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SCIENTIFIC LETTER

SARS-CoV-2 infection in neonates attended in the emergency department

Infección por SARS-CoV-2 en neonatos atendidos en Urgencias

Dear Editor:

The impact of SARS-CoV-2 infection on newborns was unknown in the early months of the pandemic. Recent studies have shown that neonatal infection is usually asymptomatic and that severe forms of disease only occur in isolated cases.[1] However, this evidence is mainly based on the monitoring of infants born to mothers with SARS-CoV-2 infection in the first days of life,[2] and few studies have been conducted in this population in other settings.

Our objective was to describe the clinical and epidemiological characteristics of neonates managed at the emergency department (ED) with a diagnosis of coronavirus disease 2019 (COVID-19) and to explore factors potentially associated with severity.

We present a retrospective, observational and descriptive study conducted at the ED of a tertiary care women's and children's hospital. The sample included all newborns (age <29 days) brought to the ED who received a diagnosis of SARS-CoV-2 infection in a 3-year period (14/3/2020-13/3/2023). We excluded cases of asymptomatic infection and repeat visits considered part of the same episode. The diagnosis of SARS-CoV-2 was based on a positive PCR test in a nasopharyngeal aspirate sample. The test used at the beginning of the study (Xpert Xpress CoV-2 plus test; Cepheid, Sunnyvale, USA) was replaced from December 2020 by a multiplex assay that allowed simultaneous testing for SARS-CoV-2, influenza A and B and respiratory syncytial virus (RVS) (Xpert Xpress CoV-2/Flu/RSV plus test; Cepheid, Sunnyvale, USA). We defined severe case as requiring admission to the Pediatric Intensive Care Unit (PICU) or the presence of sequelae at discharge. The following were assessed as possible risk factors: age, sex, pediatric assessment triangle (PAT) in the ED, fever, clinical diagnosis and detection of serious bacterial infection (SBI).

Table 1 Clinical characteristics of newborns with COVID-19, diagnostic tests performed in emergency department and clinical diagnosis.

Clinical characteristics	N = 63
Age	18 (13—24)
Male sex	42 (66.7)
History of disease	2 (2.8)[a]
Fever	50 (79.4)
Duration (hours)	4.5 (2—12)
Maximum temperature (°C)	38 (37.8—38.4)
Temperature in ED (°C)	37.4 (36.9—37.9)
Rhinorrhea	34 (54.0)
Food refusal	19 (30.2)
Cough	15 (23.8)
Irritability	11 (17.5)
Shortness of breath	5 (7.9)
Vomiting	5 (7.9)
Diarrhea	5 (7.9)
Apnea	1 (1.6)
Somnolence/lethargy	1 (1.6)
Diagnostic tests	**n = 63**
Blood count and chemistry-blood culture	45 (71.4)
Urine test-urine culture	46 (73.0)
Lumbar puncture-CSF culture	12 (19.0)
Enterovirus PCR test (blood or CSF)	24 (38.1)
Chest radiograph	1 (1.6)
Clinical diagnosis	
Upper respiratory tract infection	32 (51)
Febrile illness	20 (32)
Bronchiolitis	7 (11)
Acute gastroenteritis	4 (6)

Categorical variables expressed as No. (%) and continuous variables as median (IQR).
Abbreviations: CSF, cerebrospinal fluid; PCR, polymerase chain reaction; ED, Emergency department.
[a] One was a moderately preterm infant with incomplete right bundle branch block, the other had unilateral pyelectasis (left kidney).

The data were analyzed with the statistical software IBM SPSS Statistics for Windows, version 28. The study was approved by the ethics committee of the hospital where the study was conducted (CI PIC-193-23).

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Table 2 Clinical and epidemiological risk factors associated with severe COVID-19 (N = 63).

