

ASTHMA AND OBESITY

The Prevalence of Wheezing and its Association with Body Mass Index and Abdominal Obesity in Children

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Objective. To evaluate the relative importance of body mass index (BMI) and abdominal obesity in the prevalence of wheezing in Brazilian children. **Materials and methods.** This is a cross-sectional study of male and female students, 6–12 years old, from the public elementary schools of São Francisco do Conde, Bahia, Northeast Brazil. Reports of wheezing in the past 12 months were collected using a questionnaire from the International Study of Asthma and Allergies in Childhood Program (ISAAC) phase III, adapted to Portuguese. Anthropometric, demographic, and socioeconomic information was collected. Multivariate logistic regression analyses were used to assess the associations of interest. **Results.** Of the children surveyed, 10.6% reported wheezing. Excess weight was observed in 16.2%, 10.5%, and 7.9% of the sample, measured by BMI, waist circumference (WC), and the waist-to-height ratio (WHtR), respectively. The percentage of patients with wheezing attributable to BMI \geq 85th percentile (8.2%) slightly exceeded those identified with abdominal obesity, WC \geq 80th percentile (7.3%) and WHtR $>$ 0.5 (7.1%). **Conclusion.** The results suggest that an excess of fat deposits, either in the abdominal region or elsewhere in the body, increased the risk of wheezing. Since obesity is an important public health problem worldwide, control of this problem may partially reduce the occurrence of wheezing in youth.

Keywords abdominal obesity, body mass index, wheezing

INTRODUCTION

It is estimated that approximately 300 million people of all ages worldwide are asthmatic, with significant variations in prevalence among different countries and regions (1). The International Study of Asthma and Allergies in Childhood (ISAAC) found an average prevalence of 24.3% among young Brazilians (2). The prevalence of childhood asthma has increased dramatically over the last decades (1). Many factors have been proposed to explain the increasing asthma rates, including genetic, environmental, economic, and psychosocial aspects (3, 4).

Currently, obesity is a major health problem in both developed and developing countries (5). Reported data from Brazil indicate an increased prevalence of overweight and obese children and adolescents in recent decades (6). Currently, 34.8% of Brazilian children aged between 5 and 9 years and 21.5% aged between 10 and 18 years are overweight or obese (7). Based on the parallel rise in the prevalence of asthma and in the prevalence of obesity in

recent decades, and the existence of potential mechanisms, a connection between these two conditions has been postulated.

Obesity is a known risk factor for diabetes, cardiovascular disease, and other chronic diseases, thus influencing the morbidity and mortality of populations (8). Some studies have shown an association between obesity and both wheezing and asthma (9). Decreased pulmonary functional residual capacity and tidal volume described in obese individuals have been cited as predictors for either respiratory symptoms or more fundamental changes in the airways leading to asthma (10). However, the relationship between obesity and wheezing/asthma in youth remains controversial (9).

Studies evaluating the influence of obesity on the occurrence of asthma have commonly used body mass index (BMI) as a measure of adiposity; however, problems with this marker of adiposity have been described in the literature. In addition to other limitations, BMI does not indicate body composition and body fat distribution (11). Other studies point to waist circumference (WC) (12–14), waist-to-height ratio (WHtR) (13), and the conicity index (CI) (15) as better markers than BMI for predicting cardiovascular risk factors in adults. A growing number of

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studies have documented that WHtR is superior to WC and BMI in predicting cardiovascular risk factors in adults (12,16). Wheezing is a clinical manifestation that is characteristic of asthma (17). The investigation of the role of fat distribution in the occurrence of both wheezing and asthma among children and adolescents has been neglected (18, 19) (20). Thus, this study aimed to evaluate the relative importance of BMI and abdominal obesity in the prevalence of wheezing in children and adolescents from a low-income population of a tropical Brazilian town.

MATERIALS AND METHODS

Study Design

A cross-sectional design was used to study 6- to 12-year-old children living in São Francisco do Conde (SFC), a municipality located in the metropolitan region of Salvador, Northeast Brazil. This municipality has 33,183 inhabitants and a high urbanization rate (80.2%). Economically, the municipality has the third highest development index in the state of Bahia, and the city council is the largest local employer. However, this region experiences challenges in certain areas, including its social development index (30), level of education (139), and health indicators (178) (21).

We used data from the Education Department of the Municipality of SFC for the year 2010 to estimate the sample. Of 3734 registered students, 2649 were from rural areas and 1085 were from urban areas. These students were distributed across 22 schools in the county school system. To minimize travel costs and time for subject recruitment, the nine schools with 150 or more students were included in the sample. All students aged 6–12 years in each selected school were eligible for the study. Since the prevalence of respiratory allergies varies from 15% to 40%, the sample sizes of 531 and 834 students from urban and rural areas, respectively, were determined, taking into account a 3% error and a 95% level of confidence. We added 10% to the total sample size to account for student declining to participate in the study, resulting in 1500 students.

