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Epidemiologic evaluation of acute viral bronchiolitis (AVB) in infants hospitalized

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ABSTRACT

OBJECTIVE

To characterize the epidemiological profile of AVB and to identify prognostic factors of clinical complications of infants admitted to a pediatric intensive care unit (PICU).

METHODS

Prospective cohort study of 61 infants with a clinical diagnosis of AVB admitted to the PICU from June/2016 to July/2017. All infants were followed up during the hospitalization period for clinical and laboratory data collection. In addition, it was carried out an interview with the mothers or legal guardians to obtain socioeconomic information and morbid antecedents.

RESULTS

Mean age was 6.9 months, the length of PICU stay was 8.4 days, the prematurity rate was 27.9%, 62.7% presented anemia, and the presence of household smoking 56.7%. Pneumonia (34.4%) and atelectasis (26.2%) were the most prevalent clinical complications. In addition, pneumonia was associated with hospitalization time longer than seven days (OR=3.91, p=0.020), severe dyspnea on admission (OR=3.75, p=0.020), and thinness (OR=3.54, p=0.040). None associations were observed for atelectasis.

CONCLUSIONS

The epidemiological data presented in this study can be applied to the improvement of actions targeting ABV control actions in infants, not only by the identification of the prognostic factors associated with pneumonia but also especially by the necessity to provide greater attention and care to infants with AVB who are thinness and present severe dyspnea on admission to the PICU.

DESCRIPTORS

Pneumonia. Atelectasis. Prematurity. Thinness.

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INTRODUCTION

Bronchiolitis is characterized by an acute inflammatory response of the lower respiratory tract associated with infection caused by different viruses. Its occurrence is commonly observed in the first year of life and represents one of the main causes of infant hospitalization in many countries. Acute Viral Bronchiolitis (AVB) leads to an obstructive respiratory condition with varying degrees of intensity, in which the most frequent virus-associated is the respiratory syncytial virus (RSV)[1]. Data pointed that around 95% of all children in the world could be infected by RSV until years of age and it can lead to the occurrence of AVB[2].

According to the literature, it was estimated that more than 3 million hospital admissions worldwide were related to the occurrence of acute lower respiratory diseases and that the main factor was RSV infection, showing that this viral infection can impact significantly the economic burden on healthcare services . Furthermore, it was reported that 99% of deaths related to AVB in infants less than 2 years of age occur in developing countries[3].

In Brazil, a study cohort with 5,304 children younger than 1 year showed that 2.1% of them were hospitalized due to AVB. In addition, other studies showed that 31.9% to 64% of hospitalized patients with AVB presented RSV infection. It was also found that in 40% of AVB cases in Brazil were associated with a viral coinfection, and that the second most common virus in AVB was in which the rhinovirus[4]. Moreover, not only the occurrence, but also the death rates associated with AVB is still high, especially in developing countries, as Brazil.

Therefore, in this study, we aimed to characterize the epidemiological profile of AVB and to identify prognostic factors of clinical complications of infants admitted to a pediatric intensive care unit (PICU).

METHODS

The data presented in this prospective cohort study was obtained of 205 infants admitted to the PICU of "Hospital Municipal Dr. Carmino Caricchio" (HMCC) that belonged to the Municipal Health Secretariat of Sao Paulo, Brazil during a period of 1 year (from June 2016 to July 2017). Based on clinical and laboratory analysis, 75 infants were diagnosed with AVB and 61 infants under 2 years old were enrolled in this study. Inclusion criteria used in this study were: infants from 0 to 2 years of age hospitalized in the PICU of the HMCC; the presence of tachypnea and chest retraction, preceded or associated with cough and coryza, positive RSV infection evaluated by direct immunofluorescence examination in nasopharyngeal secretion or polymerase chain reaction (PCR) test. Infants whose suspicion of bronchiolitis was not confirmed during hospitalization or who presented other clinical complications were excluded, as shown in the flow diagram (Figure 1).

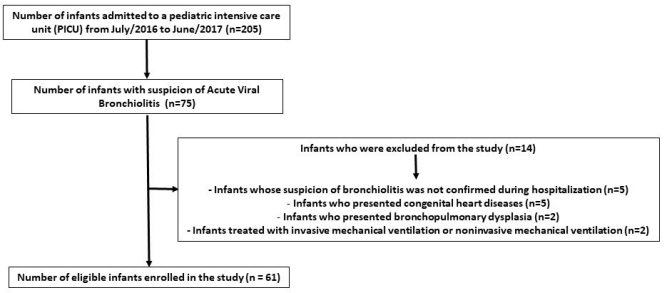

Figure 1. Flow diagram of the study.