Factor	Severe COVID-19		*P*
	No (n = 60)	Yes (n = 3)	
Age (days)	18 (13.5–23.5)	26 (15–26.5)	.487
Male sex	39 (65.0)	3 (100)	.545
History of disease	2 (3.3)	0 (0)	1
Abnormal PAT	3 (5.0)	2 (66.7)	.015
Fever	47 (78.3)	3 (100)	1
Clinical diagnosis			
Upper respiratory tract infection	32 (53.3)	0 (0)	.229
Febrile illness	20 (33.3)	0 (0)	.568
Bronchiolitis	4 (6.7%)	3 (100)	<.001
Acute gastroenteritis	4 (6.7)	0 (0)	1
SBI	4 (6.7)	0 (0)	1

Categorical variables expressed as No. (%) and continuous variables as median (IQR).
Abbreviations: PAT, pediatric assessment triangle; SBI, serious bacterial infection.

During the study period, 5498 newborns visited the ED, of who 71 (1.3%) received a diagnosis of SARS-CoV-2 infection; 8 were excluded, resulting in a sample size of 63 patients. Thirty-nine (61.9%) had a household member with SARS-CoV-2 infection (in 20 cases [31.7%], more than one household contact, with the mother being the most frequently involved household member). Five (7.9%) had a PAT with abnormal work of breathing. Table 1 summarizes the clinical and epidemiological characteristics of the patients. Fifty-three patients (84.1%) underwent collection of a nasopharyngeal aspirate sample to test for influenza and RSV at the same time as SARS-CoV-2, which turned out positive for RSV in one (1.6%). Other diagnostic tests were performed in 46 patients (63.9%) (Table 1). Four patients (6.35) had a SBI (prevalence, 6.3%; 95% CI, 2.5–15.2); 3 had a urinary tract infection involving *Escherichia coli* and one bacteremia caused by *Streptococcus agalactiae*. The primary clinical diagnosis was upper respiratory tract infection in 32 patients (51%) (Table 1). Thirty-eight newborns (60.3%) required admission. There were three severe cases (4.8%) corresponding to three patients with bronchiolitis admitted to the PICU. All three underwent testing with a multiplex respiratory panel assay in nasopharyngeal aspirate samples, leading to diagnosis of coinfection by rhinovirus in every case, one of who was the patient that had already received a diagnosis of coinfection by RSV at the ED. Table 2 presents the results of the analysis of the potential risk factors considered in the study. All patients had favorable outcomes and were free of sequelae at discharge.

This study showed that, in spite of the magnitude of the pandemic, the diagnosis of COVID-19 in newborns was rare in the ED. Although different authors have suggested that the neonatal period could be associated an increased risk of severe COVID-19,[3] most of the patients in our study had a mild presentation, with fever being the most common symptom, followed by respiratory and gastrointestinal symptoms, in agreement with other studies.[4] There is insufficient evidence to establish the mechanisms by which newborns, despite the immaturity of their immune system, have a better prognosis compared to adults. It has been hypothesized that the innate immune response, which is predominant in newborns, would prevent the hyperinflammatory response and cytokine storm that can develop in adults.[5]

Three patients had severe COVID-19 requiring admission to the PICU for respiratory support. Of the analyzed factors, only abnormal findings in the PAT and a bronchiolitis diagnosis were associated with severe disease. Similarly, in the multicenter study conducted by Akin et al.,[6] the presence of cough, tachypnea and chest retractions was associated with an increased risk of severe COVID-19. It should be noted that the three patients with severe COVID-19 in our study had coinfection by other viruses, and we were unable to determine the extent to which this factor affected the course of disease.

The limitations of the study include those intrinsic to its retrospective design. Furthermore, it was conducted in a single center, a tertiary care women's and children's hospital, so its findings may not be generalizable to other health care settings. Lastly, the low frequency of severe cases in the sample made it difficult to identify associated risk factors.

In conclusion, most cases of COVID-19 in newborns were mild, and fever and respiratory symptoms were the most common manifestations. An abnormal PAT at diagnosis and the development of bronchiolitis were associated with severe COVID-19.

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Declaration of competing interest

The authors have no conflicts of interest to declare.

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