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ORIGINAL ARTICLE

Prevalence and phenotypes of wheezing in hospitalized child

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Abstract

Wheezing is quite common in childhood. Developed countries report prevalence between 20% and 30%, with high recurrence. The definition of phenotypes and the understanding of etiological factors are fundamental for prevention and treatment strategies. The aim of this study was to evaluate the prevalence and the main wheezing phenotypes in the hospitalized child. Descriptive observational study conducted in a public hospital on the outskirts of São Paulo in 2018. The medical records of children who were hospitalized in pediatric units with wheezing symptoms were excluded, and those whose parents did not consent and who had failures in the medical records were excluded. Approval of the research ethics committee No. 2,913,139. 787 children were hospitalized, 210 (26.7%) with wheezing symptoms. Eighty-six children were excluded, totaling a sample of 124 individuals. The average age was 2.8 ± 3.1 years and most were infants (51.2%). The phenotypes found were: transient wheezing (47.2%), non-atopic wheezing (37.4%) and persistent wheezing (15.4%). It was found that the prevalence of wheezing in 2018 was high and the main phenotypes were transient wheezing and nonatopic wheezing.

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INTRODUCTION

Wheezing is a common symptom in children, it occurs due to several respiratory diseases, the most common being: asthma, bronchiolitis, pneumonia and gastroesophageal reflux¹. According to Firmida (2013)², wheezing is characterized by high-pitched and continuous adventitious pulmonary sounds, caused by partial airway obstruction and more audible in the expiratory phase of breathing. Some anatomical and functional characteristics predispose the infant to this problem, such as small airways, horizontal diaphragm, less rigid airway support, more compliant rib cage, greater resistance in the peripheral airways and poverty of Khon pores and Lambert canals².

Children with continuous wheezing for a month or at least three episodes of wheezing in a 2-month period are called wheezing children². Studies report that 40% of children wheeze in the first year of life and 20% of these will wheeze later². Wheezing may be transient, with recovery throughout childhood, but when it reaches an early age, pulmonary symptoms may persist, leading to decreased functional capacity and persistence of symptoms in adulthood². Among the phenotypes we found three patterns: transient wheezing, persistent wheezing, non-atopic wheezing³.

Transient wheezing occurs when the child has episodes in the first two/three years of age and no longer has symptoms after that age³. This predisposition is related to prematurity (airway size) and viral infections³, the latter being mostly caused by respiratory syncytial virus (RSV) belonging to the family *Paramyxoviridae* and predominant in the lower airways⁴. According to Muiño et al. (2008)³, the prognosis of this pattern is good. Persistent wheezing is characteristic of children with asthma up to six years of age, in which the first episode occurs before three years of age and lasts for another three years. This pattern is associated with an increase in immunoglobulin E (IgE) in the blood and the presence of other atopy³. It has been observed that these children may have a deficit in lung function in the future³. Finally, there is late-onset wheezing, in which the child has episodes of wheezing after six years of age and is associated with a history of family asthma and atopy³.

The high number of children hospitalized in pediatric units with wheezing aroused interest in developing this project. Knowledge of the profile of the wheezing population, as well as its predisposing factors, allows for better guidance with preventive care at home.

In this circumstance, the main objective of the present study is to survey the prevalence of hospitalization of children and adolescents in a public hospital on the outskirts of São Paulo with symptoms of wheezing and to define the main phenotypes, in addition to verifying the associated risk factors.

METHODS

Analytical cross-sectional study, carried out from January 2018 to December 2018 in a public hospital on the

outskirts of São Paulo. All newborns, infants and children admitted to the Pediatric Infirmery Unit with symptoms of wheezing described by the medical team in medical records were included. It is worth mentioning that all the children presented wheezing at the time of admission, but not all of them had the term bronchospasm in their medical records as a diagnosis. Patients whose parents or guardians did not agree to participate, those to which the researchers did not have access (holidays, weekends and holidays) and those who failed to record the variables of interest were excluded. There was approval by the Ethics Committee (nº 2,913,139) and the free and informed consent term (ICF) was signed. personal history, socioeconomic conditions, gestational age, personal history, hospitalizations, physical activity, environment, current diagnosis, use of oxygen therapy and positive pressure. In addition, those responsible answered part of the questionnaire standardized by the *International Study of Asthma and Allergies in Childhood (ISAAC)*⁵ for asthma research.

