JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Coronavirus Pandemic

Apnea or cyanosis as COVID-19 initial presentation in newborns

Carolina Tamayo-Múnera[1], Zoila Margarita Insignares Vizcaino[2], Ana Lucia Torres Millán[2], Laura Niño-Serna[3], Carolina Giraldo Alzate[1], Cesar Augusto Vanegas Diaz[1], Hernan Dario Herrera Salazar[1], Sandra Liliana Gómez Tovar[1], Maria Carolina Caicedo Baez[1], Eliana López-Barón[1]

[1] Pediatric Critical Care Unit. Hospital Pablo Tobón Uribe, Medellín, Colombia
[2] Neonatal Intensive Care Unit. Hospital Pablo Tobón Uribe, Medellín, Colombia
[3] Pediatrician. Hospital Pablo Tobón Uribe, Medellín, Colombia

Abstract

Introduction: The clinical manifestation of coronavirus disease 2019 (COVID-19) infection in newborns varies from asymptomatic infection to severe illness. Apnea or cyanosis as the earliest symptoms is rarely mentioned. The aim of this study is to describe the characteristics of newborns with COVID-19 infection admitted to the neonatal intensive care unit considering cyanosis or apnea as a form of presentation.

Methodology: This is a descriptive observational study with retrospectively collected data. All neonates under 30 days old and preterm infants with corrected gestational age of 44 weeks who had confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection with a positive antigen or reverse transcriptase polymerase chain reaction (RT-PCR) test and who were attended to between March 2020 and March 2022 were included.

Results: During the two years of the study, 410 patients were admitted to the neonatal unit. Twenty-six patients (6.3%) presented with confirmed SARS-CoV-2 infection. The main clinical characteristic at admission was apnea in 55% and cyanosis in 45%. Of the 11 patients admitted with this presentation, eight were diagnosed with COVID-19 acute upper respiratory disease, and three met the definition of COVID-19 bronchiolitis. A large proportion of the patients had a mild infection (65%, n = 17), 31% (n = 8) had a severe infection and only one patient had a critical infection, accounting for 4%.

Conclusions: Apnea and cyanosis can be a manifestation of SARS-CoV-2 infection in newborns, which suggests the need to include it in the diagnostic workup as other viral respiratory infections.

Key words: newborn; cyanosis; apnea; COVID-19; SARS CoV-2; bronchiolitis.

J Infect Dev Ctries 2023; 17(10):1401-1406. doi:10.3855/jidc.17846

(Received 12 January 2023 – Accepted 02 May 2023)

Copyright © 2023 Tamayo-Múnera *et al*. This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic has caused a high burden of morbidity and mortality worldwide, particularly among adults with severe respiratory infections and their complications. In children, ages less than two years and comorbidities have been considered risk factors for severe disease [1,2]. Studies in neonates have largely been case reports and series, and more recently, systematic reviews and meta-analyses [3,4], which have shown a variety of clinical presentations, suggesting a prevalence of mild disease. However, data continue to be scarce for the neonatal population. In the reports, most newborns with positive SARS-CoV-2 tests had asymptomatic infections or mild disease with general symptoms and recovered with hardly any complications [5]. An atypical presentation of SARS-CoV-2 infection has been mentioned in a few published case reports on newborns, with apnea as the initial and/or only presentation of the disease. This disease manifestation has been observed in other viral infections in newborns, such as influenza, respiratory syncytial virus, and metapneumovirus [6].

The objective of this study was to describe the characteristics of newborns with COVID-19 admitted to the neonatal intensive care unit (NICU) from a tertiary center, considering cyanosis or apneas, as a form of presentation that should be taken into account in the neonatal population.

Methodology

This was a descriptive observational study with retrospective data collection. Data were collected from neonates admitted to the NICU at a tertiary care center in Colombia. Most of the admitted neonates were referred from other hospitals. The hospital does not have an obstetrics department, and deliveries occur sporadically. The criteria for neonatal intensive or

intermediate care were defined according to the Colombian National Criteria for Neonatal Care [7].

