

## Prevalence and severity of wheezing in the first year of life\*

Prevalência e gravidade da sibilância no primeiro ano de vida

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### Abstract

**Objective:** To determine the prevalence and severity of wheezing in infants, using the standardized protocol devised for the “*Estudio Internacional de Sibilancias en Lactantes*” (EISL, International Study of Wheezing in Infants), as well as to determine the relationship between such wheezing and physician-diagnosed asthma, in the first year of life. **Methods:** Between March of 2005 and August of 2006, the EISL questionnaire was administered to the parents or legal guardians of infants undergoing routine procedures or immunization at public primary health care clinics in the southern part of the city of São Paulo, Brazil. **Results:** Our sample comprised 1,014 infants (mean age =  $5.0 \pm 3.0$  months), 467 (46.0%) of whom had at least one wheezing episode, 270 (26.6%) having three or more such episodes, in their first year of life. The use of inhaled  $\beta_2$  agonists, inhaled corticosteroids, or antileukotrienes, as well as the occurrence of nocturnal symptoms, difficulty breathing, pneumonia, emergency room visits, and hospitalization due to severe wheezing, was significantly more common among those with recurrent wheezing ( $p < 0.05$ ). Physician-diagnosed asthma was reported for 35 (7.5%) of the 467 wheezing infants and was found to be associated with the use of inhaled corticosteroids, difficulty breathing during the attacks, and six or more wheezing episodes in the first year of life. However, less than 40% of those infants were treated with inhaled corticosteroids or antileukotrienes. **Conclusions:** In this study, the prevalence of wheezing episodes among infants in their first year of life was high and had an early onset. The proportion of infants diagnosed with and treated for asthma was low.

**Keywords:** Asthma/diagnosis; Asthma/epidemiology; Respiratory sounds.

### Resumo

**Objetivo:** Avaliar a prevalência e a gravidade da sibilância, bem como sua relação com o diagnóstico médico de asma, em lactentes no primeiro ano de vida, utilizando o protocolo padronizado do “*Estudio Internacional de Sibilancias en Lactantes*” (EISL, Estudo Internacional de Sibilâncias em Lactentes). **Métodos:** Entre março de 2005 e agosto de 2006, os pais ou responsáveis de lactentes que procuraram unidades básicas de saúde na região centro-sul de São Paulo (SP) para procedimentos de rotina e imunização responderam ao questionário escrito do EISL. **Resultados:** A amostra foi constituída por 1.014 lactentes (média de idade =  $5,0 \pm 3,0$  meses), 467 (46,0%) dos quais apresentaram sibilância no primeiro ano de vida, sendo que 270 (26,6%) tiveram três ou mais episódios. Entre esses últimos, o uso de  $\beta_2$ -agonista inalatório, corticosteroide inalatório e antileucotrieno, assim como a presença de sintomas noturnos, dificuldade para respirar, pneumonia, idas ao pronto socorro e internação por sibilância grave, foram significativamente mais frequentes ( $p < 0,05$ ). Os pais de 35 (7,5%) dos 467 lactentes relataram o diagnóstico médico de asma, o qual foi associado ao uso de corticosteroide inalatório, percepção de falta de ar durante as crises e seis ou mais episódios de sibilância no primeiro ano de vida. Entretanto, menos de 40% desses lactentes recebiam corticosteroide inalatório ou antileucotrieno como tratamento. **Conclusões:** A prevalência da sibilância no primeiro ano de vida de lactentes no estudo foi alta e teve início precoce. A proporção de lactentes diagnosticados e tratados como asmáticos foi baixa.

**Descritores:** Asma/diagnóstico; Asma/epidemiologia; Sons respiratórios.

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## Introduction

Wheezing is one of the most common respiratory symptoms in children and can result from a number of pulmonary diseases or be of other etiologies. Regardless of the cause, wheezing is a reason for seeking emergency treatment, especially if there are recurrent episodes. Recurrent wheezing is a very common condition in children, and, in most cases, the initial episodes occur in the first year of life.<sup>(1)</sup>

In infants, there are a number of potential causes of recurrent or non-recurrent wheezing, such as acute viral bronchiolitis, aspiration syndromes, or early-onset asthma. In general, infants with recurrent wheezing require special medical care, with monitoring from the onset of symptoms, as well as appropriate treatment, in order to avoid unfavorable outcomes and higher morbidity.

