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Bronchiolitis in Pediatric Intensive Care Units in Brazil: a single centre study

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Abstract

Objective: identify the epidemiological characteristics of children with bronchiolitis hospitalized in pediatric intensive care units of a public emergency hospital. Methods: this quantitative cross-sectional study collected data from electronic medical records using a semi-structured instrument with items regarding sociodemographic and clinical characteristics of children with bronchiolitis hospitalized in the pediatric intensive care unit from April 2018 to April 2020. Results: a total of 73 children were included. Most children were under six months old (56.16%) and male (60.27%), and the most frequent causative agent of bronchiolitis was viral (75.34%). Children under invasive mechanical ventilation tended to have severe acute respiratory syndrome as a complication ($p = 0.022$) and death as an outcome ($p = 0.001$). Conclusions: prematurity, male gender, low weight, age below six months, and congenital heart disease were associated with severe bronchiolitis, which may progress to acute respiratory failure or severe acute respiratory syndrome. Mechanical ventilation reduced mortality and improved the clinical condition of children with bronchiolitis, especially in severe cases.

INTRODUCTION

Acute viral bronchiolitis (AVB) affects mainly the bronchioles, causing mucosal inflammation, edema, and congestion in airways. Also, this inflammation reduces the airway caliber and obstructs the airflow, impairing breathing.[1] AVB is one of the main acute respiratory diseases affecting infants and has clinical relevance due to the high morbidity. Moreover, the main causative agent of AVB is the respiratory syncytial virus (RSV), and its circulation increases, especially during autumn and winter. Infants born with less than 37 gestational weeks, low weight, heart or chronic lung disease (e.g., bronchopulmonary dysplasia), or immunodeficiency have a high risk of being severely infected with RSV, requiring hospitalization in pediatric intensive care units (PICU).[2,3]

RSV infection impairs lung function (especially on the fifth day), representing a major health challenge since its treatment depends on the severity and may progress to respiratory failure. Oxygen therapy is a supportive measure for mild cases, while noninvasive (NIV) and invasive mechanical ventilation (IMV) are used in moderate and severe cases involving acute respiratory failure (ARF). These measures are combined with salbutamol with hypertonic solution and bronchodilators, especially in patients with respiratory distress and requiring nasogastric tube feeding. However, the patient evolves to death if these measures are insufficient.[1,4,5]

About 75% of children with bronchiolitis hospitalized in PICU require ventilatory support, and 18% of these will need IMV because the disease severity may lead to respiratory distress. However, technological advances in PICU reduced the mortality related to severe bronchiolitis.[6,7] In this sense, AVB is one of the main causes

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of hospitalization in PICU and may cause irreversible impairment of airways, resulting in reduced lung function that may remain the entire life.[5,8]

Intrinsic (e.g., comorbidities, disease severity at admission, and age) and extrinsic factors (e.g., health team experience, available resources, and clinical protocols) influences the prognosis of a child in severe condition in PICU.[9] Thus, this study aimed to identify the epidemiological characteristics of children hospitalized with bronchiolitis in PICU at an emergency hospital.

METHODS

This quantitative cross-sectional study was conducted at two PICUs of a public emergency hospital in Goiás (Brazil) using electronic medical records of children with bronchiolitis admitted from April 2018 to April 2020.

The inclusion criteria were children with bronchiolitis of both genders and aged from 29 days to 2 years, with one or more of the following comorbidities: congenital heart or gastroesophageal reflux disease, bronchopulmonary dysplasia, pulmonary hypertension, neuropathy, immunosuppression, respiratory complications, hypoxic-ischemic encephalopathy, epilepsy, spinal muscular atrophy (type I), pertussis, asthma, hemolytic anemia, seizure, hypospadias, or perforated anus.

We excluded incomplete medical records, those registered after the analyzed period (May 2020), or children misdiagnosed with bronchiolitis.

The information technology team of the hospital provided access to the electronic medical records of all children hospitalized from April 2018 to April 2020 and classified with the following international classification of disease-10: J21.10 (acute bronchiolitis), J21.0 (acute bronchiolitis caused by RSV), J21.8 (acute bronchiolitis caused by other specified microorganisms), and J21.9 (unspecified acute bronchitis). The extubation booklet of the physical therapy team from PICU was also used to collect data and decide whether the children were eligible.

A semi-structured instrument collected the following data: sociodemographic (age, gender, and city of residence), nutritional (current weight, current weight-for-age), gestational (gestational age birth, and birth weight), and hospitalization (previous hospitalization, causative agent, use of oxygen therapy, NIV, IMV, tracheostomy, aspiration, prone position, changes in decubitus, NIV failure, respiratory complications, cardiopulmonary arrest and resuscitation, and outcome [death or hospital discharge]).

