Wheezing conditions in early childhood: prevalence and risk factors in the city of São Paulo, Brazil

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Objective To investigate the prevalence and risk factors for wheezing disorders in early childhood in São Paulo, Brazil, the largest metropolitan area of South America.

Methods A population-based cross-sectional survey of 1132 children aged 6–59 months was carried out between 1995 and 1996 to obtain information on recent wheezing and on independent variables such as demographic, socioeconomic, environmental, maternal and nutritional variables and immunization status. Intestinal parasitic infections were diagnosed using standard techniques. Multiple unconditional logistic regression was used to describe associations between outcome and independent variables.

Findings The prevalence of recent wheezing (one or more reported episodes in the past 12 months) was 12.5%; 93% of children with wheezing were also reported to have a medical diagnosis of asthma. Recent wheezing was associated with low per capita income, poor quality of housing, day-care attendance, low birth weight and infection with intestinal helminths.

Conclusion Wheezing in early childhood in São Paulo, although more common than in most developing countries, remains less prevalent than in urban areas of industrialized countries. Low income and conditions associated with poverty (poor housing, low birth weight and parasitic infections) are some of the main risk factors for wheezing disorders among young children in this city.

Keywords Respiratory tract diseases/epidemiology; Asthma/epidemiology; Prevalence; Risk factors; Helminths; Giardiasis; Air pollution, Indoor; Socioeconomic factors; Housing; Vaccination; Child; Cross-sectional studies; Brazil (*source: MeSH, NLM*).

Mots clés Respiratoires, Maladies/épidémiologie; Asthme/épidémiologie; Prévalence; Facteur risque; Helminthe; Giardiase; Pollution air ambiant; Facteur socio-économique; Logement; Vaccination; Enfant; Etude section efficace; Brésil (*source: MeSH, INSERM*).

Palabras clave Enfermedades respiratorias/epidemiología; Asma/epidemiología; Prevalencia; Factores de riesgo; Helmintos; Giardiasis; Contaminación del aire interior; Factores socioeconómicos; Vivienda; Vacunación; Niño; Estudios transversales; Brasil (*fuente: DeCS, BIREME*).

الكلمات المفتاحية: إبيدميولوجيا أمراض السبيل التنفسي؛ إبيدميولوجيا الربو؛ معدل الانتشار؛ عوامل الاختطار؛ الديدان الطفيلية؛ داء الجيارديات؛ تلوث الهواء داخل المنازل؛ العوامل الاجتماعية الاقتصادية؛ المساكن؛ التلقيح (التطعيم)؛ دراسات مستعرضة؛ البرازيل (**المصدر: رؤوس الموضوعات الطبية المكتب الإقليمي لشرق المتوسط**).

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Voir page 520 le résumé en français. En la página 520 figura un resumen en español. يمكن الاطلاع على الملخص بالعربية في صفحة **521**.

Introduction

The rising prevalence of asthma, one of the most common chronic disorders of childhood, has been associated with increased exposure to environmental allergens, air pollution and foods new to the children, and with reduced exposure to microbes as a result of more "hygienic" living conditions in developed countries (*1*, *2*). Asthma and wheezing are less frequent in developing than in developed countries (*3*), but recent increases in prevalence have been reported in the tropics (*4*, *5*). In São Paulo, Brazil, the largest metropolitan area in South America, the current prevalence of wheezing in children less than 5 years old has increased from 0.8% to 2.8% over the past decade (*6*).

Asthma in early childhood is difficult to distinguish from other wheezing disorders; transient wheeze due to viral infections, for example, differs in both pathogenesis and risk factors from atopy-related wheezing (*7*). Only 36% of the children less than 5 years old who had been diagnosed with wheezing of uncertain etiology during emergency consultations in São Paulo were diagnosed as asthmatic during the following 3 years (*8*). Moreover, some risk factors for transient wheeze, such as exposure to other children at home and at day-care centres, may protect them from atopy-related wheezing in later childhood (*9*, *10*). This report presents the prevalence and risk factors for wheezing conditions obtained in a large population-based survey of children aged less than 5 years old living in São Paulo.

