Original Article

Wheezing phenotypes from birth to adolescence: a cohort study in Pelotas, Brazil, 1993-2004*

Padrões de sibilância respiratória do nascimento até o início da adolescência: coorte de Pelotas (RS) Brasil, 1993-2004

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Abstract

Objective: To study the prevalence of wheezing patterns and their associations with independent variables. **Methods:** Cohort study of live births in 1993 in Pelotas, Brazil. A systematic subsample (20%) of the original cohort was evaluated at 6 months, 12 months and 4 years. At 10-12 years, 87.5% of the original cohort was contacted. Wheezing was categorized: transient, wheezing at 4 years but not at 10-12; persistent, wheezing at all evaluations; late-onset, wheezing at 10-12 years. Independent variables were analyzed: gender; skin color; family income; smoking/asthma during pregnancy; breastfeeding; respiratory infection/diarrhea (during the 1st year); family members with asthma/allergy (at 4 years and at 10-12); physician-diagnosed rhinitis/eczema (at 10-12 years). **Results:** The subsample comprised 897 adolescents. Wheezing patterns were expressed as prevalence (95% CI): transient, 43.9% (40.7-47.2); persistent, 6.4% (4.8-8.0); and late-onset, 3.3% (2.2-4.5). The transient pattern was more common in children from low-income families, children breastfed for less time, children with a history of respiratory infections (during the 1st year) and children with asthma in the family (at 4 years). The persistent pattern was almost twice as common in males, in children whose mothers had asthma during pregnancy, in children with respiratory infections (during the 1st year) and in children with asthma in the family (at 4 and 10-12 years). The late-onset pattern was more prevalent among those with asthma in the family (at 10-12 years) and those diagnosed with rhinitis (at 10-12 years), being less prevalent among those reporting respiratory infections (during the 1st year) and those diagnosed with eczema (at 10-12 years). **Conclusions:** Knowledge of the associations of wheezing patterns allows us to adopt preventive and therapeutic measures.

Keywords: Respiratory sounds; Asthma; Epidemiology; Hypersensitivity.

Resumo

Objetivo: Estudar a prevalência dos padrões de sibilância respiratória e suas associações com variáveis independentes. **Métodos:** Coorte de nascidos vivos, 1993, Pelotas (RS); subamostra sistemática de 20% da coorte original acompanhada aos 6 e 12 meses e 4 anos; aos 10-12 anos localizou-se 87,5% da coorte original. Definição dos padrões: transitório: chiado até 4 anos e ausência de chiado aos 10-12 anos; persistente: chiado em todos acompanhamentos; início tardio: chiado aos 10-12 anos. Variáveis independentes: gênero; cor da pele; renda familiar; fumo/asma na gravidez; amamentação; infecção respiratória/diarréia (1º ano); alergia e asma na família (4 e 10-12 anos); diagnóstico médico de rinite/eczema (10-12 anos). **Resultados:** O total da subamostra foi de 897 adolescentes. Prevalência (IC95%) dos padrões de sibilância: transitório 43,9% (40,7-47,2);persistente 6,4% (4,8-8,0); de início tardio 3,3% (2,2-4,5). O transitório foi mais freqüente em crianças de famílias de baixa renda, com menor duração da amamentação, relato de infecções respiratórias (1º ano) e história familiar de asma (4 anos); o persistente foi quase duas vezes mais freqüente em meninos, em filhos de mulheres com asma na gravidez, com infecções respiratórias (1º ano) e história familiar de asma (4 e 10-12 anos); de início tardio mostrou maior prevalência naqueles com asma na família (10-12 anos) e diagnóstico médico de rinite (10-12 anos); menor prevalência em quem relatou infecções respiratórias (1º ano) e diagnóstico médico de eczema (10-12 anos). **Conclusões:** O conhecimento das associações dos padrões sibilantes permite a adoção de medidas preventivas e terapêuticas.

Descritores: Sons respiratórios; Asma; Epidemiologia; Hipersensibilidade.