As observed in asthma in older children,<sup>(2)</sup> the prevalence and severity rates of recurrent wheezing among infants in developing countries are likely to be higher than are those found among infants in developed countries. Although the reasons for such differences remain unknown, it is likely that they are attributable to exposure to environmental risk factors, especially those related to low socioeconomic status.<sup>(3,4)</sup>

In order to conduct a worldwide comparative study of the prevalence of wheezing in infants, it is necessary to use a standardized method validated for use in the countries (cultures) involved in the study. Therefore, it is believed that the development of well-standardized protocols that are applicable to parents of infants will allow the identification of patients with recurrent wheezing and, possibly, of those with asthma.

The *Estudio Internacional de Sibilancias en Lactantes* (EISL, International Study of Wheezing in Infants) was developed to study the impact of recurrent wheezing on infants in the first year of life, as well as to determine its prevalence and associated risk factors.<sup>(5)</sup> That was an international multicenter study involving Latin American countries, as well as the Netherlands and Spain. In Brazil, eight centers, one of which was located in the southern part of the city of São Paulo, participated in that study.

The objective of the present study, in its first phase, was to determine and describe the prevalence and severity of wheezing, in the first

year of life, among infants living in the southern part of the city of São Paulo, Brazil, as well as to determine the relationship between such wheezing and physician-diagnosed asthma, using the standardized protocol devised for the EISL.

## Methods

The standardized written questionnaire for Phase One of the EISL (WQ-P1-EISL) was administered to the parents or legal guardians of infants aged 12 to 15 months who lived in the southern part of the city of São Paulo, Brazil. This region was chosen because it is the region in which the International Study of Asthma and Allergies in Childhood (ISAAC) Phase One and Phase Three were conducted.<sup>(6,7)</sup>

The infants who had parent-reported chronic diseases that could affect the respiratory system (neuropathies, myopathies, heart diseases, genetic diseases, and severe malformations) were excluded from the study, as were those for whom the questionnaire was less than 90% completed.

From among the 60 primary health care clinics in the southern part of the city of São Paulo, Brazil, we randomly selected 9, each of which is located in a different district of the city. The parents or legal guardians who agreed to participate in the study gave written informed consent and were subsequently interviewed by previously trained pediatricians or fifth-year medical students of the *Universidade Federal de São Paulo/Escola Paulista de Medicina* (UNIFESP/EPM, Federal University of São Paulo/Paulista School of Medicine). We evaluated infants examined during visits to the primary health care clinics between 2005 and 2006. These visits were for routine procedures, including immunization, or were related to one of the four immunization campaigns against childhood poliomyelitis run during the study period.

The WQ-P1-EISL is an instrument composed of 45 questions about demographic characteristics, as well as about wheezing and its potential risk factors.<sup>(5)</sup> Originally developed in Spanish, it has been translated into Portuguese and validated for use in Brazil.<sup>(8-10)</sup> A question developed for the Brazilian population was added to this questionnaire: "Has your child used oral corticosteroids?"

The data obtained with the WQ-P1-EISL were coded in a standard manner, transferred to

a database created with Microsoft Excel® 2000, and statistically analyzed via the Statistical Package for the Social Sciences for Windows, version 13.0 (SPSS Inc., Chicago, IL, USA).

The wheezing infants were divided into groups by frequency of wheezing episodes: less than three wheezing episodes; three or more wheezing episodes (recurrent wheezers); and six or more wheezing episodes (severe recurrent wheezers). Those who had never had a wheezing episode were designated non-wheezers.

The infants who had at least one wheezing episode were analyzed as to how gender affects the frequency of wheezing episodes, the symptoms presented, and the use of medications for wheezing, as well as the diagnoses of asthma, pneumonia, and upper respiratory tract infections. The wheezers diagnosed with asthma were assessed for severity factors and type of treatment given.