All mother or legal guardian of the infants participating in this study signed the consent form previously approved by the Ethical and Research Committee from Santo Amaro University (number:1,541,974) and from Hospital Municipal Dr. Carmino Caricchio (number:1,592,139). The study was performed in accordance with the Declaration of Helsinki.

Data concerning infant characteristics, demographic, clinical, and laboratory variables and also the socioeconomic status of their families were collected either through medical assistance records, which presented the daily monitoring of infants during admission to the PICU or by interviews with the mother or legal guardian. Therefore, the parameters evaluated were gender, age, birth weight, gestational age, month of hospitalization, Z scores related to physical characteristics (W/A=Weight/Age; H/A=Height/Age; and BMI=Body Mass Index/Age), and AVB severity classification using the modified Wood Downes Scale (WDS). By this scale, it was possible to classify the ABV severity using a score from 0 to 10, in which until score 3 is classified as mild AVB, between 4 to 7 as moderate, and from 8 to 10 is considered severe . In addition, it was also evaluated: the presence of cyanosis, length of stay in the PICU, the use of noninvasive or invasive mechanical ventilation, sedation, medicines, such as vasoactive drugs, antibiotics, corticoid or/and bronchodilator, nebulization with hypertonic saline solution, and oxygen (O2). The medical complications studied were pneumonia (PNM); atelectasis; cardiorespiratory arrest (CPA), acute otitis media; conjunctivitis; urinary tract infection; acute renal failure; unspecified tachycardia; pneumothorax (PNTX) and death.

The interviews were used to obtain data related to family characteristics: age and education of mother or legal guardian, parents' occupation; smoking; the occurrence of respiratory diseases; planned pregnancy; carrying out full prenatal care; breastfeeding time; the number of brothers or sisters; the number of residents in the household; the number of individuals sharing the same room with the infant patient; the presence of domestic animals and basic sanitation at home; the necessity to maintain the infant at daycare and contact with an individual with respiratory changes in the last 7 days.

The data were presented as means or prevalence with a confidence interval. Chi-square test was used in accordance to the distribution of the variables of interest. The data were analyzed using the statistical package STATA 14 and it was considered a maximum α error of 5% (p-values <0.05) as statistically different.

RESULTS

Table 1 shows the infant's physical and clinical characteristics, as well as the socioeconomic status of their families. Continuous variables are shown in mean and the categoric variables are shown in prevalence. For all variables are showed their respective confidence intervals (95% CI).

According to the data showed in Table 1, the mean age of the infants admitted in the PICU was 6.9 months; 36 were boys (59.0%); the average for weight was 7.1kg, height was 66.0cm, and BMI was 16,6kg/m^2. Regarding the Z scores, it was found an average of -0.43 for ZW/A, -0.34 for ZH/A, and -0.22 for ZBMI/A. In terms of admission, the mean length of hospital stay was 14.7 days, whereas the length of the PICU stay was 8.4 days. The interval between the day of hospitalization and admission to the PICU was, on average, 1.3 days.

As showed in Table 1, the average of the gestational age of birth was 37.6 weeks; 27.9% were premature, cesarean delivery was present in 26.2% of cases, and, on average, the exclusive breastfeeding was 2.8 months, they lived with 5 other people, in which 56.7% of them living with smokers; besides 16.4% of households were near an open sewer and 6.6% had an absence of piped water.

In relation to the maternal findings, table 1 shows that the mean age was 23.9 years, schooling was 8.9 years, 33.3% of them reported not having planned the pregnancy, and 28.8% were primigravidae, 24.6% were smokers, 18% reported that used illicit drugs, 14,8% are alcoholics, and 49.2% reported having a medical diagnosis of chronic respiratory diseases. Regarding the children's fathers, the mean age was 26 years, schooling was 9.3 years, 44.1% were smokers, 33.9% reported that used illicit drugs, 45.8% were alcoholics, and 39.7% reported having a medical diagnosis of chronic respiratory disease (Table 1).