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Introduction

The term "asthma phenotypes" refers to clinical manifestations, predominantly wheezing, and can be used to refer to patterns of wheezing. Various phenotypes have been studied in the literature.[1] However, in this article, we will analyze the phenotypes initially proposed by one author,[2] despite the fact that other phenotypes have been proposed.[3-7]

The importance of wheezing patterns is based on the fact that their determining factors and, principally, prognostic factors, are distinct, which can have various therapeutic implications.[8,9]

Wheezing is one of the symptoms typically present in asthma, although it is known that not all wheezing is synonymous with this disease. Different wheezing patterns can correspond to different clinical subtypes of asthma, and there is no consensus as to whether they correspond to the same disease or are similar manifestations of distinct diseases.[9]

According to the hypothesis of early determinants of health and disease,[10] some diseases of adulthood begin during gestation, which is also true of lung diseases. Intrauterine programming together with early environmental influences can determine permanent changes in the structure and function of the lungs, in addition to alterations in the development of the immune system, leading to diseases such as asthma or wheezing symptoms.[10]

The objective of this study was to evaluate the prevalence of certain wheezing patterns in children born in 1993, in the city of Pelotas, Brazil, monitored up to the age of 10-12 years, together with the distribution of these patterns according to sociodemographic, gestational and infectious characteristics, physician-diagnosed rhinitis and eczema, as well as family history of asthma and allergy.

Methods

Pelotas is a city located in the south of Brazil, with a population of 320,000 inhabitants, where 99% of births occur in hospitals.[11] All 5304 births occurring in 1993 at the five city hospitals were followed.[12-14] A standardized questionnaire was administered to all mothers, immediately after delivery, with questions about demographic, socioeconomic, reproductive, behavioral and morbidity characteristics.

A detailed methodology of this cohort study was published in the Brazilian Journal of Public Health in 2006.[13] During medical visits at 6 and 12 months of age, a systematic subsample of 20% of the original cohort together with all of the children with low birth weight (<2500 grams) was studied. At 4 years after the study outset, we attempted to locate the same subsample of the 1373 children visited at the last follow-up evaluation, at 12 months. We were able to locate 1273 of those children. In order to avoid overrepresentation of low weight in the subsample, 20% of the children with low birth weight were selected by random drawing thus excluding excess of low weight, and 981 children remained.

In 2004, we tried to locate all of the participants in the 1993 cohort, and managed to find 87.5% (4452 adolescents). Of the 981 children of the subsample at 4 years of age, a total of 897 adolescents (Figure 1) were located and interviewed, in 2004.

The question about wheezing in the last 12 months allowed building different wheezing patterns, since it was the question used in all of the follow-up evaluations of the cohort. The multicenter study International Study of Asthma and Allergies in Childhood also measured the prevalence of asthma or wheezing in various locations in the world using this question.[15]

The definitions of the wheezing patterns analyzed in this study were as follows:

- never presented wheezing: no wheezing in any of the follow-up evaluations before 10-12 years of age
- persistent pattern: wheezing in all follow-up evaluations (in the first year, at 4 years of age and at 10-12 years)
- irregular pattern: wheezing that does not follow the previously described patterns.

Additional variables were also investigated:

- biological: gender; skin color reported by the interviewer, determined at 4 years of age (white or not white)
- socioeconomic: family income, in number of times the minimum wage, at birth (≤3× and >3×)
- gestational: smoking and history of asthma during pregnancy
- breastfeeding at 12 months categorized by duration in months (>9; 4-8.9; 1-3.9; <1)
- acute respiratory failure (ARF) at 6 and/or 12 months (presence of one or more items:

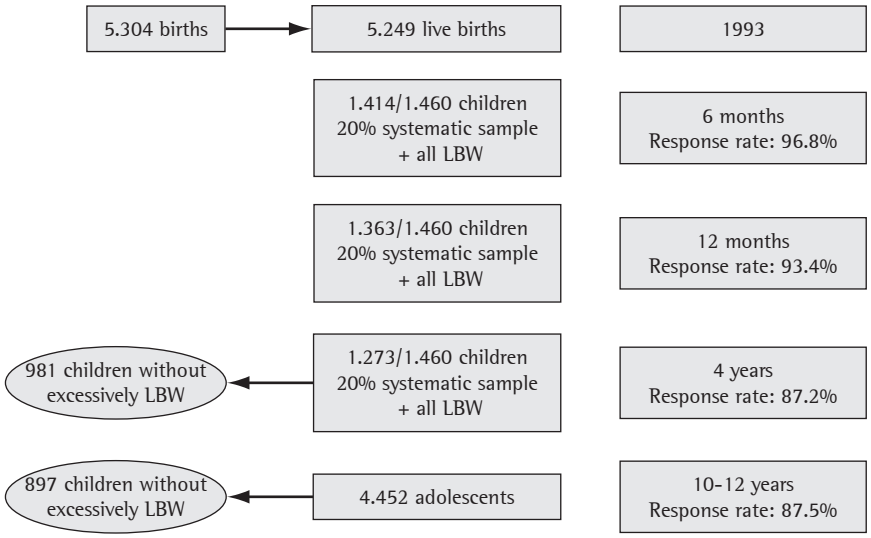

Figure 1 - Flowchart of the 1993-2004 birth cohort study, Pelotas, Brazil.

cough; fatigue; shortness of breath; sputum; rhonchiness; stuffy nose in the last week)
- diarrhea at 6 and/or 12 months (within the two weeks preceding the evaluation)
- family (maternal or paternal) history of asthma, wheezing, bronchitis or allergy (determined at 4 years of age and 10-12 years)
- history of physician-diagnosed allergic rhinitis and skin allergy/eczema (determined at 10-12 years)

The prevalence of the different wheezing patterns with respective confidence intervals (95% CIs) was measured. The associations of wheezing patterns by independent variables were measured using Fisher's exact test and a linear tendency test. Regarding the transient pattern, the associations with the variables determined at 10-12 years of age were not analyzed due to the definition of this pattern itself, that is, presence of wheezing before the age of 4 without wheezing at 10-12 years of age. The associations with the irregular pattern were not tested due to the heterogeneity of this group of adolescents. All the tests were carried out using the Stata program, version 9.0.

The study was approved by the Ethics in Research Committee of the School of Medicine, and all of the participants gave written informed consent.

Results

The characteristics of the sample as a whole (n = 897) and of the children that never presented wheezing (n = 379) are described in Table 1. In the sample as a whole, the percentage of boys and girls was similar, and most of the children were Caucasian (76.5%). Regarding socioeconomic status, approximately 60% of the families had an income less than or equal to three times the minimum wage. Approximately one third of the mothers smoked during pregnancy, and 16.3% reported having had asthma during pregnancy. More than half of the children had been breastfed for less than 4 months. Approximately one third reported having had a cough, with or without other respiratory symptoms, at 6 or 12 months of age, during the week prior to the interview. Episodes of diarrhea, within 15 days prior to the medical visits at 6 and 12 months, were reported by 85% of the children in the sample. The reported percentage of allergy in the family was higher at 4 years of age than at 12 years, despite the fact that the question referred to "ever wheezing". There was also a higher prevalence at 4 years of age than at 12 years for history of asthma in the family—investigated in the same manner as was allergy—although this difference was smaller than that for allergy in the family. During the final follow-up evaluation, physician-diagnosed rhinitis and eczema in adolescence were investigated and identified in 17.5 and 32.2%, respectively.

In the adolescents who had never presented wheezing (Table 1), a statistically significant and positive association was observed with being of the female gender, having been born into an upper-in-

Table 1 - Characteristics of the sample as a whole with the percentage of those who never presented wheezing. 1993-2004 Cohort, Pelotas, Brazil.