Data were described as absolute and relative frequencies for categorical variables or mean and standard deviation (SD) for quantitative variables. The STATA® 14 software analyzed all data, and significance was set at $p < 0.05$. The Shapiro-Wilk test verified data normality. The Mann-Whitney and Fisher's exact test compared continuous and categorical variables, respectively. The weight-for-age was also analyzed by gender using the WHO Anthro software (version 3.2.2). The Z-score < -2 indicated low weight-for-age.

This study followed the Declaration of Helsinki and Resolution 466/2012 of the National Health Council. The study was approved by the research ethics committee of the *Centro de Excelência em Ensino, Pesquisas e Projetos Leide das Neves Ferreira* (no. 28728820.7.0000.5082), and the informed consent form was not needed since we analyzed medical records.

RESULTS

A total of 73 children were included in the study from the two PICUs; mostly male (60.3%) and below six months old (56.2%), with a mean age of 7.2 months (SD 6.4 months).

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Regarding nutritional status, the mean weight was 6.7 kg (SD 1.9 kg), with a mean Z-score of -0.35 (SD 1.5). Also, about 10% of children were classified as low weight-for-age. The mean gestational age was 37.5 weeks (SD 1.9 weeks), in which 18 (33.3%) children were premature, and the mean birth weight was 3 kg (SD 0.7 kg).

We observed that 45.2% of children were hospitalized at least once before this study. The most frequent causative agent was viral (75.3%), followed by bacterial (24.7%). More than 85% of children required nasal cannula oxygen therapy for 3.6 days (SD 3.5 days). Also, 15.10% of children required IMV for 6.2 days (SD 38.7 days), and 27.4% required NIV for 1.1 days (SD 2.7 days), mostly with a nasal prong (17.8%), biphasic positive airway pressure (BiPAP) mode (19.2%), and without sedation (86.3%). About 7% of children presented NIV failure, more than 4.0% required tracheostomy, and 84.9% required aspiration. Changes in decubitus were performed in 98.6% of children, and 1.4% adopted the prone position.

The most observed comorbidity was congenital heart disease (6.8%), and bronchopulmonary dysplasia, gastroesophageal reflux disease, complications, encephalopathy, and epilepsy presented the same frequency (2.7%). Regarding medications, the most used combination were antibiotics, hypertonic solution, salbutamol, and corticosteroids (31.5%), followed by steroids, salbutamol, and hypertonic solution (19.2%), and antibiotics, hypertonic solution, and albuterol (16.4%).

Frequent complications were ARF (45,21%), severe acute respiratory syndrome (SARS) (10,96%), pneumonia (4,11%), and SARS with pneumonia (2,74%). Also, 4.10% of children presented cardiopulmonary arrest and were submitted to resuscitation. The outcome for two children (2.70%) was death, most children (94.5%) were discharged to the ward, and two (2.7%) were discharged for home care. The mean hospitalization in PICU was 12 days (SD 39.8 days), and the mean total hospitalization was 15.7 days (SD 39.9 days).

Children under IMV presented lower weight than those without IMV (p = 0.019, Table 1). They also had a lower NIV use (p = 0.007) and death outcome (p = 0.021) and a higher frequency of SARS than children without IMV (p = 0.022, Table 2). In addition, the hospitalization period (PICU and total) was longer in children under IMV than those without IMV (p = 0.001, Table 2).

Most children under NIV also required IMV (p = 0.007) (Table 2). Also, children under NIV needed more aspiration than those without NIV (p = 0.021), and total hospitalization and in PICU were longer in children under NIV than those without NIV (p = 0.001, Table 2).

Children under IMV used nasal cannula (p = 0.005) and sedation with NIV more frequently than those without IMV (p = 0.001, Table 3). Also, they spent more days in NIV (p = 0.003), had a lower frequency of NIV in synchronized intermittent mandatory ventilation mode (p = 0.002), and higher frequency of NIV failure than children without IMV (p = 0.002, Table 3). Children under NIV spent more days in IMV than those without NIV (20.9 ± 73.0 *versus* 0.7 ± 2.8; p = 0.001).

