

Prevalence of and risk factors for wheezing in the first year of life*

Prevalência e fatores de risco para sibilância no primeiro ano de vida

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Abstract

Objective: To determine the prevalence of and the risk factors for wheezing in infants under one year of age and residing in the city of Porto Alegre, Brazil. **Methods:** This was a cross-sectional study and is part of a multicenter, multinational project. The parents or legal guardians of the infants were interviewed at primary health care clinics or during home visits. We used a standardized questionnaire, validated for use in Brazil. Potential risk factors were assessed by means of a Poisson regression model with robust variance estimation, using the Wald test to determine the significance of each variable in the model. **Results:** The sample comprised 1,013 infants. The majority of those were male (53%), and the mean age was 13.5 ± 1.2 months. In 61% of the infants, there had been at least one episode of wheezing, which had recurred at least three times in one third of those infants. The mean age at the first episode of wheezing was 5.16 months (median, 5 months). Over 40% of the infants with wheezing visited emergency rooms due to wheezing, and 17% of those were hospitalized at least once in the first year of life because of this symptom. In the multivariate analysis, the risk factors for wheezing were as follows: male gender; history of pneumonia; maternal smoking during pregnancy; day care center attendance; low maternal level of education; early weaning; multiple episodes of cold; first viral infection prior to 3 months of age; existence of siblings; and history of asthma in the nuclear family. **Conclusions:** The prevalence of wheezing is high among infants in the city of Porto Alegre. We identified various risk factors for wheezing in infants.

Keywords: Respiratory sounds/epidemiology; Asthma; Infant; Risk factors.

Resumo

Objetivo: Determinar a prevalência e os fatores de risco para sibilância em lactentes com até um ano de idade e residentes na cidade de Porto Alegre (RS). **Métodos:** Estudo transversal, parte de um projeto multicêntrico e multinacional. Os pais ou responsáveis dos lactentes foram entrevistados em unidades básicas de saúde ou durante visitas domiciliares. Utilizamos um questionário padronizado e validado para uso no Brasil. Potenciais fatores de risco foram avaliados mediante um modelo de regressão de Poisson com estimativa robusta de variância, utilizando-se o teste de Wald para determinar a significância de cada variável no modelo. **Resultados:** Foram incluídos 1.013 lactentes. A maioria era do sexo masculino (53%), e a média de idade foi de $13,5 \pm 1,2$ meses. Houve pelo menos um episódio de sibilância em 61% dos lactentes, e houve recorrência do sintoma em pelo menos três ocasiões em um terço daqueles lactentes. A média de idade no início dos episódios de sibilância foi de 5,16 meses (mediana, 5 meses). Mais de 40% dos lactentes com sibilância visitaram serviços de urgência em função desse sintoma, e 17% tiveram pelo menos uma hospitalização por essa causa no primeiro ano de vida. Na análise multivariada, os fatores de risco para sibilância foram os seguintes: sexo masculino, história de pneumonia, tabagismo na gravidez, frequência a creches, baixo nível de escolaridade da mãe, desmame precoce, número elevado de resfriados, primeiro quadro viral antes dos 3 meses, presença de irmãos e história familiar de asma. **Conclusões:** A prevalência de sibilância em lactentes no município de Porto Alegre é elevada. Vários fatores de risco para sibilância em lactentes foram identificados.

Descritores: Sons respiratórios/epidemiologia; Asma; Lactente; Fatores de risco.

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Introduction

Wheezing is a quite common clinical finding in pediatric patients, especially in the first years of life. Epidemiological studies have found high prevalence rates in this age group. Surveys conducted in developed countries have found prevalence rates between 20% and 30%, recurrence rates being high.⁽¹⁻³⁾ Prevalence rates seem to be higher in developing countries.^(4,5) In a cohort of 188 neonates monitored for one year in Chile, episodes of wheezing were identified in 80% of the cases, half presenting recurrence.⁽⁶⁾

The etiologic diagnosis of wheezing in small infants varies considerably, and, in most instances, the clinical manifestations are associated with viral infection.⁽⁷⁻⁹⁾ It is presumed that asthma can manifest early in infants. However, the diagnosis of asthma is difficult in this age group, since complementary methods of investigation, such as pulmonary function tests, are available at few facilities, and the number of possible etiologies is high.