Depending on the variables analyzed, parametric tests (Student's t-test) and nonparametric tests (chi-square and Fisher's exact test) were used, as was logistic regression. Logistic regression was used for the joint analysis of the potential severity factors related to recurrent wheezing and to a prior diagnosis of asthma, in order to determine the factors independently related to the outcome. The level of significance required in order to reject the null hypothesis was set at 0.05.

The present study was approved by the Research Ethics Committees of the UNIFESP/

EPM and the São Paulo Municipal Department of Health.

## Results

We interviewed 1,054 parents or legal guardians of infants 12-15 months of age. From this sample, we excluded 30 questionnaires that were completed incorrectly and 10 that were related to infants who had heart disease or neuropathy. Therefore, the final sample comprised 1,014 questionnaires. Most respondents were mothers (82.1%), followed by fathers (10.8%) and other family members (7.1%). Of the 1,054 infants evaluated, 512 (50.5%) were male. Table 1 shows the characteristics of the infants who had at least one wheezing episode, by gender. Among the wheezing infants, the values for weight and height (at birth and at 12 months) were, as expected, slightly higher for boys than for girls, and the difference was statistically significant. There were no statistically significant differences between the genders in terms of ethnicity.

A total of 467 infants (46.0%) were found to have had one or more wheezing episodes in the first 12 months of life, and the mean age at onset was  $5.0 \pm 3.0$  months. Of those, 270 had three or more wheezing episodes (recurrent wheezing), whereas 100 had six or more wheezing episodes (severe recurrent wheezing). Table 2 shows the personal and clinical characteristics of each group of wheezers.

**Table 1** - Clinical characteristics of the infants who had had at least one wheezing episode in the first year of life by gender.

Characteristic	Male	Female	Overall	p*
	(n = 259)	(n = 208)	(n = 467)	
	n (%)	n (%)	n (%)	
Three or more wheezing episodes	159 (61.4)	111 (53.4)	270 (57.8)	0.1
Six or more wheezing episodes	57 (22.0)	43 (20.7)	100 (21.4)	0.8
Use of inhaled $\beta_2$ -agonists	218 (84.2)	184 (88.5)	402 (86.1)	0.2
Use of inhaled corticosteroids	37 (14.3)**	17 (8.2)	54 (11.5)	0.04
Use of antileukotrienes	10 (3.9)	2 (0.9)	12 (2.5)	0.09
Use of oral corticosteroids	123 (47.5)	86 (41.3)	209 (44.7)	0.2
Nocturnal awakenings sometimes	166 (64.1)	124 (59.6)	290 (62.0)	0.4
Emergency room visits	169 (65.2)	129 (62.0)	298 (63.8)	0.5
Difficulty breathing as perceived by parents	132 (50.1)	95 (45.7)	227 (48.6)	0.3
Hospitalization due to bronchitis	53 (20.5)	39 (18.8)	92 (19.6)	0.7
Physician-diagnosed asthma	24 (9.3)	11 (5.3)	35 (7.4)	0.1
Pneumonia	92 (35.5)**	52 (25.0)	144 (30.8)	0.02
Hospitalization due to pneumonia	43 (16.6)	28 (13.5)	71 (15.2)	0.4

\*Fisher's exact test or chi-square test. \*\*Statistically significant.

**Table 2** – Personal and clinical characteristics of the infants by number of wheezing episodes in the first year of life (n = 467).