Procedures

Data were collected from August to December 2010 by qualified and trained personnel. The principal of each selected school received a letter that included an explanation of the study's objectives and methodology and an invitation for their students to participate in the research study. The students' parents attended informational meetings at which they received extensive information concerning the project and were invited to enrol their children in the study. Participating parents signed a consent form and were invited to complete the study questionnaires. All anthropometric measurements were completed in the school by properly trained interviewers.

Outcome Variable

The prevalence of wheezing was measured using a previously validated ISAAC phase III questionnaire

translated into Portuguese (22). For this study, wheezing was defined based on the following two questions: (1) Has your child ever experienced asthma or wheezing in his/her lifetime? and (2) In the last 12 months, has your child experienced wheezing? The children whose parents provided positive answers to both questions or to the second question only were considered as cases.

Main Independent Variable

Anthropometric Status. Each participant's weight was obtained using a Master[®] portable digital scale and height was measured using a Leicester Height Measure[®] portable stadiometer (Seca, Hamburg, Germany). The measurements were performed in duplicate using the techniques of Lohman, Roche, and Martorell (1988) (23). To assess anthropometric status, tables from the World Health Organization (WHO) (2007) (24) with percentile values of BMI [$\text{BMI} = \text{weight (kg)/height (m)}^2$] according to age and sex were used as reference. For classification to an anthropometric status, we used the WHO 2006 (25) proposal: underweight (<3rd percentile), normal weight (≥ 3 rd percentile and <85th percentile, reference category), overweight (≥ 85 th percentile and <97th percentile), and obese (≥ 97 th percentile). For analysis, the overweight and obese categories were aggregated. Therefore, children with excess BMI were situated on or above the 85th percentile. WC measurement was performed using an inelastic tape, graduated in centimeters and millimeters, according to procedures described by Gillum et al. (26). We used the cutoff points proposed by Taylor et al. (27), which identify abdominal obesity as $\text{WC} \geq \text{P80}$. The WHtR was obtained by calculating the ratio of waist circumference (cm) to height (cm), with a cutoff value >0.5 for abdominal obesity (28).

Confounding Variables

Level of Physical Activity. To evaluate the frequency of physical activity, we used the International Physical Activity Questionnaire (IPAQ), which assesses physical activity for leisure, transport, work, and domestic purposes in the past week (28). This information allowed us to estimate the weekly time spent in physical activities by asking about the time and the frequency, during the past week, of moderate and vigorous activities and walking (28). For this study, the final score was dichotomized using a cutoff of 300 minutes/week of moderate or vigorous physical activity (29). Children with ≥ 300 minutes of activity per week were considered active (reference category) and children with <300 minutes per week were classified as inactive.

Pubertal Development

Evaluation of the stage of sexual maturity was based on breast and pubic hair characteristics in girls and genitals and pubic hair in boys. Based on this staging, adolescents were grouped according to categories described by Marshall and Tanner (30, 31) into pre-pubescent (reference category) and pubescent. The identification of these stages

was made by self-description with the help of portraits provided by the interviewers.

Other Variables

Other variables used in the study included the following: sex (male, female reference category), age (<10 years, ≥10 years reference category), education of caregiver (≤4th grade, >4th grade reference category), household location (urban, rural reference category), per capita income (<1 minimum salary (MS), ≥1 MS reference category), number of people living in the household (>3, ≤3 reference category), and presence of smokers in the house (no reference category, yes).

Statistical Analysis

For processing and construction of the database, we used Epi Info version 6.04 (Centers for Disease Control and Prevention, Atlanta, USA). Data were entered in duplicate after reviewing the questionnaires and correcting errors from the coding field.

The characteristics of the population were identified by means of descriptive analysis using categorized data for prevalence and mean and the standard deviation for continuous variables. The study of the importance of BMI, WC, and WHtR initially involved the evaluation of bivariate associations between classifications of anthropometric indicators and the occurrence of wheezing. The logistic multivariate analyses used to study the association between anthropometric indicators and wheezing were adjusted for gender, age, per capita income, pubertal development, caregiver education, number of people in household, level of physical activity, and presence of smokers in the house. The choice of variables for modeling was based on knowledge gathered from pre-existing literature (32).

The interaction was interpreted as a change in the magnitude of the effect in the presence of a third variable using the Wald test. The variables were classified as “interaction variables” when χ^2 reached a p -value ≤.05.