Population

All neonates under 30 days old and preterm infants with 44 weeks of corrected gestational age who had confirmed SARS-CoV-2 infection with a positive antigen or reverse transcriptase polymerase chain reaction (RT-PCR) test and attended between March 2020 and March 2022 were included. The institutional protocol for diagnosing SARS-CoV-2 infection requires an initial positive test (RT-PCR or antigen); hospitalized patients with an initial negative test are tested a second time with RT-PCR 48 or 72 hours after the first test.

Definitions

Apnea: The American Academy of Pediatrics defines neonatal apnea as the cessation of respiratory movements for more than 20 seconds or a shorter episode associated with bradycardia, cyanosis, or pallor [8].

Bronchiolitis refers to airway inflammation and obstruction of the lower respiratory tract, and is caused almost exclusively by a viral infection in children younger than 2 years and most commonly in the first year of life [9,10].

Table 1. Demographic and clinical presentation variables in newborns with COVID-19 infection.

Variable	N = 26
Age (days), median (IQR)	22.5 days (17.5 - 32)
Female gender, n (%)	13 (50)
Comorbidities, n (%) [a]	11 (34)
Prematurity	9 (31)
Bronchopulmonary dysplasia	3 (12)
Pierre Robin syndrome	1 (4)
ABO incompatibility	1 (4)
Initial symptoms, n (%) [b]	
Cough and rhinorrhea	17 (65)
Fever	10 (38)
Respiratory distress	7 (27)
Apnea	6 (23)
Cyanosis	5 (19)
Hypoactivity	4 (15)
Vomiting	4 (15)
Hypotonia	3 (12)
Irritability	2 (8)
Diarrhea	1 (4)
Length of hospital stay (days), median (IQR)	5 (3 - 6)
Length of PCCU stay (days), median (IQR)	1 (1 – 3)
Length of basic neonatal care stay (days), median (IQR)	2 (1 – 5)
Death from COVID-19, n (%)	1 (4)

[a] Patients may have more than one comorbidity; [b] Patients may have more than one symptom. IQR: interquartile range; PCCU: Pediatric Critical Care Unit.

Severity of COVID-19 in newborns [11]*:*

- *Mild infection:* A newborn with altered temperature regulation, cough, nasal congestion, mild hypoxemia, decreased appetite, diarrhea, or vomiting without dehydration.
- *Severe infection:* A newborn with tachypnea, hypoxemia, respiratory distress, apneas, inability to eat, dehydration, or bloody stools.
- *Critical infection:* A newborn with an altered level of consciousness, respiratory failure, need for mechanical ventilation, septic shock, or multiple organ dysfunction.

Classification of bronchiolitis severity: The Wood-Downes-Ferres severity score was used. Based on this score, this disease was classified as mild (1-3 points), moderate (4-7 points), or severe (8-14 points) [12].

Data collection

All medical records of neonates with SARS-CoV-2 infection admitted to the neonatal/pediatric unit during the first two years of the pandemic were reviewed. The data were collected using the RedCap platform, on which a form was designed with demographic data including the following variables: date of birth, gestational age, postnatal age, and gender; clinical variables such as the onset of symptoms, presenting symptoms of the disease, epidemiological contacts, and comorbidities; care setting (hospitalization, emergency room, NICU, ambulatory care); complications such as respiratory failure, shock, and the use of hemodynamic or ventilatory support; laboratory and diagnostic imaging results; length of stay; and outcome (death or discharge).

Statistical analysis

A descriptive analysis was performed. Qualitative variables were presented as frequencies and proportions, and the normality of quantitative variables was evaluated using the Shapiro-Wilk test. They were reported as the median or mean and interquartile range (IQR) or standard deviation (SD). The data were analyzed using RStudio Version 2022.02.2. This study was approved by the Institutional Ethics Committee.

Results

During the two years of the study, 410 patients were admitted to the neonatal unit, 26 (6.3%) of whom had a confirmed SARS-CoV-2 infection. The median age was 22.5 days (IQR 17.5 - 32), with a minimum age of onset of 9 days and a maximum of 90 days (corresponding to a 26-week premature infant with a corrected gestational

age of 41 + 3 weeks). The median gestational age was 41.5 weeks (IQR 38-44). The median hospital stay was five days with a minimum of two days and a maximum of 38 days. The median stay in the critical care unit was one day and two days for basic care. Forty-two percent of the patients in this group had comorbidities, as described in Table 1, along with presenting symptoms. The mortality rate in this study was 4% (N = 1).