Variable	Episodes/year					
			p*			p*
	< 3 (n = 197)	≥ 3 (n = 270)		< 6 (n = 367)	≥ 6 (n = 100)	
Male gender, n (%)	100 (21.4)	159 (34.0)	0.08	202 (43.3)	57 (12.2)	0.8
Weight at birth, kg <sup>a</sup>	3.2 ± 0.6	3.1 ± 0.6	0.06	3.2 ± 0.6**	3.0 ± 0.6	0.01
Current weight, kg <sup>a</sup>	10.1 ± 1.5	10.3 ± 1.4	0.2	10.2 ± 1.5	10.5 ± 1.4**	0.03
Height at birth, cm <sup>a</sup>	48.0 ± 3.4	47.9 ± 3.2	0.4	48.0 ± 3.4	47.9 ± 3.1	0.6
Current height, cm <sup>a</sup>	75.3 ± 5.9	74.9 ± 4.3	0.6	75.1 ± 5.3	75.1 ± 3.6	0.9
Age at wheezing onset, months <sup>a</sup>	6.2 ± 3.4**	4.1 ± 2.5	< 0.001	5.5 ± 3.1**	3.3 ± 2.3	< 0.001
Black/Mulatto, n (%)	68 (14.6)	87 (18.6)	0.7	124 (26.5)	31 (6.6)	0.6
Use of inhaled β <sub>2</sub> -agonists, n (%)	162 (82.2)	240 (88.9)**	0.04	310 (84.5)	92 (92.0)**	0.07
Use of inhaled corticosteroids, n (%)	13 (6.6)	41 (15.2)**	0.007	36 (9.8)	18 (18.0)**	0.04
Use of antileukotrienes, n (%)	4 (2.0)	8 (2.9)	0.7	9 (2.5)	3 (3.0)	0.7
Use of oral corticosteroids, n (%)	81 (41.1)	127 (47.0)	0.2	47 (12.8)	48 (48.0)	0.9
Occasional nocturnal awakenings, n (%)	88 (44.7)	202 (74.8)**	< 0.001	207 (56.4)	83 (83.0)**	< 0.001
Emergency room visits, n (%)	105 (53.3)	193 (71.5)**	< 0.001	218 (59.4)	80 (80.0)**	< 0.001
Difficulty breathing as perceived by parents, n (%)	83 (42.1)	144 (53.3)**	0.02	159 (43.3)	68 (68.0)**	< 0.001
Hospitalization due to wheezing, n (%)	30 (15.2)	62 (23.0)**	0.04	55 (11.8)	37 (37.0)**	< 0.001
Physician-diagnosed asthma, n (%)	7 (3.5)	28 (10.4)**	0.007	20 (5.4)	15 (15.0)**	0.002
Pneumonia, n (%)	40 (20.3)	104 (38.5)**	< 0.001	94 (25.6)	50 (50.0)**	< 0.001
Hospitalization due to pneumonia, n (%)	25 (12.7)	46 (17.0)	0.2	43 (11.7)	28 (28.0)**	< 0.001

<sup>a</sup>Results expressed as mean ± SD (Student's t-test). \*Chi-square test or Fisher's exact test. \*\*Statistically significant.

Multivariate analysis revealed that recurrent wheezing was independently associated with the use of inhaled corticosteroids (OR = 2.2; 95% CI: 1.1-4.4; p = 0.03), frequent nocturnal symptoms (OR = 3.5; 95% CI: 2.3-5.2; p < 0.001), emergency room visits (OR = 1.6; 95% CI: 1.1-2.5; p = 0.02), and physician-diagnosed pneumonia (OR = 3.5; 95% CI: 1.8-6.6; p = 0.005). Severe recurrent wheezing was independently associated with frequent nocturnal symptoms (OR = 2.9; 95% CI: 1.6-5.2; p < 0.001), difficulty breathing as perceived by parents (OR = 1.8; 95% CI: 1.1-2.9; p = 0.03), hospitalization due to wheezing (OR = 1.9; 95% CI: 1.1-3.3; p = 0.03), and physician-diagnosed pneumonia (OR = 1.8; 95% CI: 1.1-3.1; p = 0.02).

Physician-diagnosed asthma was reported for 35 (7.5%) of the 467 wheezing infants. Table 3 shows the comparison of the clinical characteristics of the infants with and without physician-diagnosed asthma. The multivariate analysis revealed that physician-diagnosed asthma was independently associated with the use of inhaled corticosteroids (OR = 2.97; 95% CI: 1.32-6.69; p = 0.009), difficulty breathing during the attacks (OR = 4.42; 95% CI: 1.30-14.5; p = 0.02), and having had six or more wheezing episodes (OR = 2.15; 95% CI: 1.02-4.52; p = 0.04).