Variable	Entire sample (n = 897) n (%)	Never wheezing n (%)	p
Gender			0.04*
Male	445 (49.6)	173 (38.9)	
Female	452 (50.4)	206 (45.6)	
Skin color			0.2*
White	686 (76.5)	298 (43.4)	
Non-white	211 (23.5)	81 (38.4)	
Family income at birth			0.003*
>3× the minimum wage	324 (36.7)	159 (49.1)	
≤3× the minimum wage	560 (63.4)	217 (38.8)	
Smoking during pregnancy			0.008*
No	597 (66.6)	271 (45.4)	
Yes	300 (33.4)	108 (36.0)	
Asthma during pregnancy			<0.001*
No	751 (83.7)	340 (45.3)	
Yes	146 (16.3)	39 (26.7)	
Breastfeeding (months)			0.006**
>9	241 (27.1)	115 (47.7)	
4-8.9	127 (14.3)	64 (50.4)	
1-3.9	311 (34.9)	116 (37.3)	
<1	212 (23.8)	81 (38.2)	
Acute respiratory infection (6 and/or 12 months)			<0.001*
No	582 (66.7)	275 (47.3)	
Yes	291 (33.3)	94 (32.3)	
Diarrhea (6 and/or 12 months)			0.3*
No	138 (15.4)	52 (37.7)	
Yes	759 (84.6)	327 (43.1)	
Allergy in the family[a] (4 years)			0.3*
No	469 (55.6)	209 (44.6)	
Yes	374 (44.4)	152 (40.6)	
Asthma in the family (4 years)			<0.001*
No	565 (63.7)	269 (47.6)	
Yes	322 (36.3)	107 (33.2)	
Allergy in the family (10-12 years)			1.0*
No	577 (65.4)	247 (42.8)	
Yes	306 (34.7)	131 (42.8)	
Asthma in the family (10-12 years)			<0.001*
No	585 (66.4)	294 (50.3)	
Yes	296 (33.6)	83 (28.0)	
Physician-diagnosed rhinitis (10-12 years)			0.002*
No	740 (82.5)	330 (44.6)	
Yes	157 (17.5)	49 (31.2)	
Physician-diagnosed eczema (10-12 years)			0.5*
No	618 (68.9)	256 (41.4)	
Yes	279 (31.1)	123 (44.1)	

[a]The maximum number of ignored values was 54 for the variable allergy in the family (at 4 years of age). *Fisher's exact test. **Linear tendency test.

come family, having a mother who did not smoke, having a mother who did not report having had asthma during pregnancy and having been breastfed for more than 4 months. No ARF, no asthma in the family (at 4 years of age and at 10-12 years) and no physician-diagnosed rhinitis (at 12 years) were also significantly associated with never having presented wheezing.

Figure 2 shows the prevalences of wheezing patterns and their respective 95% CIs for the subsample as a whole. We observe that approximately 40% of the participants in the cohort reported never having experienced wheezing. A similar percentage reported wheezing in some of the follow-up evaluations before the age of 4, without report of wheezing at the follow-up evaluation conducted at 10-12 years, characterizing the transient pattern (n = 394). History of wheezing in all follow-up evaluations of the cohort—persistent pattern—was reported by 6.4% of the participants (n = 57). A lower number of adolescents (n = 30) reported appearance of wheezing at 10-12 years, corresponding to the late-onset pattern (3.3%). A fourth group (n = 37) presented an irregular wheezing pattern in life (4.1%), that is, wheezing early in life, interruption of wheezing at 4 years of age and late appearance; wheezing only early in life; not wheezing at first and last follow-up evaluations but wheezing at 4 years of age.

In Table 2, we describe the frequency of the wheezing patterns, according to demographic, socioeconomic, gestational and first year of life variables. Despite the greater prevalence of all of the wheezing patterns in males, there was statistically significant difference only for the persistent pattern (p = 0.04). There was no significant difference regarding family income at birth for the persistent and late-onset patterns, whereas a greater prevalence was observed for the transient pattern in the category of lower income (p = 0.003). Report of asthma during pregnancy was significantly associated with the persistent pattern. A shorter duration of breastfeeding presented a significant association with the transient pattern. The presence of ARF was directly associated with the transient and persistent patterns and inversely associated with the late-onset pattern (p value at the threshold of statistical significance). The remaining variables in Table 2 did not present statistically significant associations.

We observed (Table 3) that a history of asthma in the family at 4 years of age was significantly associated with the transient and persistent patterns, although not with the late-onset pattern. Asthma in the family at 10-12 years of age was significantly associated with the persistent and late-onset patterns. Physician-diagnosed rhinitis (10-12 years) was positively associated with the late-onset pattern, and physician-diagnosed eczema (10-12 years) was inversely associated with the late-onset pattern. There was no significant association between the remaining variables in Table 3 and the different wheezing patterns.