The main clinical findings observed when the infants were admitted to a pediatric intensive care unit included: cyanosis (39.3%), severe dyspnea (51.8%), tachypnea (54.1%), altered SpO2 (63.9%), and fasting (68.9%). After infants' hospitalization, it was assessed the AVB severity using the modified WDS and seventeen infants (27.9%) were classified with mild symptoms, 13 infants (21.3%) with moderate symptoms, and 31 infants (50.8%) with severe symptoms of AVB (Table 1).

Table 1. Means (μ) and prevalence (P) with their respective confidence intervals (95% CI) of the characteristics of infants with the clinical diagnosis of acute viral bronchiolitis (AVB). admitted to a pediatric intensive care unit (PICU) of "Hospital Municipal Dr. Carmino Caricchio" (HMCC). São Paulo. Brazil. during a period of 1 year (from June 2016 to July 2017).

Characteristics (continuous variables)	N	μ	(CI 95%)
Age (m)	61	6.9	(5.4; 8.4)
Weight (kg)	61	7.1	(6.5; 7.8)
Height (cm)	56	66.0	(62.2; 69.9)
Birth weight (g)	59	3040	(2847; 3232)
Gestational age of birth (w)	61	37.6	(36.8; 38.4)
Neonatal length of stay (d)	59	7.1	(4.6; 9.7)
Time of exclusive breastfeeding (m)	61	2.8	(2.2; 3.4)
Z W/A	61	-0.43	(-0.95; 0.09)
Z H/A	56	-0.34	(-1.29; 0.60)
BMI	56	16.6	(15.4; 17.8)
Z BMI/A	56	-0.22	(-1.11; 0.66)
Length of PICU stay (d)	61	8.4	(7.2; 9.5)
Length of hospital stay (d)	61	14.7	(10.5; 18.9)
Hospitalization time before the PICU (d)	61	1.3	(0.85; 1.9)
Mother's age (y)	60	23.9	(22.6; 25.3)
Mother's schooling (y)	59	8.9	(8.4; 9.5)
Father's age (y)	58	26.0	(24.5; 27.5)
Father's schooling (y)	49	9.3	(8.4; 10.3)
Number of individuals residing with the infant	60	5.2	(4.7; 5.6)
Leukogram (mil/mm³)	59	14.1	(11.0; 17.2)
Platelets (mil/mm³)	59	395.2	(354.4; 436.1)

Characteristics (categoric variables)	N	P	(CI 95%)
Male gender	61	59.0	(46.0; 70.9)
Prematurity	61	27.9	(17.8; 40.7)
Low weight at birth	59	20.3	(11.7; 32.9)
Anemia	59	62.7	(49.4; 74.3)
Primigravidae	59	28.8	(18.5; 42.0)
Planned pregnancy	60	33.3	(22.3; 46.5)
Late prenatal care	58	18.9	(10.6; 31.5)
Cesarean section	61	26.2	(16.5; 39.0)
Smoking mother	61	24.6	(15.2; 37.3)
Mothers who used illicit drugs	61	18.0	(10.1; 30.1)
Alcoholism (maternal)	61	14.8	(7.7; 26.4)
Respiratory history (maternal)	59	49.2	(36.4; 62.1)
Smoking father	59	44.1	(31.7; 57.2)
Fathers who used illicit drugs	59	33.9	(22.7; 47.2)
Alcoholism (paternal)	59	45.8	(33.2; 58.8)
Respiratory history (paternal)	58	39.7	(27.6; 53.1)
Attends daycare	61	24.6	(15.2; 37.3)
Lives near an open sewer	61	16.4	(8.9; 28.3)
Absence of piped water	61	6.6	(2.4; 16.6)
Positive RSV	43	34.9	(21.8; 50.7)
Smoking at home	60	56.7	(43.6; 68.9)

N=number of infants; μ=mean; P=prevalence; CI=confidence interval; m=months; g=grams. d=days; kg=kilograms; cm=centimeters; w=weeks; y=years; RSV= respiratory syncytial virus; BMI= body mass index; Z W/A=Z score of weight/age index; Z E/I=Z score of height/age index; Z BMI/I= Z score of body mass index/age index.

Data from the medications that were administrated in the infants during the period of hospitalization are shown in Figure 2. Ten infants (16.4%) were treated with vasoactive drugs (VAD), 20 (32.8%) corticosteroids, 47 (77.0%) bronchodilators and 54 (88.5%) with antibiotic.

