Gestão & Cuidado em Saúde

Profile of suspected cases of COVID-19 in the Neonatal Intensive Care Unit: management and clinical outcomes

Perfil de casos suspeitos de COVID-19 em Unidade de Terapia Intensiva Neonatal: tratamento e desfechos clínicos

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ABSTRACT

This work aims to analyze the hospitalization profile of newborns suspected of having COVID-19 admitted to the Neonatal Intensive Care Unit, considering the clinical profile, treatment, and outcome for the newborn's hospital discharge. This is a retrospective cross-sectional observational study. Data were used from medical records of newborns admitted to COVID-19 Neonatal Intensive Care Units of a reference hospital in the northern region of Brazil. The searches were carried out using ICD-10 with codes B34.2, P220, and P229, in addition to an active search in the histories of the hospitalization sectors in the period from March 2020 to October 2021. The statistical analysis of the categorical and inferential analysis was done. Statistical processing was carried out using IBM SPSS software, adopting an alpha significance level of 5%. 67 newborns included, 55.2% (N=37) were male, with a gestational age of 34.7±3.87, from the Metropolitan region of Belém (53.7%). Of these 6 cases (8.9%) were positive for COVID-19, the female gender was predominant (66.6%), gestational age was 37.6 ± 2.1, and the route of contamination was family coexistence (83.3 %). The most used therapeutic strategy was Invasive Mechanical Ventilation, with a correlation between support time and gestational age (p-value=0.008).

The hospitalization profile during the studied period corresponded to negative cases of the disease, with children born in 2020, preterm newborns, coming from the metropolitan region of Belém, and with favorable discharge outcomes.

Keywords: COVID-19. Newborn Respiratory Distress Syndrome. Neonatal Intensive Care Units. Health Profile.

RESUMO

Este trabalho busca realizar a análise do perfil de internação de recém- nascidos com suspeita de COVID-19 internados em Unidade de Terapia Intensiva Neonatal, considerando o perfil clínico, tratamento e desfecho para alta hospitalar do recém-nascido. Trata-se de um estudo observacional transversal retrospectivo. Foram utilizados os dados de prontuários de recém-nascidos internados em Unidades de Terapia Intensiva Neonatal de COVID-19 de um hospital de referência na região norte do Brasil. As buscas se deram por meio do CID-10 com os códigos B34.2, P220, P229, além de busca ativa nos históricos dos setores de internação durante o período de março de 2020 a outubro de 2021. Aanálise estatística das variáveis categóricas e inferencial foram realizadas e o processamento estatístico realizado nos softwares IBM SPSS, adotando nível alfa de significância de 5%. 67 recém-nascidos foram incluídos, onde 55,2% (N=37) eram do sexo masculino, com 34,7±3,87 de idade gestacional, proveniente da região Metropolitana de Belém (53,7%). Destes 6 casos (8,9%) foram positivos para COVID- 19, sendo predominante o sexo feminino (66,6%), 37,6 ± 2,1 de idade gestacional, e via de contaminação por convivência familiar (83,3%). Aestratégia terapêutica mais utilizada foi a Ventilação Mecânica Invasiva, com correlação de tempo de suporte a idade gestacional (p- valor=0,008). O perfil de internação do período estudado correspondeu a casos negativos a doença, com crianças nascidas em 2020, recém- nascidos pré-termo, provenientes da região metropolitana de Belém e com desfechos de alta favoráveis.

Palavras-chave: COVID-19. Síndrome do Desconforto Respiratório do Recém-nascido. Unidade de Terapia Intensiva Neonatal. Perfil de Saúde.

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the virus identified as the causative agent of the infectious respiratory syndrome COVID-19, typically presenting asymptomatically or with mild symptoms in children and neonates. Despite generally non-specific symptoms and favorable outcomes, severe cases and fatalities have been reported. Among newborns, deaths accounted for 9% of all fatalities caused by the disease among children and adolescents, while infants aged 28 days to

under 1 year comprised 28% of these deaths (Cui *et al.*, 2021; Federal University Hospitals, 2021; Wald; Schmit; Gusland, 2021).

In Brazil, as globally, there remains an ongoing quest for high-quality scientific evidence regarding COVID-19 in newborns. Numerous documents on this subject were rapidly produced by national entities such as the Brazilian Society of Pediatrics, the Ministry of Health, and the Neonatal Resuscitation Program (BEOZZO *et al.*, 2020).