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Subjects and methods

Study design and methodology

This cross-sectional survey, carried out between September 1995 and September 1996 in the city of São Paulo, was based on a random sample of 1073 households with at least one child aged 0–59 months. Participants were selected using a multiple-stage cluster sampling procedure, with deliberate over-representation of those in low-income areas (*11*). After informed consent had been obtained, a questionnaire with questions on demographic and socioeconomic factors was administered to the mothers or guardians of 1336 (96%) of the 1390 children less than 5 years old who lived in these 1073 homes. Housing quality was described using a four-level index based on wall and floor characteristics: 1. brick walls and floor covered with parquet or wall-to-wall carpet; 2. brick walls and floor paved with glazed paving tiles; 3. brick walls and floor paved with cement, brick or other kinds of flooring; and 4. walls made of construction scraps and floor paved with cement, brick or other kinds of flooring. Each mother or guardian was given a plastic container identified with the name of each of their children aged less than 5 years and asked to provide a stool sample from each child at the next visit.

At the second visit, 92% of the children from the original sample were clinically examined by a paediatrician and had their clinical history taken. Data on recent wheezing (defined as one or more episodes of wheeze in the past 12 months) were obtained as standardized for the International Study on Asthma and Allergies in Children (ISAAC) and validated in São Paulo (*12*). Information on any previous medical diagnosis of asthma was also obtained from the mothers or guardians, but no attempt was made to investigate family history of asthma or atopy. These analyses were restricted to the 1132 children aged 6–59 months at the time of the second visit. Of these children, 932 provided stool samples. The stool samples were examined for ova, cysts and larvae of intestinal parasites (*13*). No significant differences were found between the demographic and socioeconomic characteristics of children who provided a stool sample and those of the 200 children who did not provide such a sample (*13*).

Data analysis

Multiple unconditional logistic regression models were used to describe associations between potential risk factors (independent variables) and recent wheezing. Five-level hierarchical models were constructed to investigate independent associations between explanatory and outcome variables, while controlling for potential confounders in the same or more distal hierarchical levels (*14*). The variables included at each hierarchical level are shown in Table 1: the first (distal) level included socioeconomic variables, the next levels comprised environmental, maternal and nutritional variables and the last (proximate) level comprised data on exposure to infections. Variables associated with P values < 0.20 within each level were maintained in subsequent models including variables in more proximate levels. Models were adjusted for age and sex. Tests for linear trends in the logistic models were calculated by unfactoring the following variables: per capita family income, education (number of years of schooling) of mother, housing quality index and number of siblings. The software packages used were Epi Info 2000 (Centers for Disease Control and Prevention, Atlanta, GA, USA) and version 6.0 of the Stata software package (Stata, College Station, USA).

Results

The weighted prevalence of recent wheezing, that took into account sampling weights, was 12.5%; similar figures were obtained for girls and boys (Table 1). Most children with recent wheezing (93%) were also reported, by their mothers or guardians, to have a medical diagnosis of asthma, but uncertainties in the clinical diagnosis of asthma in children in this age group limited further analysis of these results. The prevalence of recent wheezing varied according to income strata and housing conditions, with a clear dose–response effect (Table 1).

The results of the adjusted analysis of data (Table 2) did not differ substantially from those of the unadjusted analysis shown in Table 1, with the exception of attendance at a day-care centre. The following variables were independently associated with an increased risk of recent wheezing: low family income, poor housing quality, day-care centre attendance, low birth weight, and infection with intestinal helminths. The predominant helminths in this population (prevalence, 5.8%) were *Ascaris lumbricoides* and *Trichuris trichiura* (*13*). To verify whether helminthic infection was merely a marker of increased exposure to other orofaecal microbes, we also examined the association between infection with *Giardia duodenalis* (the most prevalent intestinal protozoon in this population (*13*)) and recent wheezing, and found no significant relationship (Table 2).