Table 1. Sociodemographic, nutritional, and pregnancy-related characteristics of children with bronchiolitis under or without invasive or noninvasive mechanical ventilation hospitalized in PICU of a public emergency hospital

CHARACTERISTICS	Without IMV 62 (85.1%)	Without IMV 62 (84.9%)	IMV 11 (15.1%)	IMV 11 (15.1%)	p-value	Without NIV 53 (72.6%)	Without NIV 53 (72.6%)	NIV 20 (27.4%)	NIV 20 (27.4%)
SOCIODEMOGRAPHIC									
Gender, n and %					0.223				
Female	23	37.1	6	54.5		19	35.8	10	50.0
Male	39	62.9	5	45.5		34	64.2	10	50.0

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CHARACTERISTICS	Without IMV 62 (84.9%)	Without IMV 62 (84.9%)	IMV 11 (15.1%)	IMV 11 (15.1%)	p-value	Without NIV 53 (72.6%)	Without NIV 53 (72.6%)	NIV 20 (27.4%)	NIV 20 (27.4%)
Age (months), mean and SD	7.6	6.6	4.8	4.4	0.158	7.5	6.5	6.4	6.0
Age (days), mean and SD	191.9	159.2	144.5	133.4	0.368	195.7	164.5	155.7	128.5
Age group, n and %					0.517*				
< 6 months	33	53.2	8	72.7		18	34.0	6	30.0
6 to 12 months	22	35.5	2	18.2		29	54.7	12	60.0
> 12 months	7	11.3	1	9.1		6	11.3	2	10.0
City, n and %					0.480*				
Capital	30	48.4	6	54.5		24	45.3	12	60.0
Inland	32	51.6	5	45.5		29	54.7	8	40.0
NUTRITIONAL									
Current weight (kg)	7.0	2.0	5.6	1.5	**0.019**	6.09	2.0	6.4	1.8
Current weight-for-age (Z-score)	-0.31	1.5	-0.60	1.5	0.553	-0.47	1.5	-0.03	1.3
Low weight-for-age, n and %					0.717*				
No	56	90.3	10	90.9		48	90.6	18	90.0
Yes	6	9.7	1	9.1		5	9.4	2	10.0
GESTATIONAL									

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CHARACTERISTICS	Without IMV 62 (84.9%)	Without IMV 62 (84.9%)	IMV 11 (15.1%)	IMV 11 (15.1%)	p-value	Without NIV 53 (72.6%)	Without NIV 53 (72.6%)	NIV 20 (27.4%)	NIV 20 (27.4%)
Gestational age, mean and SD	37.7	2.9	36.0	5.0	0.591	37.6	3.4	37.0	2.7
Premature, n and %					0.429*				
No	32	68.10	4	57.1		28	70.0	8	57.1
Yes	15	31.90	3	42.9		12	30.0	6	42.9
Birth weight, mean and SD	3.1	0.61	2.7	1.2	0.603	3.0	0.72	3.1	0.77

n – absolute value; SD – standard deviation; NIV – noninvasive mechanical ventilation; IMV – invasive mechanical ventilation. Mann-Whitney or * Fisher's exact test.

Table 2. Health and clinical characteristics of children with bronchiolitis under or without invasive or noninvasive mechanical ventilation hospitalized in PICU of a public emergency hospital

CHARACTERISTICS	Without IMV 62 (84.9%)	Without IMV 62 (84.9%)	IMV 11 (15.1%)	IMV 11 (15.1%)	p-value	Without NIV 53 (72.6%)	Without NIV 53 (72.6%)	NIV 20 (27.4%)	NIV 20 (27.4%)
Previous hospitalization, n and %					0.363*				
No	35	56.4	5	45.4		30	56.6	10	50.0
Yes	27	43.6	6	54.6		23	43.4	10	50.0
Causative agent, n and %					0.091*				
Viral	49	79.0	6	54.6		41	77.0	14	70.0
Bacterial	13	21.0	5	45.4		12	22.6	6	30.0
Oxygen therapy, n and %					0.659*				
Nasal cannula	55	88.7	9	81.8		44	83.0	20	100.0
Venturi mask	1	1.6	0	0.0		1	1.9	0	0.0
No	6	9.7	2	18.2		8	15.1	0	0.0

