-19-positive mothers, only four of the sample tested positive themselves, suggesting that vertical transmission is a rare event; however, the potential for vertical transmission should not be ignored, especially in cases with severe neonatal infections. The early PCR positivity recorded in Cases 1, 2, and 5 in the present study is suggestive of intrauterine transmission. Premature infants are particularly susceptible to respiratory viral infections, including respiratory syncytial virus (RSV), rhinovirus and parainfluenza viruses, which may exacerbate the clinical course of COVID-19 (7–11). The underdeveloped pulmonary structures and immature immune responses associated with such cases can contribute significantly to poor outcomes. Antigen-specific adaptive response is known to be diminished in neonatal immune systems, leaving preterm infants vulnerable to severe viral infections (11). Furthermore, the immaturity of the respiratory system in infants complicates the management of COVID-19, often leading to rapid respiratory failure (12). Of the five cases presented here, three were born preterm, predisposing them to early respiratory failure due to surfactant deficiency, underdeveloped lungs and immaturity of the immune system. These infants exhibited early respiratory distress, requiring intensive care, and the immaturity of the pulmonary and immune systems, in combination with the SARS-CoV-2 infection increased the risk of adverse outcomes substantially. One neonate developed septic shock due to an Acinetobacter baumannii infection, further complicating clinical management. Bacterial co-infections, particularly with pathogens such as Acinetobacter species, are known to worsen outcomes in the immunocompromised and preterm neonates (8). Although Acinetobacter is not a common neonatal pathogen, its involvement in hospital-acquired infections has been noted, especially among mechanically ventilated infants or those receiving prolonged antibiotics (9). Fetal inflammatory response syndrome (FIRS) has been identified as a critical pathophysiological mechanism contributing to acute respiratory distress syndrome (ARDS) in neonates born to mothers infected with SARS-CoV-2. FIRS is characterized by elevated pro-inflammatory cytokines, including IL-6 and TNF-a, which can provoke an exaggerated neonatal immune response, and such dysregulated inflammations can lead to endothelial injury, alveolar inflammation and, ultimately, ARDS. The neonatal cytokine storms associated with SARS-CoV-2 infection have been reported to cause severe respiratory distress, hypoxemia and multi-organ failure (13-16). When combined with prematurity, this inflammatory cascade creates a vicious cycle of pulmonary dysfunction and systemic inflammation, significantly increasing the mortality risk.

Cases 1, 3, 4 and 5 in the present study were placed on high-frequency oscillatory ventilation (HFOV) due to the need for elevated mean airway pressures (>12 mmHg) and the presence of pulmonary hemorrhage. HFOV increases alveolar recruitment and minimizes barotrauma by delivering rapid, small tidal volumes at a constant mean airway pressure, thereby reducing dependence on conventional mechanical ventilation and preventing ventilator-induced lung injury (17,18). The precise control of mean airway pressure is critical in COVID-19-associated ARDS (19), and the avoidance of excessive tidal volumes and pressures is important in this setting (20).

Congenital heart disease has been shown to increase the risk of severe COVID-19 outcomes in neonates, mirroring the findings in pediatric and adult populations. Children with CHD hospitalized with COVID-19 have higher rates of mechanical ventilation, respiratory failure and acute kidney injury (20). Two neonates with CHD in the presented series experienced rapid respiratory and circulatory deterioration that was attributable to the combined stress of viral infection and the underlying cardiac lesions, and developed myocardial injury, arrhythmia and refractory hypoxemia, underscoring the potential for additional complications arising from SARS-CoV-2 infection in neonates with pre-existing cardiac defects (20). This aligns with a case series in which two deaths were reported among nine pediatric CHD patients infected with COVID-19, both of whom had complex cardiac anomalies (aortic stenosis, hypoplastic left heart syndrome) (20).