Discussion

This is one of the few population-based surveys of wheezing conditions in early childhood to be carried out in a tropical urban area. In this study recent wheezing was found to be nearly as prevalent (12.5%) as in southern Tanzania (14.0%) (*15*), but less frequent than in urban preschool children living in southern Brazil (21.1%) (*16*) and in most industrialized countries (*17*).

Analyses are complicated by the heterogeneity of wheezing conditions in early childhood (*7*), but wheezing and asthma may share common risk factors in schoolchildren (*18*). Most studies in industrialized countries, with few exceptions (*19–21*), have found no relationship between asthma and socioeconomic status (*2*), whereas in tropical countries wheezing and asthma are more frequent in underprivileged children (*16*, *22–24*); other allergic conditions, such as hay fever and eczema, predominate in children from more affluent families in industrialized countries (*25*).

Day-care attendance, which was positively related to family income (frequencies of 11% and 30% in extreme strata), emerged as a significant risk factor only after controlling for socioeconomic variables (Table 2). Children attending day-care centres are at an increased risk of infections of the lower respiratory tract and transient wheeze (*26*), but may be protected from atopic conditions, including asthma, when they reach school age (*9, 27*). Low birth weight was associated with wheezing, both in our study and in surveys in the USA (*28*, *29*), possibly due to the reduced lung function in premature infants (*30*). Nearly 70% of the low-birth-weight children born in São Paulo are preterm (*31*). It remains unclear whether the early occurrence of wheeze in low-birth-weight children (whether preterm or not) is associated with the development of asthma later in childhood.

Since the early report by Tullis (*32*), helminths have been suggested either to trigger or to inhibit wheezing conditions in children and adults (*33*). This hotly debated issue has huge public health implications, because intestinal helminths infect almost one-third of the world's population (*34*). Positive associations in areas of low prevalence of helminths may result from T_H2-type

Table 1. **Prevalence (%) of wheezing in children in the previous 12 months according to putative risk factors in the city of São Paulo, Brazil, 1995–96**

Putative risk factors for childhood wheezing at different hierarchical levels	No. of subjects[a]	Wheezing in the past 12 months (%)	OR[b]	(95% CI[c])	*P*
Demographic variables					
Age (months)					0.76
6 – 11	149	11.0	1.04	(0.54–1.99)	
12 – 23	269	14.3	1.19	(0.63–2.25)	
24 – 35	245	12.1	1.11	(0.59–2.10)	
36 – 47	228	12.9	1.34	(0.73–2.45)	
⩾ 48	241	11.4	1.00		
Sex					0.27
Girls	530	11.3	0.82	(0.57–1.17)	
Boys	602	13.5	1.00		
Social variables					
Per capita family income[d]					<0.001[e]
< 0.5	109	20.4	3.16	(1.70–5.85)	
0.5 – 0.9	297	15.7	2.30	(1.40–3.79)	
1.0 – 1.9	356	13.3	1.89	(1.15–3.11)	
⩾ 2.0	370	7.5	1.00		
Education of mother (years of schooling)					0.006[e]
0 – 7	692	15.0	2.07	(1.00–4.25)	
8 – 10	391	10.2	1.34	(0.63–2.86)	
⩾ 11	112	7.9	1.00		
Environmental variables					
Housing quality index[f]					<0.001[e]
1	38	24.1	4.83	(1.95–11.97)	
2	447	16.7	3.06	(1.74–5.38)	
3	392	11.7	2.01	(1.11–3.64)	
4	255	6.2	1.00		
Exposure to smoking at home					0.03
Mother and/or relative who smokes	649	14.3	1.49	(1.02–2.16)	
None	483	10.1	1.00		
No. of siblings age < 5 years					0.28[e]
⩾ 2	96	16.2	1.44	(0.78–2.66)	
1	326	12.9	1.10	(0.73–1.64)	
0	710	11.9	1.00		
Current day-care attendance					0.43
Yes	222	14.0	1.18	(0.76–1.83)	
No	910	12.1	1.00		
Maternal variables					
Maternal age (years)					0.25
⩽ 20	95	8.6	0.64	(0.31–1.33)	
> 20	1037	12.8	1.00		
Maternal marital status					0.45
Single/divorced/widowed	168	14.3	1.20	(0.74–1.94)	
Married/living with partner	963	12.2	1.00		
Nutritional variables					
Birth weight (g)					0.005
⩽ 2500	101	21.3	2.09	(1.24–3.53)	
> 2500	984	11.5	1.00		
Duration of breastfeeding (months)					0.12
⩽ 4	603	13.9	1.33	(0.92–1.91)	
> 4	529	10.8	1.00		
Exposure to infections					
Immunization schedule					0.28
Incomplete	53	17.3	1.50	(0.73–3.10)	
Complete	1079	12.2	1.00		