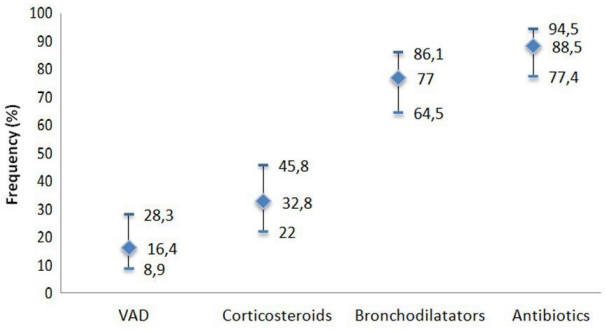

Figure 2. Frequencies and their respective confidence intervals (95% CI) of medication administrated in the infants (n=61) during their hospitalization period in a PICU.

The Figure 3 shows the medical complications observed in the infants during the period of hospitalization in a PICU. It was found that 21 (34.4%) presented pneumonia, 16 infants (26.2%) presented atelectasis, 4 (6.6%) presented cardiopulmonary arrest (CPA), which in 3 infants (4.9%) resulted in death, and 2 infants (3.3%) presented pneumothorax (PNTX).

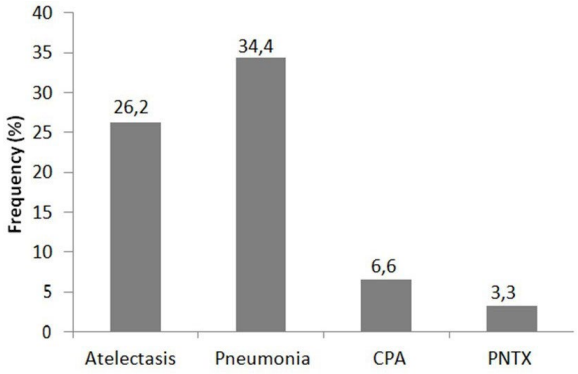

Figure 3. Frequencies of the medical complications found in the infants (n=61) during their hospitalization period in a PICU.

Based on pneumonia and atelectasis were the most medical complications observed in the infants during the PICU stay period, it was carried out evaluations to verify what factors could be associated with the occurrence of these medical complications.

As showing in table 2, significant statistical associations were found only between pneumonia and some parameters assessed. Infants that stayed in PICU for more than seven days and those presenting severe dyspnea on PICU admission had 3.9 (95% CI:1.7-16.04, p=0.020) and 3.8 (95% CI:1.07-14.16, p=0.020) greater risk to develop pneumonia, respectively. It was also found a statistically significant association with thinness (ZBMI/A<-2, p=0.040), in which infants presenting this physical condition had 3.5 (95% CI:0.86-14.60) greater risk to develop this disease.

Table 2. Odds ratios [confidence intervals (95% CI)] related to the prognostic factors for pneumonia and atelectasis in infants admitted to a pediatric intensive care unit (PICU) with acute viral bronchiolitis (AVB).