Data collection was performed during the period of hospitalization, by the physical therapist (or undergraduate student). When contacting the interviewee, the researcher identified himself and briefly explained the research objectives and handed over or read (in cases of illiterate guardians) the TCLE. After the parents/guardians agreed to participate in the research and signed the informed consent, the researcher started the interview. At the end, a folder was delivered with basic explanations on how to prevent respiratory diseases. The collected data were analyzed using the SPSS[®] statistical program (version 19). Numerical variables were expressed as mean and standard deviation or median. Categorical variables were expressed in number and percentage and compared using the chi-square test. A p value <0.05 was considered significant.

RESULTS

In 2018, a total of 787 children were hospitalized in the pediatric units of the Public Hospital in the metropolitan region of São Paulo. The composition of the sample is shown in figure 1.

The prevalence of hospitalization for wheezing was 26.7% (210/787). The contact with the guardians with acceptance to participate in the research occurred in 59% (124) of the wheezing children, composing the sample of this study. The mean age of the sample was 2.8±3.1 years (median=1.6 years, q1: 0.8 years - q3: 3.9 years). Most of the sample consisted of male infants diagnosed with pneumonia. Bronchospasm was a frequent symptom, as shown in table 1.

The phenotypes detected in the sample are shown in figure 2.

Table 2 shows the distribution of the sample in relation to the main risk factors for wheezing investigated.

The application of the modified ISAAC questionnaire revealed that 80.5% of the children had wheezing in the past

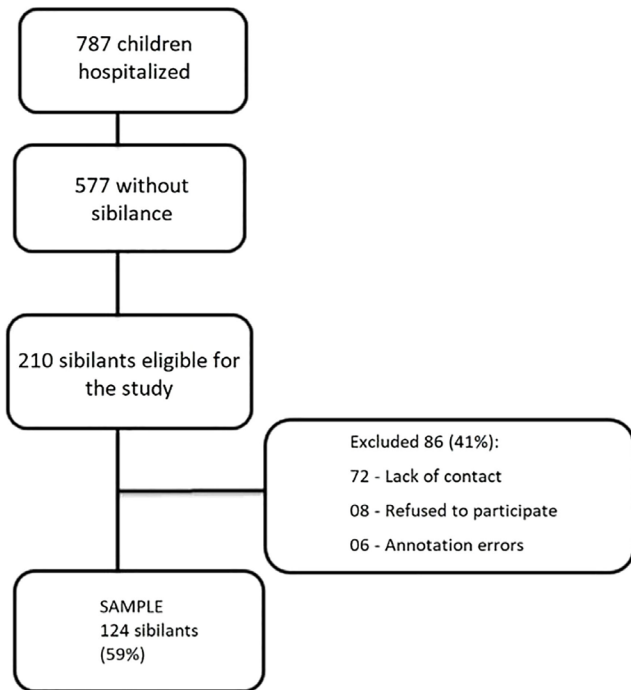


Figure 1. Sample composition flowchart.

Table 1. General characteristics of the evaluated sample.

Variables	n (%)
MALE	62 (50.4)
AGE	
Infant	63 (51.2)
Preschool	38 (30.9)
School	18 (14.6)
Adolescent	4 (3.3)
DIAGNOSES	
Pneumonia	73 (59.3)
Bronchospasm	67 (54.5)
Bronchiolitis	28 (22)
Asthma	13 (10.6)
Atelectasis	14 (11.4)
VAT	13 (2.4)
Wheezing baby	7 (5.7)
Reflux	3 (2.4)
Pleural effusion	2 (1.6)
Bronchopulmonary dysplasia	1 (0.8)
Pneumothorax	1 (0.8)

Source: The authors (2019).

and 42.5% reported a previous episode of asthma. In the last 12 months, 66.7 % had wheezing, 57.7% reported 1 to 5 attacks and 41.5% reported wheezing after physical exercise.