Studies conducted in countries such as Argentina, China, Belgium, Brazil, Italy, Spain, and the United States indicate that, thus far, manifestations have been observed primarily in the respiratory and gastrointestinal systems. These studies also provide information on the course of the disease, such as the average onset of symptoms, most common initial manifestations (e.g., fever, vomiting, cough, tachypnea), the necessity for Intensive Care Unit (ICU) admission, and the use of Invasive Mechanical Ventilation (IMV), alongside warnings about cases resulting from familial exposure (GIULIANI *et al.*, 2022; RAJAPAKSE; DIXIT, 2021; SARMAN; TUNCAY, 2021).

To enhance the characterization of the Brazilian population, particularly in the northern region of the country, this study aimed to analyze the hospitalization profile of newborns suspected of having COVID- 19 admitted to the Neonatal Intensive Care Unit (NICU), considering the clinical profile, treatment, and outcome for the newborn's hospital discharge.

1 Methodology

This is a retrospective cross-sectional observational study, utilizing data from medical records of newborns admitted to NICUs with COVID-19 at a reference hospital for high-complexity neonatal care. The records, cataloged by numbers, were archived in the Patient Data Management sector, covering the period from March 2020 to October 2021, when the hospital inaugurated specific wings for the clinical profile reported in this research.

The study was conducted in accordance with ethical principles outlined in the Declaration of Helsinki, the Nuremberg Code, and Brazilian research regulations involving human subjects (CNS Resolution 466/12) and received approval from the Ethics and Research Committee of the Santa Casa de Misericórdia Foundation of Pará (FSCMP) (No. 4.648.774).

Data collection was carried out by screening the medical records of neonates with

a history of NICU admission for COVID-19, who were admitted with symptoms of respiratory syndromes or had diagnoses recorded under ICD-10 codes B34.2 (Coronavirus infection of unspecified site), P220 (Neonatal Acute Respiratory Distress Syndrome), P229 (Unspecified Respiratory Distress of Newborn), or whose mothers had suspected or confirmed COVID-19. An active search through the electronic medical record system was also conducted.

Additionally, an active search process was implemented as a strategy to reduce potential sample losses, given that the recording pattern of these patients via ICD-10 was not well established at the pandemic's onset.

Inclusion criteria encompassed all medical records of newborns registered from March 2020 to October 2021 with a history of NICU admission for COVID-19, admitted with respiratory syndrome symptoms or having a mother with suspected or confirmed COVID-19. Excluded were records of admissions in other hospital units and individuals aged 28 days or older at the time of admission. Data were collected from medical records using an evaluation form conducted by the research team.

For statistical analysis, categorical variables were presented as frequencies and numerical variables through measures of central tendency and dispersion. Inferential statistical analysis employed the Chi-square test (χ2) for single-sample analysis. All statistical processing was performed using IBM SPSS software, adopting a 5% significance level (p-value ≤ 0.05).

2 Results

From the initial search quantity of 354 records, 67 were selected pertaining to newborns with suspected COVID-19 admitted to NICUs, meeting the inclusion criteria. The distribution by ICD-10 was as follows: B34.2 with 5 findings, P220 with 22 findings, P229 with 21 findings, and 19 from the active search (Table 1).

Table 1 – Epidemiological profile of suspected COVID-19 cases.

VARIABLES	FINDINGS	Fi[1](=N)	Fr[2](=%)
Sex	Female	30	44.7%
	Male	37	55.2%

Year of birth	2020	36	53.7%
	2021	31	46.2%
Race/color	White	8	11.9%
	Brown	59	88%
Gestational age	Pré-termo	49	73.1%
	Termo	18	26.8%
	Average age	34.7±3.87	-
Origin	Marajó	5	7.4%
	Belém Metropolitan Region	36	53.7%
	Northeast Pará	15	22.3%
	Southwest Pará	4	5.9%
	Southeast Pará	7	10.4%
Incidence of COVID-19	Positive	6	8.9%
	Negative	55	82%
	Not tested	6	8.9%
Discharge outcome	Discharged alive	59	88%
	Deceased	8	11.9%

Caption: [1]Absolute frequency; [2]Relative frequency
Source: prepared by the authors.

The use of Invasive Mechanical Ventilation and supplemental oxygen represented the majority compared to other forms of support, both in terms of their incidence of use and the average duration of applicability (Table 2).

Table 2. Use of ventilatory support.

Ventilatory Support	Fi[1] (=N)	Fr[2] (=%)	Average time in days
Invasive Mechanical Ventilation	39	58.2%	4.13
Non-Invasive Mechanical Ventilation	30	44.7%	1.53
Oxygen	50	74.6%	3.4
Nitric oxide	1	1.4%	0.05

Caption: [1]Absolute frequency; [2]Relative frequency
Source: prepared by the authors.