Prognostic factors		N	Pneumonia		Atelectasis	
			Odds Ratios	p* value	*Odds Ratios*	p* value
Socioeconomic						
Paternal education (y)	<9	49	0.28 (0.03; 1.63)	0.117	0.60 (0.09; 2.96)	0.484
	≥ 9		1.00		1.00	
Father's age (y)	<26	58	1.11 (0.31; 3.89)	0.860	0.55 (0.14; 2.04)	0.311
	≥ 26		1.00		1.00	
Paternal smoking	Yes	59	1.67 (0.48; 5.68)	0.361	1.39 (0.37; 5.13)	0.576
	No		1.00		1.00	
Maternal education (y)	< 9	59	0.78 (0.22; 2.64)	0.652	0.48 (0.11; 1.83)	0.226
	≥ 9		1.00		1.00	
Mother's age (y)	<19	60	0.52 (0.05; 3.19)	0.443	0.30 (0.01; 2.63)	0.252
	≥ 19		1.00		1.00	
Maternal smoking	Yes	61	1.38 (0.34; 5.30)	0.601	1.59 (0.35; 6.54)	0.471
	No		1.00		1.00	
Smoking in the home	Yes	60	1.23 (0.36; 4.27)	0.712	3.00 (0.74; 14.52)	0.084
	No		1.00		1.00	
Maternal respiratory history	Yes	59	1.05 (0.31; 3.54)	0.926	1.05 (0.28; 3.87)	0.937
	No		1.00		1.00	
Primigravida	Yes	59	0.32 (0.05; 1.41)	0.093	0.48 (0.08; 2.19)	0.298
	No		1.00		1.00	
Background of infants						
Gestational age of birth (w)	<37	61	0.73 (0.17; 2.77)	0.608	1.85 (0.44; 7.25)	0.317
	≥ 37		1.00		1.00	
Time of exclusive breastfeeding (m)	≤2	54	1.03 (0.29; 3.76)	0.957	3.67 (0.78; 23.01)	0.063
	>2		1.00		1.00	
Daycare attendance	Yes	61	0.94 (0.21; 3.68)	0.918	0.63 (0.10; 2.95)	0.528
	No		1.00		1.00	
Late prenatal care	Yes	58	1.11 (0.21; 5.16)	0.884	0.21 (0.01; 1.80)	0.127
	No		1.00		1.00	
Low birth weight	Yes	59	2.36 (0.52; 10.44)	0.187	1.46 (0.27; 6.70)	0.587
	No		1.00		1.00	
Hospital stay						
Modified WDS – severe	Yes	61	2.71(0.80; 9.64)	0.072	0.96 (0.26; 3.51)	0.939
	No		1.00		1.00	
Length of PICU stay (d)	>7	61	3.91 (1.07; 16.04)	0.020	3.14 (0.78; 15.13)	0.071
	≤7		1.00		1.00	
Time before admission to the PICU (d)	≥1	61	0.37 (0.10; 1.26)	0.073	2.08 (0.56; 8.17)	0.215
	<1		1.00		1.00	
Altered respiratory rate	>50	61	1.21 (0.37; 4.03)	0.730	1.12 (0.31; 4.23)	0.841
	≤50		1.00		1.00	
SpO2	>90	61	1.67 (0.47; 6.35)	0.377	0.92 (0.25; 3.69)	0.889
	≤90		1.00		1.00	
Severe dyspnea	Yes	61	3.75 (1.07; 14.16)	0.020	1.90 (0.52; 7.47)	0.277
	No		1.00		1.00	
Biological aspects						
Infant's age (m)	< 12	61	2.02 (0.33; 21.6)	0.404	Undefined*	
	≥ 12		1.00		1.00	
Gender	Male	61	0.89 (0.27; 3.00)	0.829	1.76 (0.46; 7.50)	0.357
	Female		1.00		1.00	
Z W/A	<-2	61	1.65 (0.29; 8.71)	0.493	0.31 (0.01; 2.70)	0.264
	≥-2		1.00		1.00	
Z BMI/A	<-2	56	3.54 (0.86; 14.60)	0.040	0.68 (0.10; 3.28)	0.601
	≥-2		1.00		1.00	
Z H/A	<-2	56	0.80 (0.16; 3.46)	0.741	3.19 (0.69; 14.09)	0.075
	≥-2		1.00		1.00	

DISCUSSION

In this epidemiologic study, the main findings were: a higher proportion of male infants presenting AVB; mean age of 6.9 months for admission in PICU; prematurity; more than 50% of infants lived in homes with smokers and that almost half of the infants were born of mothers with a history of respiratory disease. Concerning clinical parameters, it was found: a higher proportion of infants treated with antibiotics and/or bronchodilator drugs, more than 60% of infants presented anemia on admission date, and the main medical complications were pneumonia and atelectasis. In addition, three factors were associated with a higher incidence of pneumonia during the period in which the infants stayed in the PICU: length of stay longer than seven days, severe dyspnea on admission date, and thinness.

Corroborating our results, epidemiological studies on AVB have demonstrated that not only a higher frequency, as well as the increased severity of AVB cases were found mainly in male infants[6]. and the highest AVB incidence occurs in the first year of life, mainly between 1-6 months of age[7].

According to the literature, it has been reported a close association between prematurity and bronchiolitis, suggesting that prematurity increases the risk of infants acquiring AVB by 7 times. Furthermore, infants who born prematurely present an 80% higher rate of hospitalizations for respiratory disease and also 24.5 times higher probability of PICU admission as compared to full-term infants[8].