Of the parents or legal guardians of the wheezing infants, 429 (91.9%) responded to the

question about the use of oral corticosteroids, and, of those, 209 (48.7%) reported having used oral corticosteroids to treat wheezing. The analysis of the relationship of the use of oral corticosteroids as an associated factor with higher frequency and greater severity of wheezing episodes revealed no significant association between the variables.

## Discussion

In Brazil, the city of São Paulo is one of the areas with the highest prevalence of wheezing and asthma among children and adolescents.<sup>(11,12)</sup> However, there have been only a few studies evaluating the prevalence of wheezing in infants in the metropolitan area of São Paulo, the largest urban area in South America. The situation is not different in other large urban areas in Brazil, nor is it different in other developing countries.

More than one decade ago, the prevalence of recent wheezing (one or more episodes in the last 12 months) among children aged 12 to 23 months and living in the city of São Paulo was estimated to be 14.3%.<sup>(13)</sup> A birth cohort study involving individuals at high risk of developing asthma (parents with atopy), conducted on the outskirts of the southern part of the city, documented that, at 30 months, 52% of the participating children had recurrent wheezing.<sup>(3)</sup> In the present study, we found a high prevalence

**Table 3** – Personal and clinical characteristics of the infants with and without physician-diagnosed asthma.

Characteristic	With asthma	Without asthma	p*
	(n = 35)	(n = 432)	
	n (%)	n (%)	
Male gender	24 (68.6)	235 (54.4)	0.1
Use of inhaled $\beta_2$ -agonists	35 (100.0)**	367 (85.0)	0.008
Use of inhaled corticosteroids	11 (31.4)**	43 (10.0)	< 0.001
Use of antileukotrienes	3 (8.6)	9 (2.1)	0.06
Use of oral corticosteroids	22 (62.9)**	187 (43.3)	0.03
Pneumonia	17 (48.6)**	127 (29.4)	0.02
Hospitalization due to pneumonia	11 (31.4)**	60 (13.9)	0.01
Six or more wheezing episodes	15 (42.9)**	85 (19.7)	0.004
Three or more wheezing episodes	28 (80.0)**	242 (56.0)	0.007
Nocturnal symptoms	29 (82.9)**	261 (60.4)	0.01
Emergency room visits	32 (91.4)**	266 (61.6)	< 0.001
Difficulty breathing as perceived by parents	26 (74.3)**	201 (46.5)	0.002
Hospitalization due to wheezing	16 (45.7)**	76 (17.6)	< 0.001

\*Fisher's exact test. \*\*Statistically significant.

of wheezing in a representative sample of the population in the southern part of the city, and slightly less than half of the infants had had at least one wheezing episode in the first year of life. The variation observed between previous studies and the present study might be related to the lack of standardization of the methods used to identify infants, to the type of study conducted, to the definition of wheezing, and to the age group studied.

Among the wheezers, there was a predominance of male infants, who also had a higher frequency of pneumonia episodes and received inhaled corticosteroids for the treatment of wheezing more frequently than did female infants (Table 1). Studies have demonstrated that male gender is a risk factor for wheezing in children, and it has been suggested that the smaller airway diameter in boys at birth is an explanation for this.<sup>(1)</sup>

Nearly 1 in every 4 infants evaluated had recurrent wheezing, which was defined as the report of three or more wheezing episodes in the first year of life. The infants in this group had earlier onset of episodes (Table 2), received inhaled corticosteroids more frequently, and more often showed signs of greater severity than did those in the group with non-recurrent wheezing (multivariate analysis). Isolated studies have suggested that the prevalence and severity of recurrent wheezing are higher in developing countries than in developed countries.<sup>(4,14,15)</sup> It is likely that this is related to environmental

factors and to the poor socioeconomic status of the populations in those areas. In studies using the same instrument and method to evaluate infants in the same age group, the prevalence rates in the city of Curitiba, Brazil, were found to be similar for wheezing (45.4%) and recurrent wheezing (22.6%),<sup>(16)</sup> whereas the prevalence rates in the Netherlands were found to be lower for wheezing (28.5%) and recurrent wheezing (14.5%).<sup>(17)</sup>