Aspects such as the gestational age profile of the newborn concerning the use of IMV and length of stay in the NICU were analyzed (Table 3) to understand the influence of these factors on the characterization of hospital stay for these individuals.

Table 3. Association between gestational age, invasive mechanical ventilation, and length of hospital stay among Neonatal Intensive Care Unit patients suspected of COVID-19.

VARIABLES	GESTATIONAL AGE (weeks)				p-value £
	24 – 36		37 – 41		
	N	%	N	%	
IMV[1]					
Yes	34	70.8	5	26.3	0.008*
No	14	29.2	14	73.7	
Length of stay					
Up to 14 days	29	60.4	12	63.2	0.091
15 to 30 days	12	25.0	1	5.3	
30 days or more	7	14.6	6	31.6	
Total	48	71.6	19	28.4	

Caption:[1] Invasive Mechanical Ventilation; £ Chi-Square; *p value < 0.05
Source: prepared by the authors.

Among the inclusion group of this study, 67 (55.2%) newborns were male, with a gestational age of 34.7±3.87 weeks, and the Metropolitan Region of Belém had the highest number of individuals, accounting for 53.7%. Regarding the profile of positive cases, there were 6 positive cases, representing 8.9% of the total cases. The predominance of cases was in females (66.6%), with an average birth age of 37.6 ± 2.1 weeks, and contamination occurred in a familial environment (Table 4).

Table 4. Clinical profile of positive cases.

VARIABLES	FINDINGS	Fi[1](=N)	Fr[2] (=%)
Gestational age	Preterm	2	33.3%
	Term	4	66.6%
	Average age	37.6 ± 2.1	-
Weight	Low	1	16.6%
	Normal	5	83.3%
Sex	Male	2	33.3%
	Female	4	66.6%
Symptoms	Lung secretion	4	66.6%
	Fever	4	66.6%
	Jaundice	3	50%

	Hypoactivity	2	33.3%
	Respiratory discomfort	2	33.3%
X-ray	Infiltrators	2	33.3%
	Opacity	1	16.6%
	No abnormal findings	3	50%
Tests	Rapid test	3	50%
	RT-PCR	3	50%
Form of contamination	Family coexistence	5	83.3%
	Cesarean section	1	16.6%

Caption: [1]Absolute frequency; [2]Relative frequency
Source: prepared by the authors.

3 Discussion

This study aimed to analyze the hospitalization profile of 67 newborns with suspected COVID-19 admitted to NICUs, where 6 (8.9%) cases were confirmed positive, similar to findings in a parallel study conducted in São Paulo, which reported 3 positive cases out of 49 neonates, corresponding to 6.1%. This study also provided comparable information regarding the clinical profile of these patients (BEOZZO *et al.*, 2020; PAVÃO *et al.*, 2020).

The most frequent clinical manifestations in these neonates were pulmonary secretions, fever, jaundice, hypoactivity, and signs of respiratory distress. These findings align with the neonatal COVID-19 clinical profile observed in other studies, which predominantly noted asymptomatic or mild to moderate symptoms in individuals (BENTLIN *et al.*, 2020; CHEN *et al.*, 2020).

The characterization of contamination revealed that 83.3% of cases were due to family contact. This is explained by the fact that one of the primary sources of infection is contact with respiratory droplets from individuals infected with the 2019-nCoV virus, whether symptomatic or not. Close contact, such as family interaction, is a significant transmission source, posing risks through contact with the nose and ocular conjunctiva via contaminated hands and objects (SANTOS *et al.*, 2022; SMITH *et al.*, 2020).

One newborn had contact only with the mother during a cesarean delivery; the mother was not tested for COVID-19 but exhibited flu-like symptoms, which could indicate a case of vertical transmission or contamination through aerosols produced by the mother, healthcare professionals, or other sources in the hospital environment.

Regarding transmission and the type of delivery, whether cesarean or vaginal, there is growing evidence (MOTTA *et al.*, 2024) suggesting a low correlation between

vertical transmission and delivery type. This is consistent with other authors who suggest that factors such as delayed umbilical cord clamping, skin-to-skin contact, feeding methods, or rooming-in also have low transmission rates (KOSTENZER *et al.*, 2021; VARDHELLI *et al.*, 2021).

Neonatal symptoms, such as mild and transient respiratory difficulty observed in other studies (MOTTA *et al.*, 2024), showed a higher correlation with late prematurity or elective cesareans due to severe maternal conditions, rather than with neonatal COVID-19 infection. This suggests that, generally, newborns of mothers diagnosed with COVID-19 are born in good condition.