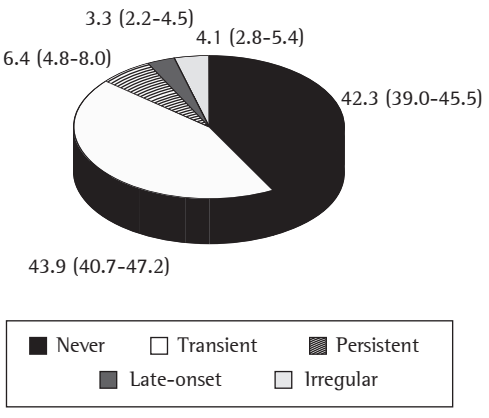

Figure 2 - Prevalence (95% CI) of wheezing patterns from birth to 10-12 years of age (n = 897). Birth cohort study, 1993, Pelotas, Brazil.

Discussion

The longitudinal design of the present study, with its various follow-up evaluations at different ages, allowed the prevalence of wheezing patterns to be assessed from birth to adolescence. One of the important biases that can occur in a cohort study—losses to follow-up—was avoided in our study through numerous search strategies, and a high percentage of children submitted to follow-up evaluation over 11 years of monitoring was achieved (87.5%).

Wheezing patterns were defined based on other studies in the literature,[2-4] sometimes adapted in accordance with the dates of the follow-up visits of our cohort. There is no standardization or consensus in the literature as to the cut-off points, in terms of age bracket, for the definitions of wheezing patterns. Most studies define the transient wheezing pattern

Table 2 - Wheezing patterns, according to demographic, socioeconomic, gestational and first year of life variables. 1993-2004 Cohort, Pelotas, Brazil.

Variable	Transient n (%)	p	Persistent n (%)	p	Late-onset n (%)	p
Gender (n)		0.6*		0.04*		0.7*
Male (445)	199 (44.7)		36 (8.1)		16 (3.6)	
Female (452)	195 (43.1)		21 (4.7)		14 (3.1)	
Skin color of the child (n)		0.2*		0.5*		0.8*
White (686)	292 (42.6)		46 (6.7)		24 (3.5)	
Non-white (211)	102 (48.3)		11 (5.2)		6 (2.8)	
Family income at birth (n)		0.003*		0.7*		1.0*
>3× MW (324)	120 (37.0)		22 (6.8)		11 (3.4)	
≤3× MW (560)	265 (47.3)		34 (6.1)		19 (3.4)	
Smoking during pregnancy (n)		0.7*		0.4*		0.07*
No (597)	259 (43.4)		35 (5.9)		15 (2.5)	
Yes (300)	135 (45.0)		22 (7.3)		15 (5.0)	
Asthma during pregnancy (n)		0.1*		0.001*		0.3*
No (751)	321 (42.7)		38 (5.1)		23 (3.1)	
Yes (146)	73 (50.0)		19 (13.0)		7 (4.8)	
Breastfeeding, in months (n)		0.03**		0.9**		0.7**
≥9 (241)	100 (41.5)		14 (5.8)		6 (2.5)	
4-8.9 (127)	44 (34.7)		11 (8.7)		3 (2.4)	
1-3.9 (311)	141 (45.3)		17 (5.5)		17 (5.5)	
<1 (212)	106 (50.0)		15 (7.1)		4 (1.9)	
ARF at 6 and/or 12 months (n)		0.002*		0.04*		0.05*
No (582)	233 (40.0)		30 (5.2)		25 (4.3)	
Yes (291)	149 (51.2)		26 (8.9)		5 (1.7)	
Diarrhea at 6 and/or 12 months (n)		0.7*		0.6*		0.2*
No (138)	63 (45.7)		10 (7.3)		7 (5.1)	
Yes (759)	331 (43.6)		47 (6.2)		23 (3.0)	

MW: minimum wage; and ARF: acute respiratory failure. *Fisher's exact test. **Linear tendency test.

as that which occurs only in the first years of life (typically before the age of 4). The persistent pattern occurs when wheezing is always present during the various follow-up evaluations before adolescence. The late-onset pattern depends on the follow-up evaluation ages, but refers to those who did not present wheezing in the first years of life and began to present wheezing later on. There is also a group of individuals who present wheezing and then stop wheezing in yet a different pattern than those already mentioned, and this group was designated as presenting an irregular pattern of wheezing. Due to the great heterogeneity of this group, we opted for not analyzing its associations by different exposures, since any result found would be inconsistent with a specific wheezing pattern.