In the present study, having been diagnosed with pneumonia and having been hospitalized due to pneumonia were found to be independently associated with recurrent wheezing and severe recurrent wheezing. It is likely that the number of infants diagnosed with pneumonia was overestimated in our sample, because the limitations, difficulties, and contradictions in the diagnosis of acute infectious pulmonary diseases in children are extremely common in clinical practice.<sup>(18)</sup> However, the high percentage of infants who had respiratory infection with pulmonary impairment in this sample is still a cause of concern. According to the Brazilian National Ministry of Health, respiratory diseases were responsible for 34.5% of all hospital admissions of children less than one year of age nationwide in 2006. In the city of São Paulo, this rate was 34.9%.<sup>(19)</sup> The association between wheezing and pneumonia is well known<sup>(20)</sup> and clearly points to recurrent wheezing as a serious public health problem. However, in Brazil and in other developing countries, although

the morbidity and mortality associated with respiratory infections are high in the first year of life,<sup>(21)</sup> the true prevalence of wheezing in this age group was unknown at the time.

We found the occurrence of nocturnal symptoms, emergency room visits, difficulty breathing as perceived by parents, and wheezing to be quite common in all groups of wheezers, a higher frequency of episodes translating, as expected, to a statistically significant percentage increase (Table 2). The infants with severe recurrent wheezing had the first attack early, at 3 months on average (Table 2). Although severe recurrent wheezing was independently associated with signs of severity, such as difficulty breathing during the attacks and hospitalization due to wheezing, only 18.0% and 3.0% of the infants received inhaled corticosteroids or antileukotrienes, respectively, as a specific treatment (Table 2). This is likely due to the low percentage of wheezers identified as having asthma.

Diagnosing asthma in the first year of life is known to be difficult, since many diseases can manifest as recurrent episodes of cough or wheezing, or both, in this period.<sup>(22)</sup> However, asthma is the most prevalent chronic respiratory disease in children,<sup>(22)</sup> and the intensity of the symptoms in the first two years of life is strongly associated with late prognosis.<sup>(23)</sup> One prospective study found that most of the children with wheezing had had the first episodes in the first year of life. Of those, half continued to have wheezing episodes until 6 years of age, being classified as having asthma,<sup>(1)</sup> which indicates the need for improvements in the diagnosis and early treatment of asthma and wheezing.

In Brazil, and especially in the state of São Paulo, the term “bronchitis” is frequently employed when referring to asthma in children, which produces an additional bias in epidemiological assessments.<sup>(24)</sup> This might have contributed to the underdiagnosis of asthma in the present study. However, it is of interest that the diagnosis of asthma also was much less common than was the occurrence of wheezing episodes in the last 12 months among older children (aged 6 and 7 years) and adolescents (aged 13 and 14 years) who participated in the ISAAC in Brazil.<sup>(25)</sup> Recently, one group of authors, who evaluated different criteria for the diagnosis of asthma in children and adolescents,

demonstrated that the use of the overall ISAAC score<sup>(12)</sup> and the enquiry regarding the occurrence of wheezing episodes in the last 12 months was more reliable than was the enquiry regarding physician-diagnosed asthma or bronchitis.<sup>(24)</sup>

In the present study, the infants diagnosed with asthma had more wheezing attacks and more often showed signs of severity than did the other wheezing infants, pneumonia and hospitalizations being more common among the former (Table 3). Logistic regression revealed that physician-diagnosed asthma was significantly associated with a larger number of wheezing attacks, difficulty breathing as perceived by parents, and the use of inhaled corticosteroids. This indicates that physician-diagnosed asthma is likely to be limited to the more severe presentations of wheezing. Nevertheless, although there was a formal prescription for inhaled corticosteroids or antileukotrienes, less than 40% of the children with asthma received the recommended treatment. The treatment of asthma in children is characterized by its greater complexity, which results from the difficulties in adapting the inhalation techniques, from the different patient phenotypes, and from the potentially more serious risks from the side effects of the medications.<sup>(22)</sup> These factors are likely to have negatively affected the percentage of wheezing infants receiving specific treatment in the present study.