Table 2: *Laboratory Findings of Cases*

Parameter	Case 1	Case 2	Case 3	Case 4	Case 5	Normal range
White Blood Cell Count ($x10^9$/L)	27,16	16,78	12,27	33,10	26,26	4-10
Red Blood Cell Count ($\times10^{12}$/L)	6,01	4,32	4,58	4,18	4,67	3,5-5,5
Hemoglobin (g/dL)	21,9	15,3	14,3	8,7	7,7	10-16
Hematocrit (%)	74,2	48,2	48,2	26,4	24,1	55-68
Platelet Count ($\times10^9$/L)	65	186	254	14	9	150-450
Neutrophil Count ($\times10^9$/L)	7,29	9,73	5,92	31,26	1,73	2-7
Lymphocyte Count ($\times10^9$/L)	2,68	4,86	4,58	0,44	0,87	0,8-4,0
Blood Urea Nitrogen (BUN) (mg/dL)	120	17	14	104,8	192	5-20
Creatinine (µmol/L)	1,17	0,83	0,46	1,75	1,12	0,3-0,7
Creatine Kinase (CK) (U/L)	1512	1720	-	450	4639	24-172
Aspartate Aminotransferase (AST) (U/L)	175,3	186,4	81	917,9	211,1	5-34
Alanine Aminotransferase (ALT) (U/L)	212,9	23,1	13,9	189,6	24,4	0-55
Albumin (g/L)	21	18	25	17	17	32-53
Total Bilirubin (mg/dL)	8,28	3,34	1,27	7,18	10,53	0,2-1,2
Direct Bilirubin (mg/dL)	1,09	0,46	0,54	4,09	5,59	0-0,5
Lactate Dehydrogenase (LDH) (U/L)	4294	1231	-	6000	3056	5-746
Sodium (mmol/L)	144	138	140	160	154	135-145
Potassium (mmol/L)	5,02	4,76	4,46	2,74	8,83	3,7-5,9
Ferritin (µg/L)	3755	-	-	1333	-	0-10
Procalcitonin (ng/mL)	2,92	-	0,985	-	4,32	<0,5
D-Dimer (µg/mL)	3,29	-	-	8,7	-	<0,5
Fibrinogen (mg/dL)	206	-	-	296	-	125-300
C-Reactive Protein (CRP) (mg/L)	41,5	2	11,5	125	239	<2
Prothrombin Time (PT) (sec)	15,8	28,7	-	25,2	-	9,5-13,5
Activated Partial Thromboplastin Time (aPTT) (sec)	52,2	94,2	-	46,3	-	<65
International Normalized Ratio (INR)	1,72	2,58	-	2,34	-	<1,3

Table 2: *Continued*

pH	6,34	6,15	6,76	6,78	6,89	7,35-7,45
PCO_2 (mmHg)	146,8	169,2	108,8	84,3	70,5	38-42
PO_2 (mmHg)	19,6	12,8	12,9	22,7	28,1	75-100
HCO_3^- (mEq/L)	10,4	9,4	18,3	6,3	6,1	22-28
Base Excess (BE) (mEq/L)	-17,3	-21,9	-16,1	-21,4	-23,1	-4+4
Lactate (mmol/L)	16,48	16,76	9,33	26	23	0,26-2,21
Oxygen Saturation (%)	25,7	19,3	46	30,5	34,2	94-100

COVID-19-related coagulopathy is a recognized complication in adults and children with CHD (18). This hypercoagulable state, driven by endothelial injury and systemic inflammation, predisposes the patient to thrombotic events, as observed in Case 4, who developed portal vein thrombosis and bleeding complications. Neonates with ARDS and SARS-CoV-2 infection are particularly susceptible to severe hemorrhage due to inflammation-induced vascular fragility and impaired hemostasis. These factors likely contribued to the pulmonary hemorrhages preceding the deaths of several infants in this series (8,9). The combined effects of hypoxemia and systemic inflammation due to SARS- CoV-2 infection can impair intestinal perfusion, promote mucosal ischemia and exacerbate inflammatory injury, thereby increasing the risk and severity of necrotizing enterocolitis (NEC) (13–16). Previous studies have reported cases of term neonates with confirmed perinatal COVID-19 who developed NEC, similar to Case 4 in the present study, highlighting SARS-CoV-2-induced intestinal ischemia and inflammation as a potential mechanism (16). Although vertical transmission remains rare, our findings, and those of other studies, indicate that neonates can test PCR-positive early in life, likely due to intrauterine or intrapartum transmission. This is supported by the early PCR positivity recorded in Cases 1, 2 and 5. Conversely, the delayed PCR positivity recorded in Cases 3 and 4 is likely due to peripartum or nosocomial postnatal exposure, possibly from infected healthcare workers or family members. In all cases, either the mother or father developed COVID-19 symptoms and tested positive postpartum, suggesting lateral transmission in addition to vertical routes. These findings underscore the complexity of SARS-CoV-2 transmission in neonates and emphasize the need for rigorous infection control, including both postnatal screening and the vigilant monitoring of the vertical and horizontal transmission routes.