The prevalence of wheezing patterns found in the present study ranged from 43.9% for the transient pattern to 3.3% for the late-onset pattern. The comparability of these results with those in the literature is difficult since not all studies have used the same cut-off points. However, we will mention the principal cohort studies that evaluated wheezing patterns using definitions similar to the ones used here, comparing their principal findings with ours.

It is important to note that none of the other studies discussed here were carried out in Brazil. In a cohort study conducted in Tucson, Arizona (USA),[2] 826 children were evaluated at birth, at 3 years of age and at 6 years, and "ever wheezing" was reported in 49%: 20% presented transient wheezing (wheezing during the first 3 years of life); 14% presented persistent wheezing (wheezing at 3 years of age and at 6 years); and 15% presented late-onset wheezing (wheezing that started at the age of 6). In England,[4] a cohort study (n = 1034) with follow-up evaluations

Table 3 - Wheezing patterns, according to genetic factors and family history. 1993-2004 Cohort, Pelotas, Brazil.

Variable	Transient n (%)	p	Persistent n (%)	p	Late-onset n (%)	p
Allergy in the family[a] at 4 years (n)		0.8*		0.8*		0.08*
No (469)	201 (42.9)		31 (6.6)		11 (2.4)	
Yes (374)	164 (43.9)		22 (5.9)		17 (4.6)	
Asthma in the family at 4 years (n)		0.01*		<0.001*		0.1*
No (565)	229 (40.5)		22 (3.9)		15 (2.7)	
Yes (322)	159 (49.4)		34 (10.6)		15 (4.7)	
Allergy in the family at 10-12 years (n)		-		0.2*		0.08*
No (577)	-		32 (5.6)		15 (2.6)	
Yes (306)	-		24 (7.8)		13 (4.3)	
Asthma in the family at 10-12 years (n)		-		<0.001*		0.05*
No (585)	-		21 (3.6)		14 (2.4)	
Yes (296)	-		35 (11.8)		15 (5.1)	
Physician-diagnosed rhinitis at 10-12 years (n)		-		0.3*		0.01*
No (740)	-		44 (6.0)		19 (2.6)	
Yes (157)	-		13 (8.3)		11 (7.0)	
Physician-diagnosed eczema at 10-12 years (n)		-		0.08*		0.009*
No (618)	-		33 (5.3)		27 (4.4)	
Yes (279)	-		24 (8.6)		3 (1.1)	

[a]The maximum number of ignored values was 54 for the variable allergy in the family at 4 years of age. *Fisher's exact test. **Linear tendency test.

at 1, 2, 4 and 10 years of age, detected a 32.5% prevalence of transient wheezing (wheezing before 4 years of age but not at 10 years), a 12.1% prevalence of persistent wheezing (wheezing at 4 years of age and at 10 years) and an 8% prevalence of late-onset wheezing (wheezing beginning at 5 years of age and still present at 10 years). In the German Multicentre Allergy Study,[3] conducted in 2003, children were evaluated at birth, at 3 years of age and at 7 years, with 71.5% of the children (n = 939) still in follow-up evaluation at 7 years. The prevalences of wheezing found by the author were as follows: 22.8% for the transient pattern (wheezing during the first 3 years stopping by 7 years); 4.4% for the persistent pattern (wheezing at 3 years of age and at 7 years); and 4.8% for the late-onset pattern (wheezing that started at 7 years). These data are similar to ours.

As can be observed in previous studies, the transient wheezing pattern is the one with the highest prevalence and the remaining patterns present lower prevalences.