In contrast, practically half of the wheezing infants received oral corticosteroids as rescue medication during the attacks. In accordance with the guidelines for the treatment of wheezing in children,<sup>(22)</sup> the use of oral corticosteroids is recommended for more severe wheezing attacks. However, this association was not observed in the present study. It is likely that this medication was prescribed for the treatment of milder cases, or even for the treatment of other diseases, such as viral bronchiolitis, which represents a potential information bias for the severity of wheezing in this population. In addition, the fact that the prescription of oral corticosteroids has become commonplace causes concern regarding their potential side effects, which are not always borne in mind. In the literature on the treatment of wheezing in infants and small children, there is no scientific basis for this approach. Recently, a study compared the use of oral prednisolone with that of placebo in preschool children with

mild to moderate wheezing, together with viral infection, and found no difference between the groups in terms of the progression or severity of the symptoms.<sup>(26)</sup>

Due to the magnitude of the problem of asthma in children, it is essential that infants with recurrent wheezing be investigated and correctly diagnosed from the first year of life. One group of authors proposed an asthma predictive index for infants who have three or more wheezing episodes, and the use of that index facilitates early intervention.<sup>(27)</sup> In the index, a family history of asthma and the presence of eczema are considered major criteria, whereas allergic rhinitis, eosinophilia, and wheezing in the absence of viral infections are considered minor criteria. An infant with recurrent wheezing who met one major criterion or two minor criteria would be considered as potentially having asthma.<sup>(27)</sup> However, there are difficulties in applying this index in Brazil. In the city of Pelotas, Brazil, a birth cohort study was conducted to assess wheezing patterns and their associations with independent variables. The authors of that study observed that a family history of asthma was associated not only with persistent wheezing (at 4 and 10-12 years of age), but also with transient wheezing (present at 4 but not 10-12 years of age), indicating that this criterion cannot be used in order to distinguish between these two phenotypes.<sup>(28)</sup> In addition, the diagnosis of atopic dermatitis is often underestimated in Brazil, especially in relation to the milder forms of the disease,<sup>(7)</sup> and eosinophilia over 4%, as a laboratory criterion, is questionable due to its low specificity in developing countries, where the prevalence of parasitoses is high. These data show the need for local studies to identify the different wheezing patterns, the associated risk factors, and, mainly, the infants who are at risk of developing persistent asthma.

One limitation of the present study is the fact that we used a questionnaire with questions to which the responses depend on the memory of parents. It is known that wheezing sounds might be mistaken for other respiratory sounds, leading to underestimation or overestimation of the true prevalence of wheezing.<sup>(29)</sup> However, studies using written questionnaires have shown that parents are able to remember common events and diseases such as asthma, as well as being able to remember use of medication

and symptom perception, with good levels of accuracy.<sup>(30)</sup>

We conclude that, among infants in the southern part of the city of São Paulo, Brazil, the prevalence of wheezing in the first year of life is high, wheezing has an early onset and high morbidity, with approximately 27% of the infants having recurrent episodes with higher morbidity and greater severity, and the high prevalence of wheezing increases the incidence of pneumonia, requiring that such infants receive specialized care. Infants with physician-diagnosed asthma more often experienced episodes of wheezing, and those episodes were more severe than were those experiences by infants without physician-diagnosed asthma. However, less than half of the infants with physician-diagnosed asthma received specific asthma treatment. The high prevalence of wheezing, combined with low rates of physician-diagnosed asthma and the adoption of a therapeutic approach different from the one recommended for such cases, indicates the magnitude of the problem of asthma in children and underscores the need for public health measures targeting this population.

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