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CHARACTERISTICS	Without IMV 62 (84.9%)	Without IMV 62 (84.9%)	IMV 11 (15.1%)	IMV 11 (15.1%)	p-value	Without NIV 53 (72.6%)	Without NIV 53 (72.6%)	NIV 20 (27.4%)	NIV 20 (27.4%)
Days under O_2, mean and SD	3.3	3.0	4.9	5.7	0.607	3.4	3.2	3.9	4.2
NIV, n and %					**0.007***				
No	49	79.1	4	36.4		49	92.4	13	65.0
Yes	13	21.0	7	63.6		4	7.5	7	35.0
TQT, n and %					0.057*				
No	61	98.4	9	81.8		52	98.1	18	90.0
Yes	1	1.6	2	18.2		1	1.9	2	10.0
Aspiration, n and %					0.143*				
No	11	17.7	0	0.0		11	20.7	0	0.0
Yes	51	82.3	11	100.0		42	79.3	20	100.0
Changes in decubitus, n and %					0.151*				
No	0	0.0	1	9.1		1	1.9	0	0.0
Yes	62	100.0	10	90.9		52	98.1	20	100.0
Prone position, n and %					0.151*				
No	62	100.0	10	90.9		53	100.0	19	95.0
Yes	0	0.0	1	9.1		0	0.0	1	5.0
Complications, n and %					**0.022***				
None	24	38.7	2	18.2		20	37.7	6	30.0
ARF	30	48.4	3	27.3		27	50.9	6	30.0
Pneumonia	2	3.2	1	9.1		2	3.8	1	5.0
SARS	4	6.4	4	36.4		3	5.7	5	25.0
SARS and pneumonia	1	1.6	1	9.1		1	1.9	1	5.0
CPA and CPR, n and %					0.057*				
No	61	98.4	9	81.8		51	96.2	19	95.0
Yes	1	1.6	2	18.2		2	3.8	1	5.0

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CHARACTERISTICS	Without IMV 62 (84.9%)	Without IMV 62 (84.9%)	IMV 11 (15.1%)	IMV 11 (15.1%)	p-value	Without NIV 53 (72.6%)	Without NIV 53 (72.6%)	NIV 20 (27.4%)	NIV 20 (27.4%)
Death, n and %					**0.021***				
No	62	100.0	9	81.8		51	96.2	20	100.0
Yes	0	0.0	2	18.2		2	3.8	0	0.0
Discharge to ward, n and %					**0.001***				
No	0	0.0	4	36.4		3	5.7	1	5.0
Yes	62	100.0	7	63.6		50	94.3	19	95.0
PICU hospitalization (days), mean and SD	5.9	7.4	46.5	97.7	**0.001**	5.3	4.6	29.6	74.2
Total hospitalization (days), mean and SD	9.7	9.7	49.4	97.0	**0.001**	8.9	**6.0**	33.6	73.9

n – absolute value; SD – standard deviation; O_2 – oxygen; NIV – noninvasive mechanical ventilation; IMV – invasive mechanical ventilation; TQT – tracheostomy; ARF – acute respiratory failure; SARS – severe acute respiratory syndrome; CPA – cardiopulmonary arrest; CPR – cardiopulmonary resuscitation; PICU – pediatric intensive care unit. Mann-Whitney or * Fisher's exact test.

Table 3. Characteristics of noninvasive mechanical ventilation in children with bronchiolitis under or without invasive mechanical ventilation hospitalized in PICU of a public emergency hospital

CHARACTERISTICS	Without IMV 62 (84.9%)	Without IMV 62 (84.9%)	IMV 11 (15.1%)	IMV 11 (15.1%)	p-value
NIV interface, n and %					**0.005***
Nasal	1	1.6	2	18.2	
Facial	5	8.1	0	0.0	
Prong	8	12.9	5	45.4	
No	48	77.4	4	36.4	
NIV use (days), mean and SD	0.6	1.6	3.5	5.4	**0.003***

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CHARACTERISTICS	Without IMV 62 (84.9%)	Without IMV 62 (84.9%)	IMV 11 (15.1%)	IMV 11 (15.1%)	p-value
Use of sedation for NIV, n and %					**0.001***
No	59	95.2	4	36.4	
Yes	3	4.8	7	63.6	
NIV mode, n and %					**0.002***
CPAP	2	3.2	3	27.3	
BiPAP	11	17.7	3	27.3	
No	49	79.1	4	36.4	
SIMV	0	0.0	1	9.1	
NIV failure, n and %					**0.022***
No	60	96.8	8	72.7	
Yes	2	3.2	3	27.3	

n – absolute value; SD – standard deviation; NIV– noninvasive mechanical ventilation; IMV – invasive mechanical ventilation; CPAP – continuous positive airway pressure; BiPAP – biphasic positive airway pressure; SIMV – synchronized intermittent mandatory ventilation. Mann-Whitney or * Fisher's exact test.