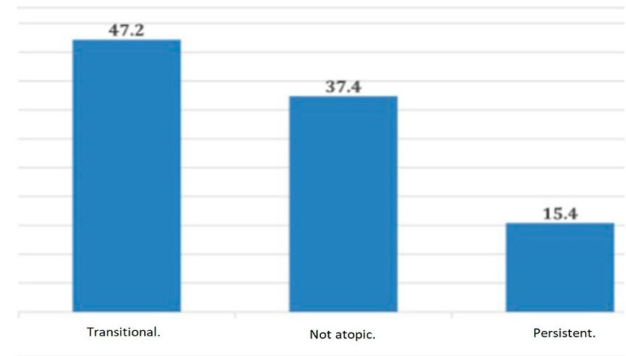


Figure 2. Distribution of the sample according to the phenotypes presented. Source: The authors (2019).

Table 2. Prevalence of the main risk factors for wheezing in the sample.

Variables	n (%)
Smoking in pregnancy	16 (13.0)
Lack of breastfeeding	109 (11.4)
Fastroesophageal reflux	32 (26.0)
Previous hospitalizations for respiratory problems	101 (82.1)
Rhinitis	24 (19.5)
Atopic dermatitis	22 (17.9)
Family history of asthma/ bronchitis	36 (26.8)
Smokers in the house	48 (39.0)
Animals	33 (26.8)
Mold or mildew on the walls	33 (26.8)
Pollution where you live	89 (72.4)
Number of rooms	
1 to 3	61 (49.6)
4 to 6	56 (45.5)
7 to 9	4 (3.3)
Number of people	
1 to 3	40 (32.5)
4 to 6	73 (59.3)
7 to 9	9 (7.3)
Mother's education	
Elementary School	26 (21.1)
High school	83 (67.40)
University education	14 (11.5)
Family income	
Unemployed	7 (5.7)
up to minimum wage	45 (36.6)
1 to 3 minimum wages	65 (53.6)
> 3 minimum wages	5 (4.1)

The risk factors related to the main wheezing diseases were: Pneumonia: previous hospitalizations for respiratory problems ($p=0.007$), passive exposure to smoking ($p=0.013$) and previous episodes of asthma ($p=0.033$). Bronchiolitis: age younger than 2 years ($p<0.001$), and family history of asthma

($p=0.025$). Asthma: age greater than 10 years ($p=0.009$), previous episode of asthma ($p<0.001$) and presence of wheezing in the chest after physical exercise in the last 12 months ($p=0.029$); there was a tendency for a greater number of asthmatics with mothers with low maternal schooling ($p=0.076$).

DISCUSSION

The prevalence of children hospitalized with wheezing in 2018 in a public hospital on the outskirts of São Paulo was high (26.7%), especially in the age group from 0 to 2 years old. The main phenotypes observed were transient wheezing (47.2%) and non-atopic (37.4%), persistent wheezing occurred less frequently, 15.4%.

These results are in agreement with the literature, as according to Solé (2008)⁵ there is a higher rate of transient sibilants in the first two years of life, due to smaller airways, greater susceptibility to viral infections and passive exposure to maternal smoking and tends to improve after 2-3 years. Within this group, there are those with acute symptoms associated with atopic factors, which are distinguished from the more common clinical picture associated with genetic factors (history of asthma), eczema, allergic sensitization and eosinophilia, and who, over the years, present with recurrence of wheezing, these being classified as persistent wheezing⁵. Finally, non-atopics develop “wheezing” due to contact with a pathogen that damages the epithelial tissues of the airways, inducing an inflammatory process and consequent bronchial hyperresponsiveness⁵.

It is worth mentioning that the classification of phenotypes in this study was carried out through the application of a questionnaire to those responsible, not taking into account allergic sensitization and eosinophilia, thus presenting some limitation, being subject to alterations in the presence of these tests.