(Table 1, cont.)

Putative risk factors for childhood wheezing at different hierarchical levels	No. of subjects[a]	Wheezing in the past 12 months (%)	OR[b]	(95% CI[c])	*P*
Current infection with intestinal helminths					<0.001
Yes	50	31.3	3.19	(1.68–6.07)	
No	882	12.5	1.00		
Current infection with *Giardia duodenalis*					0.97
Yes	56	13.3	0.98	(0.43–2.24)	
No	876	13.4	1.00		

[a] Number of children analysed was 1132. For some variables, the totals are fewer than 1132 because some values are missing.
[b] OR = Odds ratio.
[c] CI = Confidence intervals.
[d] Per capita monthly income in relation to the country's official minimum wage in 1996.
[e] Test for linear trend.
[f] Housing quality was described using a four-level index based on wall and floor characteristics: 1. brick walls and floor covered with parquet or wall-to-wall carpet; 2. brick walls and floor paved with glazed paving tiles; 3. brick walls and floor paved with cement, brick or other kinds of flooring; and 4. walls made of construction scraps and floor paved with cement, brick or other kinds of flooring.

Table 2. **Risk factors for wheezing in children in the last 12 months, the city of São Paulo, Brazil, 1995–96**

Risk factors for childhood wheezing at different hierarchical levels	Wheezing in the last 12 months		
	Adjusted OR[a]	(95% CI[b])	*P*
Per capita family income			<0.001[c]
< 0.5	3.10	(1.66–5.80)	
0.5–0.9	2.33	(1.41–3.85)	
1.0–1.9	1.91	(1.17–3.13)	
⩾ 2.0	1.00		
Housing quality index[d]			0.001[c]
1	3.48	(1.31–9.21)	
2	2.52	(1.36–4.67)	
3	1.89	(1.03–3.46)	
4	1.00		
Exposure to smoking at home			0.68
Mother and/or relative who smokes	1.43	(0.97–2.10)	
None	1.00		
Current day-care attendance			0.03
Yes	1.71	(1.05–2.79)	
No	1.00		
Maternal age (years)			0.08
⩽ 20	0.50	(0.24–1.09)	
> 20	1.00		
Birth weight (g)			0.02
⩽ 2500	1.93	(1.12–3.32)	
> 2500	1.00		
Current infection with intestinal helminths			0.002
Yes	2.84	(1.43–5.63)	
No	1.00		
Current infection with *Giardia duodenalis*			0.66
Yes	0.81	(0.32–2.08)	
No	1.00		

[a] Odds ratio adjusted for variables at the same or higher hierarchical levels.
[b] CI = Confidence intervals.
[c] Test for linear trend.
[d] Housing quality was described using a four-level index based on wall and floor characteristics: 1. brick walls and floor covered with parquet or wall-to-wall carpet; 2. brick walls and floor paved with glazed paving tiles; 3. brick walls and floor paved with cement, brick or other kinds of flooring; and 4. walls made of construction scraps and floor paved with cement, brick or other kinds of flooring.