It is believed that the different wheezing patterns have their peculiarities and that, depending on the age studied, different prevalences can be detected.

The transient wheezing pattern was more prevalent in families with lower income, in children who were breastfed for a short time, with occurrence of respiratory infections in the first year of life and family history of asthma at 4 years of age. The literature shows that this wheezing pattern is of good prognosis, and breastfeeding for longer periods[7] is typically a protective factor. One of the mechanisms suggested for transient wheezing is the combination of viral infections and smaller airway diameter at birth. The association between wheezing and respiratory infections in the first year possibly results from low income and lack of breastfeeding, which would lead these children to present wheezing only during the first years of life. There are conflicting data in the literature regarding the association of this pattern with asthma or allergy in the family.[2,7,9] In a cohort study in Italy,[7] for example, a 90% higher risk was detected for transient wheezing in those whose mothers reported a history of asthma, although this risk was greater for the persistent wheezing pattern (OR = 3.27). In the present study, although the transient pattern was more prevalent in those who reported asthma in the family (determined at 4 years of age), the same was

not observed for allergy in the family (determined in the same follow-up evaluation—at 4 years of age).

The persistent wheezing pattern is typically associated with high levels of atopy and bronchial hyperreactivity, and the principal risk factors found in the literature for this type of pattern are being of the male gender, probably due to the smaller airway diameter compared to that of the female gender,[8] and maternal/paternal history of asthma and atopy.[4,9] In our study, being of the male gender corresponded to a higher risk for the persistent pattern and having a mother who presented asthma during pregnancy corresponded to 2.5 times higher frequency of this type of pattern, which also corroborates the finding of history of asthma in the family. In addition, the persistent pattern was more common in those who reported asthma in the family, determined at 4 years of age and at 10-12 years.

Regarding infections early in life, there is an ongoing discussion in the literature as to its potential to be a risk factor or protective factor for persistent or late-onset wheezing. In accordance with the hygiene hypothesis,[16-18] bacterial or parasitic infection early in life can protect against the later appearance of asthma. In the present study, the persistent pattern was found to be more prevalent in children who reported having had respiratory infections in the first year of life, which was not true for those having had diarrhea in the first year of life. The prevalence of the late-onset pattern was lower in those who reported early respiratory infections (although the p value was a borderline 0.05), as has been shown in the literature.[16-18] The positive association with physician-diagnosed eczema and the negative association with physician-diagnosed rhinitis have not been explained in other studies.

There are some considerations (or disadvantages) to bear in mind when we analyze the findings of the present study. One is the fact that all of the children studied in the Pelotas cohort came from urban areas. Therefore, their contact with certain substances or allergens might differ from that of children residing in rural areas. The classification of the distinct wheezing groups or patterns was based exclusively on data from questionnaires. Therefore, there are no other data such as atopy test results, immunoglobulin levels, pulmonary function test results and bronchial hyperreactivity test results.

The information on upper respiratory tract infections and diarrhea collected from the mothers, without validation from other sources, and, in order to avoid memory bias, we questioned the mothers only in reference to a short period prior to the interview. Therefore, these variables do not reflect the full history of infections in children less than one year of age.

Knowledge of wheezing patterns has important implications for patients. Knowing that the prognosis of the persistent pattern is worse and that these individuals might present impaired pulmonary function throughout their lifetimes, therapy with inhaled corticosteroids, for example, might be an important element of the treatment of this group of patients. The fact that adolescents breastfed for longer periods presented a lower prevalence of transient wheezing has preventive implications, although some authors have reported that breastfeeding is a risk factor for late-onset wheezing.[19] Another important preventive measure is smoking reduction or cessation during pregnancy. Although there was no statistical significance, the persistent and late-onset patterns were more common in children whose mothers smoked during pregnancy.

The findings of this study are the first in the Brazilian literature on wheezing patterns in a cohort monitored from birth to adolescence. The high prevalence of wheezing—58% of the children born in 1993 presented episodes of wheezing before early adolescence—demonstrates the relevance of this clinical manifestation. It is known that many of these adolescents will not present wheezing. However, some of them not only will continue to present wheezing but might also present impaired pulmonary function in the future.

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