The importance of each anthropometric indicator in determining wheezing was quantified by calculating the population attributable fraction (PAF) using the following formula: $[H - 1/H \times 100]$, with $H = f1 \times 1 + f2 \times OR2 + f3 \times OR3 + f4 \times OR4$, where $f1$ is the frequency of subjects in the baseline category of the anthropometric indicator (unexposed to risk); $f2$, $f3$, and $f4$ are the frequencies in the risk categories of the indicator; and OR2, OR3, and OR4 are the adjusted odds ratios (ORs) for wheezing in each risk category for that indicator (33).

Ethical Issues

Ethical approval was provided by the Ethics Research Board of the School of Nutrition, Federal University of Bahia, Brazil, under registration number 27-09/CEPNUT, and the study was conducted in accordance with the Declaration of Helsinki of 1975, as revised in 2000. Written, informed consent detailing all procedures to be carried out was signed by a parent or legal guardian of each participant.

RESULTS

Of the total number of students initially selected (1500 students), 193 (12.8%) declined or discontinued participation in the study (due to refusal, family moving to another city, or children transferring to another school), resulting in 1307 students of both sexes, aged 6–12 years. A total of 1187 students who presented complete information for the variables used here were included in the present analysis.

In the present study, there were slightly higher percentages of male students (53.3%) and those aged between 6 and 10 years (50.6%). Other characteristics of the studied population are shown in Table 1. It was also found that 10.6% [confidence interval (CI): 95% 8.9%–12.31%] of study participants had experienced wheezing within the last 12 months. Excess weight was observed in 16.2% (CI 95% 14.4%–18.5%) of the sample, as measured by BMI. Abdominal obesity, measured by WC and WHtR, was observed for 10.5% (CI: 95% 8.5%–12.2%) and 7.9% (CI: 95% 6.4%–9.3%) of the study participants, respectively.

There were no associations between wheezing and demographic or socioeconomic factors. The level of physical activity and the presence of smokers in the house were

TABLE 1.—Characteristics of caregivers and children and adolescents aged 6–12 years enrolled in public schools in São Francisco do Conde, Bahia, Brazil, 2010.

Variables	Population number		Wheezing within last 12 months		<i>p</i> -Value
	<i>n</i>	%	<i>n</i>	%	
Gender					
Male	633	53.3	69	10.9	.657
Female	554	46.7	56	10.1	
Age (years)					
6 to <10	601	50.6	71	11.8	.145
≥10 to <13	586	49.4	54	9.2	
Pubertal development					
Prepubertal	712	60.0	72	10.1	.565
Pubertal	475	40.0	53	11.2	
Caregiver education					
≥4 years	820	69.1	84	10.2	.630
<4 years	367	30.9	41	11.2	
Per capita income ^{a,b}					
>1 MS	945	79.7	95	10.1	.270
≤1 MS	240	20.3	30	12.5	
Household location					
Rural	779	65.6	73	9.4	.072
Urban	408	34.4	52	12.7	
No. of people at the household					
≤3	281	23.7	24	8.5	.214
>3	906	76.3	101	10.8	
Level of physical activity ^b					
Active	285	24.0	16	8.0	.120
Inactive	902	76.0	109	11.3	
Smokers at the household ^b					
No	929	79.9	92	9.9	.131
Yes	223	20.1	31	13.3	

Notes: ^aMeasured in Brazilian minimum salary (BMS; value in 2010; BRL510.00, equivalent to US\$ 290.7). ^bDifferent totals because of nonavailable data.

TABLE 2.—Crude and adjusted ORs of the association between excess weight and asthma among children and adolescents enrolled in public schools in São Francisco do Conde, Bahia, Brazil, 2010.

Variables	Studied population		Wheezing		Crude OR (IC95%)	Adjusted OR (IC95%) ^a
	<i>n</i>	%	<i>n</i>	%		
BMI						
<85	995	83.3	99	9.6	1	
≥85	192	16.2	26	13.5	1.41(0.89–2.51)	1.61(1.02–2.68)
PAF ^b (%)	8.2					
WC						
<85	1061	89.5	106	10.0	1	1
≥85	125	10.5	19	15.2	1.61(0.95–2.73)	1.78(1.03–3.07)
PAF ^b (%)	7.3					
WHtR						
<0.50	1092	92.1	109	10.0	1	1
≥0.50	94	7.9	16	17.0	1.85(1.04–3.28)	2.01(1.11–3.65)
PAF ^b (%)	7.1					

Notes: ^aAdjusted for gender, age, per capita income, puberal development, caregiver education, number of people in household, level of physical activity, and presence of smokers in the house. ^bPopulation attributed fraction. Boldface numbers are statistically significant.

not significantly different between those who had or had not experienced wheezing in the previous 12 months (Table 1).