T-cell responses elicited by acute infections, with increased levels of immunoglobulin E, eosinophilia, mastocytosis and allergic reactions (*35*). In addition, the pulmonary phase of larval migration of some intestinal nematodes, such as *Ascaris lumbricoides* and hookworm, may cause asthma-like symptoms (the so-called Loeffler's syndrome). Anthelminthic treatment resulted in clinical improvement of asthma in patients in Venezuela (*36*). The light burden of helminthic infections in our study population (*13*) fits well within this scenario of low prevalence, whereas in children in Africa who are heavily exposed, chronic helminthic infections may suppress inflammatory responses by mast cell saturation, blocking IgG4 antibodies, tolerance to aeroallergens and T-cell hyporesponsiveness (*35*, *37*).

In contrast to previous studies, we found no significant association between wheezing and male sex (*2*, *16*), parental smoking (*2*, *16*, *38*), low number of siblings (*24*, *39*, *40*), young maternal age (*18*), maternal marital status (*41*), bottle-feeding (*42*) or immunizations (*43*). Large surveys have similarly failed to detect associations between wheezing and risk factors such as bottle-feeding (*44*, *45*), passive smoking (*46*) and immunizations (*47*). We did not investigate parental history of asthma and atopy, a powerful determinant of childhood asthma (*2*, *16*) that can modify the effect of exclusive breastfeeding (*42*).

The recent rise in wheezing conditions in early childhood in São Paulo (*6*) did not result from increases in the proportion children of low-income families; living in poor-quality houses; or from exposure to intestinal helminths, because these risk factors have become less prevalent in the population of São Paulo over the past decade (*13*, *48*, *49*). The prevalences of low birth weight and preterm birth remained stable in São Paulo between 1993 and 1998 (*31*). The recent increase in attendance at day-care centres (*6*) and some variables not assessed here, such as exposure to air pollutants and indoor aeroallergens, and dietary factors (*6*, *17*), may account for the rise in the prevalence of wheezing and represent additional targets for public health interventions. ■

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Conflicts of interest: none declared.

Résumé

Episodes de respiration sifflante chez le jeune enfant : prévalence et facteurs de risque en ville de São Paulo (Brésil)

Objectif Etudier la prévalence et les facteurs de risque des épisodes de respiration sifflante chez le jeune enfant à São Paulo (Brésil), la plus grande métropole d'Amérique du Sud.

Méthodes Une enquête transversale portant sur 1132 enfants de 6 à 59 mois a été réalisée dans la population entre septembre 1995 et septembre 1996 afin d'obtenir des informations sur les épisodes récents de respiration sifflante et sur des variables indépendantes telles que variables démographiques, socio-économiques, environnementales, maternelles et nutritionnelles et statut vaccinal. Les parasitoses intestinales ont été diagnostiquées selon les méthodes classiques. On a utilisé la régression logistique multiple non conditionnelle pour décrire les associations entre les observations et les variables indépendantes.

Résultats La prévalence des épisodes récents de respiration sifflante (un ou plusieurs épisodes rapportés au cours des 12 derniers mois) était de 12,5 % ; chez 93 % des enfants atteints, un diagnostic d'asthme était également rapporté. Les épisodes récents de respiration sifflante étaient associés aux variables suivantes : faible revenu par habitant, qualité médiocre de l'habitat, fréquentation d'une crèche, faible poids de naissance et helminthiases intestinales.

Conclusion Les épisodes de respiration sifflante chez le jeune enfant à São Paulo, bien que plus répandus que dans la plupart des pays en développement, ont une prévalence plus faible que dans les zones urbaines des pays industrialisés. Un faible revenu et des facteurs associés à la pauvreté (qualité médiocre de l'habitat, faible poids de naissance et parasitoses) figurent parmi les principaux facteurs de risque de respiration sifflante chez les jeunes enfants de cette ville.

Resumen

Cuadros con sibilancias en la primera infancia: prevalencia y factores de riesgo en la ciudad de São Paulo, Brasil

Objetivo Investigar la prevalencia y los factores de riesgo de sufrir cuadros con sibilancias en la primera infancia en São Paulo, Brasil, el área metropolitana más extensa de América del Sur.