In this article, 73.1% of the newborns were premature, with an average gestational age of 34 weeks and 1 day. A cross-sectional study conducted in Western Europe in 2021 presented similar data, where the majority of participants were parents of preterm newborns (PTNs), accounting for about 71% (KOSTENZER *et al.*, 2021). This aligns with the integrative review linking prematurity to COVID-19, with an average gestational age of 30 weeks and 2 days (COLLETI JUNIOR *et al.*, 2020; PONTUAL *et al.*, 2021).

PTNs are all infants born before 37 weeks and 6 days of gestation (BLENCOWE *et al.*, 2013; GRUENDING *et al.*, 2023). This population, due to their pulmonary immaturity, may have a surfactant deficiency in the alveoli, compromising lung function. The low alveolar tension caused by a lack of surfactant facilitates pulmonary atelectasis and difficulties in maintaining respiratory comfort (YUE *et al.*, 2021).

Newborns may present varying levels of respiratory distress, depending on their gestational age and the degree of hyaline membrane disease, resulting in a greater need for respiratory support (ALMEIDA *et al.*, 2022; ARAUJO *et al.*, 2021). This condition can also complicate the differentiation of COVID-19 diagnosis when the newborn has risk factors such as a mother with a confirmed COVID-19 diagnosis (DA SILVA *et al.*, 2021).

The comparison of gestational age and hospitalization duration in this study did not show the proposed statistical significance. However, it indicated that PTNs have a longer hospital stay compared to term infants. Articles discussing maternal complications have shown that gestational complications can promote prematurity and its clinical conditions, as well as increase hospitalization time. Clinical instability in the mother can lead to fetal distress and reduced nutrient and oxygen supply (ALBERT EINSTEIN, 2023; DE FREITAS; ALVES; GAÍVA, 2020).

Regarding the use of IMV in neonates, 58.2% of cases required this type of ventilatory assistance. This result differs from Oncel *et al*. (2021), where the rate was only 6.4% out of 125 neonates, and Vardhelli *et al*. (2021), which reported 2% out of 692 newborns. The average duration of IMV use found in this study was 4 days.

In comparing term and preterm neonates, there is a higher rate of invasive ventilatory support use among preterm newborns, 70.8% (p=0.008). These findings are consistent with other studies, such as Lima *et al*. (2015), conducted at the same reference hospital, which showed that the hospitalization profile of newborns indicated prematurity as the main cause of NICU admission, with 69.1% of cases requiring IMV and 92.1% requiring physiotherapeutic assistance.

A 2021 study at a maternal-infant care reference hospital in China analyzed mechanical ventilation use in hospitalized PTNs and found that 33.5% of preterm infants needed IMV, with pulmonary and neural immaturity as the primary risk factors for these patients' lives (YUE *et al*., 2021).

The use of supplemental oxygen had a rate of 74.6%, with an average duration of 3 days. These high percentages can be explained by prematurity-related causes (LIMA *et al*., 2015; ONCEL *et al*., 2021; VARDHELLI *et al*., 2021). It is important to note that, so far, there is no clarity about the safety of respiratory support care strategies or mortality risk.

The choice of respiratory support therapy should be based on the newborn's physiology and pathophysiology, following the best available evidence in neonatal intensive care according to international guidelines (DE FREITAS; ALVES; GAÍVA, 2020).

The general clinical treatment for positive newborns is symptomatic and supportive, involving homeostasis maintenance, close monitoring of blood tests, chest radiography, prevention and treatment of complications, and initiation of respiratory support if necessary. One priority is detecting acute neonatal respiratory disorders to classify clinical severity and provide ventilatory support according to guidelines and the best available evidence (SANTOS; BARROS; DELDUQUE, 2019).

This study has some limitations. Although conducted at the largest maternal-infant reference unit in the State of Pará, being limited to a single specialized care center restricted the research quantity since other hospitals were also receiving this patient profile. Additionally, the article focused on high-complexity hospitalizations, leading to potential sample losses of neonates with milder symptoms. Moreover, newborns of

mothers with flu-like syndrome but negative COVID-19 test results were included, posing a bias risk.

Final considerations

The findings of this study indicate that the hospitalization profile of newborns with suspected COVID-19 in the NICU of a reference hospital in the State of Pará between 2020 and 2021 corresponds to negative cases of the disease, preterm newborns, primarily from the metropolitan region of Belém, with favorable discharge outcomes.

The results provide a temporal snapshot of the disease's impact and characteristics on the neonatal population at one of Pará's reference hospitals. Besides representing the northern region of Brazil, which has unique geographical characteristics, this study raises the possibility of extending findings to other reference centers in Brazil and worldwide, contributing to increasingly robust data on the neonatal population.

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