Passive smoking is also a risk factor associated with AVB hospitalizations since passive exposure to tobacco leads to a higher risk of respiratory complications[9]. In Brazil, the risk of hospitalization for AVB is 57% higher in children exposed to maternal smoking[10].

Interestingly, the administration of antibiotics and bronchodilators drugs was high in our sample. It is noteworthy to highlight that there is no consensus in the medical and scientific literature about the effectiveness of these medicines in the AVB treatment[8,9,11-14].

By using the modified WDS, a well-accepted scale for AVB severity[14], it was verified that 31 infants (50.8%) presented severe BVA, following the criteria in the literature[4,15].

Particularly, infants with higher clinical disease severity scores frequently present pneumonia. In this respect, a large retrospective, time-series study reported that RSV infection was associated with a 20% increase in the incidence of pneumonia in infants[16]. However, our results did not show a significant association between them.

Our data concerning severe dyspnea showed that half of the infants presented this medical complication and that this finding raises the risk of them acquiring pneumonia. Dyspnea frequency in neonates with RSV was higher than neonates without RSV and also that pneumonia was diagnosed in 53% of neonates with RSV, whereas the diagnosis of pneumonia was found 15.6% of neonates without RSV[17,18]. Children presenting dyspnea and pneumonia have respiratory distress characterized by the presence of tachypnea, intercostal, and subdiaphragmatic circulation[19]. In addition, AVB is characterized by respiratory discomfort associated with tachypnea and mild to moderate hypoxemia, associated or not with other symptoms such as wheezing[20]. Since that dyspnea is a symptom that can be observed both in AVB and pneumonia, it is very important to consider the presence of dyspnea at the admission of PICU, not only as a factor of greater probability of clinical worsening by favoring the development of secondary infection but also as a factor related to a more serious respiratory infection already present.

The length of hospital time in PICU longer than seven days can putatively increase the risk of infants acquiring pneumonia by approximately four times[8,9,21]. Although our results showed an average of infant hospitalization of 14.7 days for the treatment of AVB, the average length of PICU stay in this study (8.4 days) was similar to the report in other studies[9,15]. Despite the finding that the risk of infants acquiring pneumonia was higher when the length of hospital stay in PICU is longer than seven days, we believe that a significant question needs to be raised: it would be the length of stay that favored the development of pneumonia or the existence of subclinical pneumonia led the longest hospital stay for these infants? Unfortunately, our results did not allow us to respond clearly to the question raised above.

Here, the infants with low ZBMI/I presented a higher risk of acquiring pneumonia during the length of stay at the PICU for AVB treatment. It widely accepted that thinness is associated with malnutrition[22]. Evidence showed that malnutrition is frequently observed in the hospital admissions for pneumonia and also that when the malnutrition is not adequately managed by the health teams is associated with a negative effect in the length of hospital stays[7,12,20,23,24].

Concerning this issue, our results showed that the duration of exclusive breastfeeding was an average of 2.8 months, which is lowest than the recommendation found in the Guidelines of the United Nations Children's Fund (UNICEF) and the Ministry of Health of Brazil. It is widely known that exclusive breastfeeding is recommended until the sixth month of age and that after this period the breastfeed is also recommended[25]. According to Chatzimichael et al.[23] children hospitalized for AVB with breastfeeding for less than 4 months presented a higher risk for severe evolution and longer hospital stay. Although we did not verify a significant association between the shortest duration of exclusive breastfeeding and pneumonia or atelectasis, these findings do not diminish the importance of strategies to encourage the exclusive breastfeeding in the first 6 months of life.

It is important to mention that the missing of the data about the pneumonia diagnosis in all infants may not reflect the absence of this infectious disease upon admission in the pediatric PICU and can difficult to establish a real causal relationship between the prognostic factors and the occurrence of pneumonia.

CONCLUSION

In this study, we were able to report that male gender, prematurity, age less than 6 months, malnutrition, and passive smoking were the epidemiological hallmarks in the studied sample. In addition, the most frequent clinical complications were pneumonia and atelectasis, and that antibiotic therapy and bronchodilator drugs had been widely used in the infants. These data can putatively contribute to the improvement of actions targeting ABV control actions in infants, especially by the identification of the prognostic factors associated with pneumonia.

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