Métodos Entre 1995 y 1996 se llevó a cabo una encuesta transversal basada en la población entre 1132 niños de 6-59 meses con objeto de obtener información sobre los antecedentes recientes de sibilancias y sobre variables independientes relacionadas con características demográficas, socioeconómicas y ambientales, con el estado de la madre y la nutrición y con el estado de inmunización. Se diagnosticaron los casos de parasitosis intestinal mediante técnicas de uso común. Para describir las relaciones entre las variables dependientes y las independientes se utilizó el método de regresión múltiple incondicional.

Resultados La prevalencia de sibilancias recientes (notificación de uno o más episodios en los 12 últimos meses) fue del 12,5%; al 93% de los niños con sibilancias se les había diagnosticado también asma. Las sibilancias recientes se asociaron a unos ingresos per cápita bajos, una vivienda de calidad deficiente, la asistencia diurna, un bajo peso al nacer y la presencia de infección por helmintos intestinales.

Conclusión La prevalencia de sibilancias en la primera infancia en la ciudad de São Paulo, aunque superior a la de la mayoría de los países en desarrollo, sigue siendo menor que en las zonas urbanas de los países industrializados. Los ingresos bajos y los problemas asociados a la pobreza (vivienda deficiente, bajo peso al nacer e infecciones parasitarias) son algunos de los principales factores de riesgo de trastornos causantes de sibilancias entre los niños pequeños en esa ciudad.

ملخص

حالات الأزيز في الطفولة المبكرة: معدل الانتشار وعوامل الاختطار في مدينة ساو باولو، البرازيل

الغرض: تقصي معدل انتشار اضطرابات الأزيز وعوامل الاختطار المقترنة بها في مرحلة الطفولة المبكرة في مدينة ساو باولو، في البرازيل، والتي تعد أكبر مدن أمريكا الجنوبية.

الطريقة: تم إجراء مسح سكاني يشمل مختلف القطاعات غطى ١١٣٢ طفلاً من عمر ٦ أشهر إلى ٥٩ شهراً وذلك في الفترة من عام ١٩٩٥ إلى عام ١٩٩٦، بغرض الحصول على معلومات حول الإصابة الحديثة بحالات الأزيز وحول متغيرات أخرى مستقلة مثل العوامل الديموغرافية، والاجتماعية الاقتصادية، والبيئية، والتغذوية، والعوامل المتعلقة بالأمومة وبحالة التمنيع. وتم تشخيص حالات العدوى الطفيلية المعوية باستخدام الطرائق المعيارية. وتم استخدام طريقة التحوف اللوجستي (الإمدادي) المتعدد غير المشروط لوصف الارتباط بين المتغيرات الناتجة والمتغيرات المستقلة.

الموجودات: بلغ معدل انتشار الأزيز الحديث (نوبة واحدة أو أكثر تم الإبلاغ عنها خلال الأشهر الإثني عشرة الأخيرة) ١٢,٥٪؛ كما شخصت حالة ٩٣٪ من الأطفال الذين يعانون من الأزيز على أنهم مصابون أيضاً بالربو. وقد لوحظ ارتباط بين حالات الأزيز الحديثة وبين انخفاض دخل الفرد، وانخفاض جودة المسكن، وسوء الرعاية النهارية للأطفال، وانخفاض الوزن عند الولادة، والعدوى بالديدان الطفيلية المعوية.

الحصيلة: بالرغم من أن الأزيز في مرحلة الطفولة المبكرة أكثر شيوعاً في ساو باولو بالمقارنة مع معظم البلدان النامية، إلا أنه مايزال أقل انتشاراً منه في المناطق الحضرية للبلدان الصناعية. وقد تبين أيضاً أن انخفاض الدخل والظروف المقترنة بالفقر (مثل سوء المسكن، وانخفاض الوزن عند الولادة، والعدوى الطفيلية) تأتي ضمن عوامل الاختطار الرئيسية المسببة لاضطرابات الأزيز بين صغار الأطفال في ساو باولو.

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