DISCUSSION

Despite the low mortality, bronchiolitis has high morbidity. Death by respiratory failure in bronchiolitis is rare, affecting 5.3 per 100,000 infants under 12 months old in the USA, where resources for intensive care and research advance and reduce this rate.[10]Also, the mortality rate was low even in children with comorbidities (e.g., low weight, young age, and premature birth) and those under IMV for a long period (i.e., more than seven days).[11-13]This rate was associated with low breathing patterns in children with bronchiolitis. However, children with bronchiolitis under IMV and who progressed to SARS presented increased complications and mortality rates since it is a viral infection that impairs the respiratory system.[11,13]

Two children with low birth weight died in this study; one had congenital heart disease, and the other had SARS. Although both children were under IMV, they died due to severe bronchiolitis, which caused hemodynamic instability.[14,15] Similarly, severe bronchiolitis was previously associated with young and low-weight children who developed ARF followed by SARS since bronchiolitis may increase the respiratory pattern by sixfold. [1,13]

Younger (i.e., less than six months old) and premature infants presented severe bronchiolitis with adverse respiratory impairment, needing ventilatory support. Mechanical factors (e.g., small airway caliber) may increase airway resistance, which is further increased by the inflammation and swelling of the airways due to the disease. Also, immunological factors, such as the weak immune system in younger and premature infants, may hamper innate immune responses, and these infants become susceptible to viral infections and require ventilatory support.[16,17]

The NIV is one of the initial supportive measures for acute bronchiolitis, which may progress to IMV in severe cases, especially in children with comorbidity and low weight. These cases require continuous positive airway pressure and BiPAP, which may not reverse the respiratory distress.[12] Corroborating this data, one child in the present study was intubated even after using NIV. However, a previous study showed that children under early NIV improved their respiratory condition, requiring only nasal cannula oxygen therapy with a low flow. [18] Thus, ventilatory support using NIV may avoid IMV and its complications in most cases.[19]

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The treatment of bronchiolitis depends on its severity since this disease may impair lung function on the fifth day. Thus, oxygen therapy is designated and changed to NIV in case of increased severity, progressing to intubation with IMV in case of NIV failure. In this sense, the three measures are related, and the inverse process may also occur (i.e., an extubated patient may need NIV followed by oxygen therapy in case of improved condition). These measures are commonly combined with salbutamol, hypertonic solution, and bronchodilators, especially in children with respiratory distress and requiring nasogastric tube feeding.[4,5]

In this study, the risk of severe bronchiolitis caused by RSV was higher in male than female children, possibly due to differences in lung structure, airway development, and genetic factors.[20]The present study corroborated previous studies considering male gender, congenital heart disease, and young age (from one to six months) as risk factors for bronchiolitis; these conditions require bronchial washing and aspiration due to excess mucus.[21-23] The comorbidities with the highest risk for bronchiolitis were congenital heart disease and bronchopulmonary dysplasia.[20]

Children younger than 24 months old, with less than 37 gestational weeks, and low weight birth also presented an increased risk for prolonged hospitalization in PICU.[17,24] Although the hospitalization period was not associated with aspiration, children under IMV and NIV were hospitalized for longer than those without IMV and NIV. Even with technological advances in ventilatory support, which reduced hospitalization costs and period and support-related lung injury, the most severe cases required IMV, NIV, and prolonged hospitalization to obtain clinical improvement and stability.[12,24,25,26]

In the present study, the hospitalization period ranged from 5 to 15 days in cases requiring IMV or NIV, with a mean of 12 days in PICU and 15.71 days of the total hospitalization period. Also, 94.52% of children were discharged to the ward, and two were discharged for home care. In this sense, the hospitalization period was directly associated with the virus incubation (about four to five days) and factors increasing the condition severity. Long hospitalization was previously associated with high costs, emotional burdens, and health-related issues.[21] Parents accompanying the children during hospitalization missed workdays, affecting their income. In addition, anxiety was associated with the children condition, which may cause long-term consequences for the family.[21]

CONCLUSION

The coronavirus disease (COVID-19) may have limited the sample size since one of the PICU became a reference in pediatric treatment for this disease simultaneously to the focus of bronchiolitis, and the number of beds was allocated and reduced for other respiratory diseases. Also, social distancing reduced the exposure to etiological agents of bronchiolitis since the children did not go to schools or daycare centers, and some parents performed home office, reducing the cases between 2020 and 2021.

In conclusion, RSV was the main causative agent of bronchiolitis. Prematurity, male gender, low weight, age below six months, and congenital heart disease were associated with severe bronchiolitis that tended to progress with ARF and especially SARS. IMV was beneficial for children with severe bronchiolitis since it reduced mortality and improved clinical condition. However, bronchiolitis is still challenging, requiring protocols and multidisciplinary teamwork to minimize the morbidity caused by this disease and IMV. Thus, further studies need to address this issue to help health professionals classify the severity of bronchiolitis.

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