Pneumonia was the main cause of hospitalization, followed by bronchiolitis. Bronchospasm was a frequent symptom and the atelectasis occurred as a complication of hypersecretivity. This data is in agreement with the literature, whose data show that, worldwide, among children under five years of age, community-acquired pneumonia occurs around 0.29 episodes per year, which is equivalent to an incidence of 150.7 million, with that 7 to 13% of cases require hospitalization⁶. According to DATASUS⁷, in 2012, there were 44,619 hospitalizations for pneumonia among children <4 years of age in São Paulo. According to Andrade et al. (2018)⁸ the prevalence of pneumonia reached 60% of the child population in 2015, being the leading cause of mortality among children <5 years, with a prevalence of 15%. However, national and international data from 2018 show a significant reduction in pneumonia mortality rates, due to an improvement in the socioeconomic situation, an increase in vaccination policies, greater availability of antibiotics and greater access to health care⁹.

Bronchiolitis was identified as the second leading cause of hospitalization in the study. According to data published in the USA, approximately 800 million infants required medical care in the first 12 months of life due to respiratory infections¹⁰. The main causative agent of infections is the respiratory syncytial virus (RSV), which affects 90% of patients under 24 months of age¹⁰. In Brazil, Alvarez et al. (2013)¹¹ reports that 2.1% of infants aged <1 year were hospitalized due to AVB caused by RSV, with 2.7% requiring ICU care, 2.1% using mechanical ventilation and 0.2% died, demonstrating the serious proportion that the pathology can reach.

Bronchospasm was a recurrent symptom in the study. This phenomenon is characterized by an increase in bronchial smooth muscle tone, causing bronchoconstriction¹². This happens due to pulmonary hyperresponsiveness, leading to a cascade of events, namely: hypersecretivity, airway obstruction, hypoventilation, increased surface tension and consequent alveolar collapse, resulting in atelectasis¹². According to Johnston e Carvalho (2008)¹³ atelectasis occurred due to probable hypoventilation and accumulation of secretion due to the characteristics of the population. The same author reports that children in the first years of life have less development of collateral ventilation performed through the intra-alveolar pores and communications of the alveolar bronchioles, called Kohn's pores and Lambert's channels respectively, which justifies a higher frequency of atelectasis in infants¹³.

In addition to the anatomical and physiological characteristics of children's respiratory system that favor respiratory infections, some factors are also associated with greater airway hyperresponsiveness, triggering a wheezing crisis and favoring respiratory infections².

Breastfeeding is relevant in protecting against infections and respiratory problems in much of the current literature. Sorio et al. (2017)¹⁴ argues that breast milk has anti-inflammatory, immunomodulatory and growth factors that protect the child from allergic sensitization during and shortly after the end of this phase. However, some studies are controversial. According to Brandão et al. (2017)¹⁵ exclusively maternal nutrition up to the fourth month of the infant's life contributes to its protection against AVB, due to the presence of immunological, immunomodulatory and anti-infective factors in breast milk. Breastfeeding has antiviral and bacterial substances, with immunologically active cells that stimulate the child's immune system, with a strong protective effect against pneumonia and lower respiratory infections¹⁶. In the present study, there was no statistical significance with breastfeeding and the diseases evaluated.

Maternal smoking during pregnancy remains an important insult to the developing lung and a factor associated with low birth weight, preterm birth, intrauterine growth restriction and sudden infant death¹⁷. Experimental studies with several animal models have shown that intrauterine exposure to nicotine leads to smaller lungs, with a reduced number of alveoli, alveolar changes suggestive of aging and

low capillary density¹⁸. In addition, prenatal exposure to nicotine causes abnormalities in the ramifications and dimensions of the airways and results in increased muscle and collagen deposition, with subsequent airflow limitation, reduced forced expiratory volume in the first second, and airway hyperreactivity, in animal models¹⁹.

Smoking at home, maternal postnatal, exposes the child passively to smoke, increasing the risk of respiratory infection in infants. In the meta-analysis by Jones et al. (2011)²⁰ on the effect of smoking by both parents, it showed a statistically significant increase in the chances of pulmonary infection, mainly bronchiolitis. When analyzing only pre and postnatal maternal smoking, a significant increase was observed, with stronger effects on the chances of respiratory infections and bronchiolitis²⁰.