Regardless of the etiology, many factors are related to the risk of wheezing and of the recurrence of wheezing in infants. A history of asthma in the nuclear family, especially a maternal or paternal history, significantly increases the risk. Other risk factors have been identified⁽¹⁰⁻¹⁶⁾: prematurity; low birth weight; siblings in the household; day care center attendance; early weaning; exposure to smoking during pregnancy and in the postnatal period; low parental socioeconomic status; and low parental level of education. Knowledge of local prevalence and associated risk factors can inform decisions regarding treatment and risk prevention, as well as the planning of public health measures.

Population-based studies assessing the prevalence of wheezing in infants are still scarce, and those using similar methodologies so that populations from different localities can be compared are even scarcer. The first multicenter, multinational study designed with this goal in mind was the *Estudio Internacional de Sibilancias en Lactantes* (EISL, International Study of Wheezing in Infants). The EISL involved localities in Latin American countries, as well as in Spain and in the Netherlands, and, with the use of questionnaires validated for use in those communities, aimed to obtain data that

could elucidate questions regarding wheezing in infants.⁽¹⁷⁾

The objective of the present study was to determine the prevalence of wheezing and the associated risk factors in infants residing in the city of Porto Alegre, Brazil.

Methods

This was a prevalence study, conducted as part of the EISL—a multicenter, multinational project involving centers in Latin America, Spain, and the Netherlands and designed to analyze data regarding wheezing in infants.⁽¹⁸⁾ Each center was responsible for the local logistics involved in validating the questionnaire, as well as for collecting, tabulating, and subsequently sending the data. The present study was conducted between June and December of 2006 in the city of Porto Alegre, Brazil.

In the city of Porto Alegre, public health care is provided at primary health care clinics, which are organized into six regional districts. In addition, the population is treated at clinics affiliated with public and private hospitals. During the data collection period, the parents or legal guardians of infants between 12 and 15 months of age were interviewed and completed a standard written questionnaire, duly validated for use in Brazil.⁽¹⁹⁾ This questionnaire comprises 45 questions regarding demographic aspects, socioeconomic aspects, and wheezing episodes in the first year of life. According to data from the Center for Epidemiological Surveillance of the Porto Alegre Municipal Department of Health, during the study period, the population of the city included 3,639 children in the target age group. To achieve the minimum number of 1,000 infants, we conducted the interviews during the vaccination campaign carried out at the primary health care clinics (25 centers involving all of the health management districts in the city) and during home visits, as well as during the wait to schedule pediatric appointments and visits for vaccination at family health care clinics. The parents or legal guardians of all of the subjects gave written informed consent, and the confidentiality of data was ensured.

The sample size, previously determined by the coordinators of the study, was such that, in the overall data analysis, it was representative of each center, and the number of participants at each center was similar, allowing comparisons

among those centers and thereby making it possible to implement local and system-wide measures. The necessary minimum number of interviews per center was estimated at 1,000.⁽¹⁷⁾

Frequencies were determined for categorical variables, whereas means and standard deviations were determined for ordinal variables. The chi-square test and Fisher's exact test were used in order to compare the means.

Continuous variables are presented as means, with prevalence ratios and 95% CIs, whereas categorical variables are presented as absolute and relative frequencies.

In the bivariate and multivariate analyses, the prevalence ratio was calculated by means of a Poisson regression model with robust variance estimation, considering that the prevalence of wheezing was 60% in this population. The Wald test was used in order to determine the significance of each variable in the model. Initially, all covariates that presented $p < 0.10$ were included in the multivariate model. The next step was the individual exclusion of the covariates that presented critical p values (values that were not significant). This step was repeated until all variables remaining in the model presented $p < 0.10$.