The main admitting diagnosis among the hospitalized patients was a brief resolved unexplained event (BRUE), which occurred in up to 42% (n = 11), and was related to apnea in 55% of these cases and cyanosis in 45% (Table 2). However, once the workout was completed for these patients, eight of the patients admitted for BRUE met the diagnosis of COVID-19 acute upper respiratory disease, and three met the definition of COVID-19 bronchiolitis. The second most common diagnosis was late-onset sepsis. Regarding severity, a large proportion of the patients had a mild infection (65%, n = 17), 31% (n = 8) had a severe infection and only one patient had a critical infection, accounting for 4%. A second test was required for diagnosis in 12% (n = 3) of patients. Only one case was considered an incidental finding in a newborn diagnosed with pyloric hypertrophy who presented with gastrointestinal symptoms and developed a systemic inflammatory response after surgery. The infant had a history of close contact with a relative with active COVID-19 infection, which led to testing.

Table 2. Clinical presentation characteristics of newborns with COVID-19 infection.

Variable	n (%)
Admitting diagnosis, n (%) [a]	
BRUE	11 (42)
Apnea	6 (55)
Cyanosis	5 (45)
Late-onset neonatal sepsis	9 (35)
Acute bronchiolitis	3 (12)
Acute respiratory infection	2 (7)
Pyloric hypertrophy	1 (4)
Final diagnosis, n (%)	
COVID-19 acute respiratory infection	16 (62)
COVID-19 acute bronchiolitis	5 (20)
Late-onset neonatal sepsis	3 (12)
Acute sepsis and bronchiolitis	1 (3)
Severe COVID-19 pneumonia with ARDS	1 (3)
COVID-19 infection characteristics, n (%)	
Mild	17 (65)
Severe	8 (31)
Critical	1 (4)
First test, n (%)	
Positive	23 (88)
Negative	3 (12)

[a] Patients may have more than one diagnosis. ARDS: acute respiratory distress syndrome.

The laboratory and diagnostic imaging characteristics of patients are presented in Table 3. As part of the imaging studies performed, seven patients had echocardiograms, with the described findings and chest images ranging from normal chest X-rays to pneumothorax.

According to the admission and severity criteria established by the Colombian Association of Neonatology, five (19%) patients required admission to the neonatal intensive care unit for acute respiratory failure (critical COVID-19 infection) and severe COVID-19 infection. Eighteen of the admitted patients had intermediate neonatal unit criteria and only three were admitted to basic care from onset.

Three patients (12%) had complications: one with acute respiratory distress syndrome (ARDS) and two (8%) with acute respiratory failure requiring a high-flow nasal cannula. The patient with severe ARDS also had acute kidney failure but did not require renal replacement therapy. Myocarditis was not diagnosed or suspected in any of the patients. The treatments are listed in Table 4.

The only fatality reported was a 40-week newborn with a history of uncomplicated hospital delivery that was admitted at nine days old due to nasal congestion, respiratory distress, and fever, with oxygen requirements on admission to the hospital. He was diagnosed with COVID-19 bronchiolitis and was

Table 3. Laboratory and diagnostic imaging findings in newborns with confirmed COVID-19 infection.

Variable	Result
Laboratory tests	
CRP, median (IQR)	0.05 (0.03 - 0.16)
Leukocytes, mean (SD)	7,965 (2,695)
Neutrophils, median (IQR)	2,500 (1,372 - 2,888)
Lymphocytes, mean (SD)	3,982 (1,831)
Hemoglobin, mean (SD)	13.4 (2.44)
Platelets, mean (SD)	406,650 (187,898)
Sodium, mean (SD)	137.5 (2.9)
Diagnostic imaging	
Chest x-ray [a], n (%)	15 (58)
Normal	7 (27)
Interstitial pattern	7 (27)
Air trapping	3 (12)
Atelectasis	2 (8)
Alveolar pattern	1 (4)
Pneumothorax	1 (4)
Echocardiogram [a], n (%)	7 (19)
Patent foramen ovale	5 (19)
Closing ductus arteriosus	4 (15)
Mild pulmonary branch stenosis	4 (15)
Mild pulmonary hypertension	1 (4)
Severe pulmonary hypertension	1 (4)
Right ventricular dysfunction	1 (4)

[a]: Patients may have more than one finding. IQR: interquartile range; SD: standard deviation; CRP: C-reactive protein.