Study Limitations

This case series has several limitations, including the small sample size and single-center design, both of which restrict the generalizability of the findings. The lack of uniformity in the timing of PCR tests and the methods used may have affected diagnostic accuracy, particularly concerning vertical transmission. Furthermore, the absence of placental and amniotic fluid testing limits the definitive evaluation of in utero transmission. Furthermore, the lack of maternal vaccination data and long-term neonatal outcome data precludes the assessment of the potential protective effects of the vaccine.

CONCLUSION

Neonatal SARS-CoV-2 infections can have fatal consequences, especially in infants with underlying vulnerabilities such as prematurity or congenital heart disease. The immaturity of the immune and pulmonary systems of infants predisposes them to rapid respiratory deterioration, thrombotic complications and multi-organ failure. Early recognition, aggressive respiratory support, careful coagulopathy monitoring and multidisciplinary management are essential for the improvement of outcomes. Clinicians should maintain a high index of suspicion for COVID-19 in neonates, even when the initial PCR results are negative, and particularly in those with such risk factors as prematurity or comorbidities.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - L.Ş., N.O.; Planning and Design - L.Ş., N.O.; Supervision - L.Ş., N.O.; Funding - L.Ş., N.O.; Materials - L.Ş., N.O.; Data Collection and/or Processing - L.Ş., N.O.; Analysis and/or Interpretation - N.O., L.Ş.; Literature Review - L.Ş., N.O.; Writing - L.Ş., N.O.; Critical Review - L.Ş., N.O.