Results

Between June and December of 2006, 1,013 infants were included in the analysis. The majority of those were male (53%), and the mean age was 13.5 ± 1.2 months. In 61% of the infants included, there had been at least one episode of wheezing. In one third of those infants, there had been at least three episodes, and those infants were characterized as having recurrent wheezing. The mean age at the first episode of wheezing was 5.16 months (median, 5 months). Regarding severity, more than 40% of the infants had received emergency room treatment for wheezing, and 17% had been hospitalized for wheezing at least once in the first year of life (Table 1).

More than half of the infants had been treated with bronchodilators, and some been treated with inhaled corticosteroids and leukotriene receptor antagonists, despite the fact that such treatment is not indicated during the acute phase of wheezing. The use of the latter groups of drugs illustrates the severity of the presentation of the episodes of wheezing (Table 1).

The prevalence of allergic disease and asthma, as well as of rhinitis or dermatitis, in any member of the family was, respectively,

Table 1 - Demographic characteristics of the population analyzed.

Characteristic	Wheezers, %	Non-wheezers, %	p
Male gender	57	47	< 0.01
History of pneumonia	17	5	0.05
Hospitalization for pneumonia	10	3	< 0.01
Passive smoking	50	42	0.011
Maternal smoking	29	22	0.016
Maternal smoking during pregnancy	23	14	< 0.01
History of asthma in the nuclear family (parents or siblings)	47	30	< 0.01
History of rhinitis in the nuclear family	69	62	< 0.01
History of atopic dermatitis in the nuclear family	37	30	0.04
Day care center attendance	24	12	< 0.01
Pets in the household at the time the infant was born	53	50	0.3
Pets in the household during the infant's first year of life	51	52	0.9
Mother with less than 8 years of schooling	79	72	< 0.01
Less than 2 months of exclusive breastfeeding	62	52	0.02
Less than 2 colds in the first year	26	48	0.06
First cold prior to 3 months of age	42	29	0.09
Siblings in the household	68	59	0.01
≤ 3 people in the household	35	41	0.06
Atopic dermatitis	64	56	0.02

40%, 66%, and 34%. Smoking was a common finding among the parents and siblings of the infants evaluated. Nearly half of the infants had been exposed to smoking in the household, and maternal smoking was identified in 26% of the families. One fourth of the mothers were found to have smoked during pregnancy.

Among other risk factors analyzed, day care center attendance was an uncommon finding, reported for only 15% of the infants. Most of those infants were less than 5 months of age when they started attending a day care center. Early weaning from breast milk was common. Half of the families reported having pets in the household at the time the infants were born and in their first year of life.

More than two thirds of the mothers or family members of the infants included in the study had a low level of education. In most cases, the infants had only one sibling, and, on average, four people lived in the same household.

The multivariate analysis revealed the following risk factors for wheezing in the first year of life: male gender (in 57%); history of pneumonia (in 17%); maternal smoking during pregnancy (in 23%); day care center attendance (in 24%); low maternal level of education (in 79%); early weaning (in 62%); multiple episodes of cold (in 21%); first viral infection prior to 3 months of age (in 40%); siblings in the household (in 68%); and history of asthma in the nuclear family—parents or siblings (in 47%). Other data regarding a history of allergy, such as rhinitis and dermatitis, in the nuclear family

did not achieve statistical significance. Other factors associated with risk of wheezing in the first year of life, such as environmental exposure to smoking, maternal smoking, hospitalization for pneumonia, and atopy (dermatitis) in the infant, despite showing statistical significance in the bivariate analysis, did not maintain this significance in the multivariate analysis model (Table 2).

Discussion

The 61% prevalence of wheezing obtained in the present study is comparable to that reported in population-based studies conducted in other developing countries.⁽⁴⁻⁶⁾ In addition, the risk factors found, such as male gender, history of pneumonia, maternal smoking during pregnancy, day care center attendance, low maternal level of education, early weaning, multiple episodes of cold, first viral infection prior to 3 months of age, siblings in the household, and history of asthma in the nuclear family (parents or siblings), are in accordance with the findings obtained in previous studies.^(4,5,10-14)

Various population-based studies have attempted to determine the clinical importance of wheezing in childhood. Its complexity makes prevalence rates vary, depending on the time of data collection, the area, and the population assessed, as well as on the research tool used. The fact that the present study primarily involved families from poor peripheral areas in the city of Porto Alegre who sought treatment

Table 2 - Risk factors for wheezing in the first year of life (multifactorial analysis).