Table 4. Treatment received by patients.

Variable	n (%)
Oxygen	11 (42)
Simple nasal cannula or mask	8 (31)
High-flow cannula	2 (8)
Invasive ventilation	1 (4)
Prone ventilation	1 (4)
Vasopressor support	1 (4)
Antibiotic	11 (42)
Dexamethasone for COVID-19	1 (4)

started on dexamethasone. Late-onset neonatal sepsis was suspected, and no viral co-infection was found. During the stay, his respiratory condition deteriorated, and pneumothorax was found with secondary respiratory failure and invasive mechanical ventilation. The disease progressed to ARDS, with hypoxemia refractory to conventional mechanical ventilation, starting with high-frequency mechanical ventilation and inhaled nitric oxide. He also had a catecholamine-refractory shock with an inotropic score of 21.5; echocardiographic findings indicated severe pulmonary hypertension, right ventricular dysfunction, and patent ductus arteriosus. The patient was diagnosed with acute kidney injury without the need for dialysis. The total length of hospital stay for this patient was 12 days. Death was directly related to COVID-19 disease.

Discussion

This was a descriptive study of a neonatal population with documented SARS-CoV-2 infection admitted to a tertiary care hospital in a middle-income country during the two years of the COVID-19 pandemic. SARS-CoV-2 infection was documented in 6.3% of newborns admitted to the neonatal unit, whose main clinical characteristic was apnea or cyanosis, followed by late-onset neonatal sepsis, acute bronchiolitis, and only one incidental finding due to another disease. Most cases were considered mild, with only one associated death representing 4% of the series. Prematurity was the main comorbidity associated with positive cases but not with death.

Most of the literature to date on SARS-CoV-2 infection in newborns comes from cases and case series, such as those first reported in China and more recent ones like those reported in Turkey [13,14]. Our population had a 6.3% incidence, which differs from reports such as a recent systematic review that included 72 studies with 236 newborns (mostly case reports or series and descriptive studies) [3], with the largest sample derived from the United Kingdom reporting a 0.6% incidence, and a percentage of these cases being infants born to COVID-19 positive mothers [15]. It also differs from other studies, such as the one in Brazil, which sought to evaluate the epidemiological characteristics of one of the populations most affected by COVID-19, reporting a 23.3% incidence of SARS-CoV-2 infection in newborns [16], or a study published more recently in Turkey, with the highest number of cases worldwide, including 176 cases from 44 neonatal intensive care units [14]. Colombian data reported by the National Institute of Health show 2,158 cases in the newborn population thus far during the pandemic, mostly late-onset (after day 8, 72.5%), with 0.4% mortality directly due to COVID-19 infection [17].

One of the significant findings of our study, which differs from some case series and descriptive studies in this population to date, is the initial clinical presentation with apnea or cyanosis, requiring inpatient monitoring and additional studies, which accounted for 42% of our cases. Respiratory syncytial virus and other respiratory infections in children and newborns are known to present with cyanosis and apnea [18–20]; however, this presentation has not been related to COVID-19 infection. This relationship has been described in scarce and isolated case reports, which included premature and term infants without comorbidities or with comorbidities such as hypoxic-ischemic encephalopathy who presented with critical disease [21–24]. The most significant case series thus far describes five patients with apnea as a manifestation of COVID-19; four of the cases had no comorbidities and occurred in term newborns, except for one patient with a gestational age of 34 weeks [25]. The initial diagnosis for these children was BRUE, since the etiology was not clear at admission, corresponding to 42% of the patients who were later diagnosed with COVID-19 [26]. To our knowledge, this is the largest number of patients reported to date with this manifestation of neonatal COVID-19 infection. Unlike the series described, in which no patient comorbidities were reported, 45% of the patients in our series with cyanosis or apnea as the initial presentation had comorbidities (with prematurity being the most common in up to 36% of the patients), although most did not. Unlike some previously reported cases of critical disease, no other complications occurred in this presentation.