In the study in question, no relationship was detected with prenatal smoking and hospitalization for pneumonia, bronchiolitis and asthma. Regarding the current contact with smokers at home, a relationship was observed only with hospitalization for pneumonia. This fact can be explained by the low number of smokers, both during pregnancy and after the child's birth. Investigations with a larger sample size are needed to confirm this fact.

The environment factor is directly related to disorders of the respiratory system, since the child, who is more susceptible, is exposed to several factors throughout their development, which can corroborate the triggering of pathological conditions¹⁵.

An important factor related to the environment where the child is inserted is the interaction with animals, in which the literature is controversial. According to the study by Magalhães et al. (2018)²¹, there is a significant relationship, since there is an increase in sensitization associated with contact with the fur of dogs and cats in the first year of life, being more susceptible in children with atopic predisposition²¹. In study Perzanowski et al. (2008)²² it was observed that exposure to cat hair caused a reduction in the frequency of wheezing in the first few years of life in infants at risk for developing asthma, while exposure to dog hair was unrelated to wheezing. In the current study, there was no significant difference in hospitalization for asthma, pneumonia and bronchiolitis with the presence of animals in the residence.

The presence of moisture and mold in the home environment has a great influence on the symptoms of respiratory diseases. According to Magalhães et al. (2018)²¹, signs of mold and mildew on the walls of a home indicate the presence of humidity, thus, there is a greater probability of proliferation of mites and fungi, which are the real triggers of asthma attacks in already sensitized patients. In this study, there was a greater tendency of children hospitalized with asthma and bronchiolitis in a home with mold/mold, confirming the findings in the literature.

According to Amâncio and Nascimento (2012)²³, atmospheric pollution is characterized by the amount of sulfur

dioxide (SO₂) and ozone (O₃), which can be harmful to the body, especially in children who, due to higher respiratory rates and higher levels of physical activity, are more exposed to pollutants. There is no concrete histological explanation for the damage caused by air pollution, however, it is believed that it causes lesions in the lung parenchyma, thus increasing the harmful effects of viruses and allergens²³. According to KKarr et al. (2006)²⁴ air pollutants intensify the lung parenchyma response to RSV, thus increasing the severity of bronchiolitis. In the current study, living in a region with pollution was not related to hospitalization for pneumonia, bronchiolitis and asthma.

The literature is conflicting regarding the effect of socioeconomic conditions on children's lung health. Bronchiolitis may be associated with the child's socioeconomic status, since factors such as income and maternal schooling can influence both the development of the pathology and its worsening. According to Albernaz et al. (2003)²⁵, mothers who attended school for less than five years increase the chances of their child developing bronchiolitis by five times, this is due to the fact that they do not have sufficient knowledge for the basic care of the child. Another important factor is family income, considering that families with greater financial resources provide better preventive conditions, as well as better child care²⁵. Lower family income can increase the hospitalization rate by up to three times, therefore, families with lower income levels are more susceptible to having children with bronchiolitis²⁵. In the studied sample, there were no statistically significant differences in hospitalization for respiratory diseases with the number of rooms and people in the house, family income and mother's education. There was only a trend of hospitalizations for asthma whose mothers had a lower level of education.

Regarding the modified ISAAC questionnaire, it was observed that most children had previous wheezing (80.5%), and 66.7% of them had wheezed in the last 12 months. About 16.3% had more than 5 crises in the last 12 months. It was observed that, in children hospitalized with pneumonia, there was statistical significance with the presence of a previous asthma episode and a significant trend with the presence of previous wheezing. Hospitalizations with a diagnosis of asthma showed significance with the presence of a previous asthma episode and the presence of wheezing in the chest after physical exercise.

The high prevalence of hospitalization of children with wheezing, mainly due to pneumonia and bronchiolitis, demonstrates the need for public policies to better monitor this population in order to prevent such symptoms. Special attention should be given to infants, children of asthmatic parents and smokers.

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