Characteristic	PR (95% IC)	p
Male gender	1.102 (1.030-1.211)	0.043
Pneumonia	1.183 (1.070-1.307)	0.001
Maternal smoking during pregnancy	1.135 (1.023-1.259)	0.017
Asthma (parents)	1.203 (1.090-1.329)	< 0.001
Asthma (siblings)	1.172 (1.030-1.333)	0.016
Day care center attendance	1.295 (1.172-1.431)	< 0.001
Mother with less than 8 years of schooling	1.332 (1.009-1.759)	0.043
Mother with 8-11 years of schooling	1.277 (0.947-1.723)	0.109
Siblings in the household	1.144 (1.032-1.269)	0.011
Less than 2 months of exclusive breastfeeding	1.129 (1.021-1.249)	0.018
More than 6 episodes of cold	1.440 (1.245-1.666)	< 0.001
Between 3 and 6 episodes of cold	1.197 (1.043-1.373)	0.01
First cold prior to 3 months of age	1.244 (1.042-1.486)	0.016
First cold between 3 and 6 months of age	1.187 (0.994-1.417)	0.058

PR: prevalence ratio.

at municipal primary health care clinics might partially explain the high prevalence found. In a study conducted in the city of Pelotas, Brazil,⁽²⁰⁾ involving a population with the same socioeconomic profile, the reported prevalence of wheezing (55%) was very similar to that reported here. However, reports of wheezing made by family members or caregivers might be biased due to the fact that, in small infants, the sound of wheezing can be confused with sounds caused by the accumulation of upper airway secretions.⁽²¹⁾

Another study that was part of the EISL was conducted in the state of Paraná, Brazil, and the authors of that study reported a lower prevalence of wheezing (45%).⁽⁴⁾ The duration of the studies might explain this difference. The present study, conducted during the winter and spring, when the prevalence of respiratory diseases is higher, was carried out over a 5-month period. Therefore, the recollection of family members regarding clinical findings and measures taken in the management of the wheezing is likely to have been better in the present study than in the other study, which was carried out over a longer period (18 months). In addition, it is likely that the study conducted in the state of Paraná included a greater proportion of families of higher socioeconomic status, as mentioned by the authors.⁽⁴⁾ In the present study, the majority of the mothers had less than 8 years of schooling, compared with only approximately a third of those included in the study conducted in Paraná. A study conducted in the state of Rio Grande do Sul, Brazil,⁽¹²⁾ showed that the risk of wheezing in children under 5 years of age was directly related to a low maternal level of education.

A history of asthma in the nuclear family and male gender are risk factors for wheezing, being almost universally described in international studies.^(13,22) In our study, having parents or siblings with asthma translated to a 20% higher risk of wheezing in the first year of life. The risk of wheezing was found to be similar in male and female infants. These data are in accordance with those reported in the literature and possibly reflect the smaller airway diameter in the males in the first years of life.⁽²³⁾

Day care center attendance was associated with a nearly 30% higher risk of wheezing. In some studies,^(22,24) involving populations in European countries, there was also an association between day care center attendance and the

risk of early wheezing. It should be considered that, on average, the children in those studies were more than 6 months old when they started attending a day care center. A birth cohort study of 922 children in England⁽²⁴⁾ found that entering day care between 6 and 12 or after 12 months of age, respectively, was significantly and inversely associated with current wheeze (at 5 years of age), and that entering day care between 6 and 12 months of age reduced the risk of persistent wheezing (at 5 years of age). In a cross-sectional study, such as ours, it is not possible to assess the various presentations of wheezing in relation to day care center attendance.