Another COVID-19 manifestation was fever, which led to the suspicion of late-onset neonatal sepsis that occurred in 38% of the patients and was confirmed in 12% of the total population. In another series of patients aged < 60 days who were hospitalized for sepsis, almost 40% had SARS-CoV-2 infection, with fever being the most relevant symptom [27]. The most recent systematic review of COVID-19, which included 236 newborns, reported fever as one of the main symptoms

(found in up to 43.2% of cases), along with respiratory symptoms such as cough, respiratory distress, and tachypnea (46.6%), gastrointestinal symptoms (35.2%), neurological symptoms (primarily lethargy) (23.7%), and dermatological and cardiovascular symptoms [3]. This variety and frequency of symptoms are similar to those reported in our study for most of them (fever and gastrointestinal symptoms), and differs from a multicenter descriptive study of 178 patients in Turkey, whose main presentation was fever (in up to 64% of cases) [14].

Finally, there was only one death in our study, which corresponds to 4% of the described population, unlike the 0.4% reported in Colombia by the National Institute of Health [17], which could be related to the sample size. A systematic review published by García *et al.* reported a 1.7% mortality rate in populations from high- and low-income countries [3]. However, compared with the mortality from other countries with similar limited resource conditions, this mortality rate is lower, considering that studies such as Shah *et al.* reported 16.7% fatalities in a neonatal population, which is somewhat different from the patients presented in Turkey with 0.6% mortality and Brazil with 0.8% [14,16,28]. The latter was similar to what has been reported for high-income countries, such as the United Kingdom, with a 2% mortality rate; however, this was not related to COVID-19 infection, as in our series [15]. The differences in mortality between these populations are caused by multiple factors, ranging from the sample size to the type of neonatal population cared for, together with the treatment arsenal provided. In our setting, no vertical transmission was found, as there were no deliveries at our institution.

The strengths of this study include the fact that it exclusively describes newborn patients cared for at a tertiary care center, where patients with or without comorbidities could be captured, and inpatient observation and follow-up were possible. In addition, it is the largest series reported with an initial diagnosis of BRUE manifesting as apnea or cyanosis as a COVID-19 presentation, which led us to include it in the differential diagnosis of patients admitted with a diagnosis of BRUE. The weaknesses that could affect the case descriptions in this study include the fact that it deals with a neonatal population that is likely to be present at an older postnatal age. Therefore, early onset and vertically transmitted cases reported in other studies may have been lost, with the age of symptom onset in this population being 22.5 days [14,27].

Conclusions

This study describes the largest population of newborn COVID-19 patients initially presenting with cyanosis or apnea. These symptoms can be considered a clinical manifestation of SARS-CoV-2 infection in newborns, which suggests the need to include them in the initial diagnostic tests, as is done with other viral respiratory infections. Although most studies have reported that neonatal COVID-19 infections are mild to moderate, it should be noted that some of these patients may have serious complications requiring specialized care. A stricter, multicenter record of neonatal presentations in middle-income countries is needed to expand the description of these types of presentations, which may change according to geographic and socioeconomic conditions, and to establish diagnostic suspicion patterns with a better assessment of severity and associated mortality.