REFERENCES

1. Jiehao C, Jin X, Daojiong L, Zhi Y, Lei X, Zhenghai Q, et al. A Case Series of Children with 2019 Novel Coronavirus Infection: Clinical and Epidemiological Features. Clin Infect Dis 2020; 12:1547-51. [CrossRef]
2. Fu L, Wang B, Yuan T, Chen X, Ao Y, Fitzpatrick T, et al. Clinical Characteristics of Coronavirus Disease 2019 (COVID-19) in China: A Systematic Review and Meta-Analysis. J Infect 2020; 80:656-65. [CrossRef]
3. Zamaniyan M, Ebadi A, Aghajanpoor S, Rahmani Z, Haghshenas M, Azizi S. Preterm Delivery, Maternal Death, and Vertical Transmission in a Pregnant Woman with COVID-19 Infection. Prenat Diagn 2020; 40:1759-61. [CrossRef]
4. Kirtsman M, Diambomba Y, Poutanen SM, Malinowski AK, Vlachodimitropoulou E, Parks WT, et al. Probable Congenital SARS-Cov-2 Infection in a Neonate Born to a Woman with Active SARS-Cov-2 Infection. CMAJ 2020; 192:E647-E650. [CrossRef]
5. Gale C, Quigley MA, Placzek A, Knight M, Ladhani S, Draper ES, et al. Characteristics and Outcomes of Neonatal SARS-Cov-2 Infection in the UK: A Prospective National Cohort Study Using Active Surveillance. Lancet Child Adolesc Health 2021; 5:113-21. [CrossRef]
6. Oncel MY, Akın IM, Kanburoglu MK, Tayman C, Coskun S, Narter F, et al. A Multicenter Study on Epidemiological and Clinical Characteristics of 125 Newborns Born to Women Infected with COVID-19 by Turkish Neonatal Society. Eur J Pediatr 2021; 180:733-42. [CrossRef]
7. Lingappan K, Karmouty-Quintana H, Davies J, Akkanti B, Harting MT. Understanding the Age Divide in COVID-19: Why Are Children Overwhelmingly Spared? Am J Physiol Lung Cell Mol Physiol 2020; 319:L39-L44. [CrossRef]
8. Alassaf A, Ellithy K, Mehta T, Aljbawi W, Ali H, Soliman A, et al. Severe Pulmonary Hemorrhage in a 3-Week-Old Neonate with COVID-19 Infection: A Case Report. Clin Case Rep 2022; 10:e6189. [CrossRef]
9. Russo A, Gavaruzzi F, Ceccarelli G, Borrazzo C, Oliva A, Alessandri F, et al. Multidrug-Resistant Acinetobacter Baumannii Infections in COVID-19 Patients Hospitalized in Intensive Care Unit. Infection 2022; 50:83-92. [CrossRef]
10. García H, Allende-López A, Morales-Ruíz P, Miranda-Novales G, Villasis-Keever MÁ. COVID-19 in Neonates with Positive RT-PCR Test. Systematic Review. Arch Med Res 2022; 53:252-62. [CrossRef]
11. Collins A, Weitkamp JH, Wynn JL. Why Are Preterm Newborns at Increased Risk of Infection? Arch Dis Child Fetal Neonatal Ed 2018; 103:F391-F394. doi: 10.1136/archdischild-2017-313595.12. [CrossRef]
12. Eber E, Zach MS. Long term sequelae of bronchopulmonary dysplasia (chronic lung disease of infancy). Thorax 2001; 56:317-23. [CrossRef]
13. Nomiyama M, Nakagawa T, Yamasaki F, Hisamoto N, Yamashita N, Harai A, et al. Contribution of Fetal Inflammatory Response Syndrome (FIRS) with or without Maternal-Fetal Inflammation in The Placenta to Increased Risk of Respiratory and Other Complications in Preterm Neonates. Biomedicines 2023; 11:611. [CrossRef]
14. Beraud M, Hashami SA, Lozano M, Bah A, Keith P. Role of Therapeutic Plasma Exchange in the Management of COVID-19-Induced Cytokine Storm Syndrome. Transfus Apher Sci 2022; 61:103433. [CrossRef]
15. Schoppen ZJ, Stearns K, Dielentheis K. Severe Maternal Morbidity and Neonatal Mortality after COVID-19 Infection: Case Report. WMJ 2022; 121:E37-E41.
16. Sidatt M, Sghair YM, Ghaddour T, Ahmed MS, Kader FA, Habib L, et al. Neonatal Necrotizing Enterocolitis due to COVID 19: A Case Report. J Neonatal Perinatal Med 2023; 16:165 168.
17. Yang G, Qiao Y, Sun X, Yang T, Lv A, Deng M. The Clinical Effects of High-Frequency Oscillatory Ventilation in the Treatment of Neonatal Severe Meconium Aspiration Syndrome Complicated with Severe Acute Respiratory Distress Syndrome. BMC Pediatr 2021; 21:560. [CrossRef]
18. Barnes ME, Feeney E, Duncan A, Jassim S, MacNamara H, O'Hara J, et al. Pulmonary Haemorrhage in Neonates: Systematic Review of Management. Acta Paediatr 2022; 111:236-44. [CrossRef]
19. Zheng YR, Chen YK, Lin SH, Cao H, Chen Q. Effect of High-Frequency Oscillatory Ventilation, Combined with Prone Positioning, in Infants with Acute Respiratory Distress Syndrome after Congenital

Heart Surgery: A Prospective Randomized Controlled Trial. J Cardiothorac Vasc Anesth 2022; 36:3847-54. [CrossRef]

20. Haji Esmaeil Memar E, Pourakbari B, Gorgi M, Sharifzadeh Ekbatani M, Navaeian A, Khodabandeh M, et al. COVID-19 and Congenital Heart Disease: A Case Series of Nine Children. World J Pediatr 2021;17:71-8.[CrossRef]