Smoking was a very common finding in the present study, intrauterine exposure to smoking being associated with the risk of wheezing in the multifactorial analysis. However, no association was found between postnatal exposure to smoking in the household and the risk of wheezing. In a large birth cohort study of children in Denmark,⁽²²⁾ maternal or paternal smoking, in combination with a history of asthma in the nuclear family, tripled the risk of wheezing, compared with a history of asthma in the nuclear family alone.

The design of the present study might explain the difference found in relation to exposure to smoking, since transient early wheezing seems to be more closely associated with intrauterine exposure and the consequent changes in fetal immune function⁽¹⁰⁾ in the postnatal period and in pulmonary function, whereas exposure to smoking in the household increases the risk of asthma.⁽²⁵⁾ A study conducted in the city of Fortaleza, Brazil, and involving more than 1,000 children under 5 years of age⁽²⁶⁾ identified a two-fold higher risk of wheezing or dyspnea among children who were passive smokers. In addition, in a cohort in the city of Rio Grande, Brazil,⁽¹²⁾ the risk of wheezing was 30–40% higher among children whose family members smoked. In the birth cohort study of children in Denmark,⁽²²⁾ the authors observed that maternal smoking during pregnancy was also related to wheezing in the first years of life, although not to atopic disease. Another group of authors,⁽²⁷⁾ studying a population with characteristics similar to those of our study population, found that, after a multifactorial analysis, only maternal smoking during pregnancy was associated with wheezing in the first year of life. In another study,⁽²⁸⁾ intrauterine exposure to smoking was also associated with the transient wheezing phenotype. One limitation to a better

understanding of the association between passive smoking and wheezing is the lack of objective measures. However, as demonstrated in one study,⁽²⁹⁾ the tendency for parents and caregivers of children with respiratory disease to underreport the frequency of smoking might indicate that these associations are more significant. In that study, approximately 20% of the children who were hospitalized for acute viral bronchiolitis had high urinary cotinine levels, despite the fact that their mothers denied exposure to smoking.⁽²⁹⁾

Various studies have suggested that weaning from breastfeeding is associated with the risk of wheezing and other allergic diseases. In the present study, early weaning was associated with wheezing regardless of a history of asthma or atopy in the nuclear family. In a cohort of children monitored from birth to 2 years of age, early weaning and a history of asthma in the nuclear family were found to be associated with an increased risk of wheezing.⁽²⁾ In the study conducted in Denmark,⁽²²⁾ weaning was also associated with transient wheezing, although not with atopic disease. Early weaning is a risk factor for infection, which is in turn related to an increased risk of wheezing in infants, whereas early bacterial exposure could be a protective factor against the subsequent onset of allergic diseases, such as asthma.⁽³⁰⁾ This might also explain the fact that the existence of older siblings was independently related to an increased risk of wheezing in the first year of life, since the risk of transmission of viral infectious diseases is higher in environments with a greater number of people, especially if those people are other children.

Studies such as this one are subject to bias, since they require a large group of interviewers and involve questions whose interpretation is not always easy. The definition of wheezing is limited because it does not involve physician diagnosis, and the characteristic of an educationally and economically disadvantaged population might explain some of the differences found in relation to studies conducted in developed countries. It should also be borne in mind that, because the information was obtained by means of a questionnaire, the prevalence of certain factors, such as smoking in the household and maternal smoking during pregnancy, might have been underestimated. In addition, the exposure to smoking was not quantified in the present study.

The objective of a large population-based study, such as the EISL, is to assess potential differences among populations with different socioeconomic and cultural characteristics, and this makes it necessary to wait for a larger amount of data from the various centers participating in the study so that comparisons and analysis can be made. Based on the results of present study, we can conclude that there is a high prevalence of wheezing among infants residing in the city of Porto Alegre, Brazil, and that there is significant related morbidity. Measures such as maternal smoking cessation during pregnancy and the promotion of breastfeeding would have a potential impact on reducing the prevalence of wheezing in this population. Since this was a single-center study involving limited comparisons, it is difficult to draw conclusions on the basis of our findings. The body of data coming from the various centers will show whether the risk factors found in the present study will remain and whether they will eventually have an even greater impact.

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