References

1. Gonzalez-Dambrauskas S, Vasquez-Hoyos P, Camporesi A, Cantillano EM, Dallefeld S, Dominguez-Rojas J, Francoeur C, Gurbanov A, Mazzillo-Vega L, Shein SL, Yock-Corrales A, Karsies T; Critical Coronavirus and Kids Epidemiological (CAKE) Study Investigators. (2022). Paediatric critical COVID-19 and mortality in a multinational prospective cohort. Lancet Reg Health Am. 12:100272. doi: 10.1016/j.lana.2022.100272.
2. Kalyanaraman M, Anderson MR (2022) COVID-19 in children. Pediatr Clin North Am 69: 547–571. doi: 10.1016/j.pcl.2022.01.013.
3. García H, Allende-López A, Morales-Ruíz P, Miranda-Novales G, Villasis-Keever MÁ (2022) COVID-19 in neonates with positive RT-PCR test. Systematic review. Arch Med Res 53: 252–262. doi: 10.1016/j.arcmed.2022.03.001.
4. Trevisanuto D, Cavallin F, Cavicchiolo ME, Borellini M, Calgaro S, Baraldi E (2021) Coronavirus infection in neonates: a systematic review. Arch Dis Child Fetal Neonatal Ed 106: F330–335. doi: 10.1136/archdischild-2020-319837.
5. Hobbs CV, Woodworth K, Young CC, Jackson AM, Newhams MM, Dapul H, Maamari M, Hall MW, Maddux AB, Singh AR, Schuster JE, Rowan CM, Fitzgerald JC, Irby K, Kong M, Mack EH, Staat MA, Cvijanovich NZ, Bembea MM, Coates BM, Halasa NB, Walker TC, McLaughlin GE, Babbitt CJ, Nofziger RA, Loftis LL, Bradford TT, Campbell AP, Patel MM, Randolph AG; for the Overcoming COVID-19 Investigators (2022) Frequency, characteristics and complications of COVID-19 in hospitalized infants. Pediatr Infect Dis J 41: E81–86. doi: 10.1097/INF.0000000000003435.
6. Ricart S, Rovira N, Garcia-Garcia JJ, Pumarola T, Pons M, Muñoz-Almagro C, Marcos MA. (2014) Frequency of apnea and respiratory viruses in infants with bronchiolitis. Pediatr Infect Dis J 33: 988–990. doi: 10.1097/INF.0000000000000365.
7. Troncoso-Moreno G, Galvis-Díaz C, Solano-Suarez JM, Arias-Fernandez D, Cortés-Céspedes H, Navarro-Marroquín SM, Tamayo-Pérez ME, Celis-Castañeda LA, Fernández-Mercado JC. (2020). Criteria for neonatal unit admission and

discharge. Colombian Association of Neonatology 2: 1-22. [Article in Spanish].
8. American Academy of Pediatrics. Task Force on Prolonged Infantile Apnea (1985) Prolonged infantile apnea: 1985. Pediatrics 76: 129-131. doi: 10.1542/peds.76.1.129.
9. Silver AH, Nazif JM (2019) Bronchiolitis. Pediatr Rev 40: 568–576. doi: 10.1542/pir.2018-0260.
10. National Institute for Health and Care Excellence (NICE) (2021) Bronchiolitis in children: diagnosis and management. In: National Institute for Health and Care Excellence: Guidelines. Available: https://www.ncbi.nlm.nih.gov/books/NBK573086/. Accessed: 9 October 2022.
11. Gómez IM, Ramírez DM, Vargas YA, Bertolotto AM, Montealegre AP, López JC (2021) Practical approach to SARS-CoV-2 in newborns. Univ Medica 62: 1-16: e31628.
12. Wood DW, Downes JJ, Leeks HI (1972) A clinical scoring system for the diagnosis of respiratory failure. Preliminary report on childhood status asthmaticus. Am J Dis Child 123: 227–228. doi: 10.1001/archpedi.1972.02110090097011.
13. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, Tong S (2020) Epidemiology of COVID-19 among children in China. Pediatrics, 145: 1-16. doi: 10.1542/peds.2020-0702.
14. Akin IM, Kanburoglu MK, Tayman C, Oncel MY, Imdadoglu T, Dilek M, Yaman A, Narter F, Er I, Kahveci H, Erdeve O, Koc E (2022) Epidemiologic and clinical characteristics of neonates with late-onset COVID-19: 1-year data of Turkish Neonatal Society. Eur J Pediatr 181:1933–1942. doi: 10.1007/s00431-021-04358-8.
15. Gale C, Quigley MA, Placzek A, Knight M, Ladhani S, Draper ES, Sharkey D, Doherty C, Mactier H, Kurinczuk JJ (2021) Characteristics and outcomes of neonatal SARS-CoV-2 infection in the UK: a prospective national cohort study using active surveillance. Lancet Child Adolesc Heal 5: 113–121. doi: 10.1016/S2352-4642(20)30342-4.
16. Leung C (2021) The younger the milder clinical course of COVID-19: even in newborns? Pediatr Allergy Immunol 32: 358–362. doi: 10.1111/pai.13371.
17. National Institute of health. Colombia. (2022) Coronavirus: pregnant and newborns. COVID-19 in Colombia report. Available: https://www.ins.gov.co/Noticias/Paginas/coronavirus-gestantes-y-neonatos.aspx. Accessed: 12 September 2022. [Document in Spanish].
18. Pichler K, Assadian O, Berger A (2018) Viral respiratory infections in the neonatal intensive care unit-a review. Front Microbiol 9: 2484. doi: 10.3389/fmicb.2018.02484.
19. Bochner R, Tieder JS, Sullivan E, Hall M, Stephans A, Mittal MK, Singh N, Delaney A, Harper B, Shastri N, Hochreiter D, Neuman MI; Brief Resolved Unexplained Event Research And Quality Improvement Network (2021) Explanatory diagnoses following hospitalization for a brief resolved unexplained event. Pediatrics 148: e2021052673. doi: 10.1542/peds.2021-052673.
20. Staat MA, Henrickson K, Elhefni H, Groothuis J, Makari D (2013) Prevalence of respiratory syncytial virus-associated lower respiratory infection and apnea in infants presenting to the emergency department. Pediatr Infect Dis J 32: 911–914. doi: 10.1097/INF.0b013e31828df3e3.
21. Loron G, Tromeur T, Venot P, Beck J, Andreoletti L, Mauran P, Bednarek N (2020) COVID-19 associated with life-threatening apnea in an infant born preterm: a case report. Front Pediatr 8: 568. doi: 10.3389/fped.2020.00568.
22. Needleman JS, Hanson AE (2020) COVID-19-associated apnea and circumoral cyanosis in a 3-week-old. BMC Pediatr 20: 382. doi: 10.1186/s12887-020-02282-8.
23. Marsico C, Capretti MG, Aceti A, Vocale C, Carfagnini F, Serra C, Campoli C, Lazzarotto T, Corvaglia L (2022) Severe neonatal COVID-19: challenges in management and therapeutic approach. J Med Virol 94: 1701–1706. doi: 10.1002/jmv.27472.
24. González Brabin A, Iglesias-Bouzas MI, Nieto-Moro M, Martínez de Azagra-Garde A, García-Salido A (2020) Neonatal apnea as initial manifestation of SARS-CoV-2 infection. An Pediatr (Engl Ed) 93: 215–216. doi: 10.1016/j.anpedi.2020.05.008.
25. Krajcar N, Marić LS, Roglić S, Tešović G (2022) Among young infants with uncomplicated COVID-19: should we broaden diagnostic tests for infectious causes of apnea? Pediatr Infect Dis J 41: E301–302. doi: 10.1097/INF.0000000000003536.
26. Tieder JS, Bonkowsky JL, Etzel RA, Franklin WH, Gremse DA, Herman B, Katz ES, Krilov LR, Merritt JL 2nd, Norlin C, Percelay J, Sapién RE, Shiffman RN, Smith MB, Subcommittee On Apparent Life Threatening Events (2016) Clinical practice guideline: brief resolved unexplained events (formerly apparent life-threatening events) and evaluation of lower-risk infants: executive summary. Pediatrics: 137: e20160591. doi: 10.1542/peds.2016-0591.
27. Hassan M, Khalil A, Magboul S, Alomari O, Abdalla T, Alsliman H, Alhothi A, Al Maslamani E, AlAmri M, Soliman A (2021) Neonates and young infants with COVID-19 presented with sepsis-like syndrome: a retrospective case-controlled study. Front Pediatr 9: 634844. doi: 10.3389/fped.2021.634844.
28. Shah B, Dande V, Rao S, Prabhu S, Bodhanwala M (2021) Outcome of COVID-19 positive newborns presenting to a tertiary care hospital. Indian Pediatr 58: 177–179. doi: 10.1007/s13312-021-2136-3.

Corresponding author
Eliana López-Barón, MD, MHPE
Hospital Pablo Tobón Uribe, Calle 78b # 69-240,
Medellín, Colombia. 050034.
Tel: +57 3002516091
E-mail: elopezb@hptu.org.co

Conflict of interests: No conflict of interests is declared.