The data were analyzed by multivariate unconditional logistic regression, adjusted for gender, age, per capita income, pubertal development, caregiver education, the number of people in the household, physical activity level, and the presence of smokers in the house. Obesity was significantly associated with wheezing, as assessed by BMI (OR = 1.61, CI: 95% 1.02 to 2.68), WC (OR = 1.78, CI: 95% 1.03–3.07), and WHtR (OR = 2.01, CI: 95% 1.11–3.65) (Table 2; Supplementary Table). There were no significant interactions between gender and the anthropometric indicators (gender_WC $p = .134$, gender_WHtR $p = .074$, gender_BMI $p = .715$). In addition to the adjusted ORs, the corresponding fractions of disease attributable to anthropometric indicators (PAFs) are presented in Table 2. The fraction of wheezing attributable to BMI (8.2%) slightly exceeded the fraction identified for abdominal obesity, as measured by WC (7.3%) and WHtR (7.1%).

DISCUSSION

During the previous 12 months, 10.6% of the studied individuals had experienced wheezing according to the mother. This prevalence is lower than those recorded in other regions of Brazil (1). A possible explanation for this phenomenon is that most studies in Brazil have been held in large cities, while the present study was conducted in a small town and its surrounding rural areas. However, this prevalence is consistent with those described in urban areas of Argentina, Chile, and Mexico (1). The prevalence of overweight children (16.2%) was slightly higher than that reported previously by Souza (34) and Matos et al. (35) in Salvador, but was consistent with those identified by the vast majority of other studies among children and adolescents in other regions of Brazil (6).

The results of multiple logistic regression analysis showed, after adjustment, positive and significant

association of all anthropometric indicators with wheezing. Thus, in the present study, participants with excess weight, as measured by BMI ≥ 85th percentile, WC ≥ 80th percentile, and WHtR > 0.5, were 61%, 78%, and 100% more likely to have experienced wheezing, respectively. The results of this study reinforce the influence of excess weight in the occurrence of wheezing, which has also been reported by other studies in Brazil (35–37) and elsewhere (38, 39) in populations of the same age range.

Another important finding in the present study was the absence of major differences in the fraction of wheezing attributable to the three anthropometric indicators used (range 7.0 to 8.2%). To the best of our knowledge, only one study in the literature on this subject used the PAF to evaluate the importance of excess weight in determining asthma (40). In that study, the PAF estimated that 28% of asthma occurring in women after age 9 was due to excess weight (40), as measured by BMI. In the present work, the explanatory power of these indicators for the occurrence of wheezing was slightly higher for BMI than for abdominal obesity. This suggests that greater fat deposits, either in the abdominal region or elsewhere in the body, increase the risk of wheezing. We know of no other study employing the same analytical procedure to evaluate the role of anthropometric indices on the occurrence of asthma or wheezing; the PAF is commonly used in studies assessing risk factors for cardiac diseases (41, 42). Thus, comparisons between reports in the literature and the present study are not straightforward. For instance, our results differ from those reporting greater robustness of abdominal obesity compared to standard BMI measures in the occurrence of wheezing (or asthma) in children and adolescents (19) or adults (43).

BMI, WC, and WHtR correlate with the amount of visceral adipose tissue, although some studies have shown the WC to be the anthropometric measure that best correlates with the amount of visceral adipose tissue (44). Visceral adipose tissue is considered a risk factor for various metabolic disorders and cardiovascular risk at all stages of life (45–47). Insulin resistance and metabolic syndrome appear to increase

the risk of asthma occurrence (48). However, the mechanisms by which these illnesses promote wheezing/asthma have not yet been clearly elucidated. Obesity has more recently been thought of as an inflammatory condition because pro-inflammatory cytokines produced by adipocytes, such as IL-1, TNF-alpha, leptin, and adiponectin, lead the immune system toward a T_H2 response. Such polarization might, consequentially, worsen a pre-existing sensitization, thus pushing the individual to develop asthma and rhinitis (49). In obese people, symptoms of breathlessness and wheezing may be due to the increased work of breathing (50). Alternatively, obesity may have a direct effect on the respiratory system physiology by altering lung volume, airway calibre, or respiratory muscle strength (51). In addition to the quantity of fat, the distribution of fat may also play a role in wheezing (asthma). Adipose tissue in the chest and abdomen leads to a reduction of lung tidal volume and functional residual capacity (52). Even without considering the distribution of fat, pulmonary function has been shown to be impaired in the presence of obesity, such as in children in Salvador-Brazil, where overweight children had higher rates of asthma and reduced respiratory capacity (35).

It should be noted that this study has limitations inherent to cross-sectional studies, particularly in estimating relationships between the variables, response, and exposure simultaneously, as well as not considering the temporality between events. Thus, this study design did not allow us to establish a cause and effect relationship. However, improvements in respiratory function with weight reduction have been demonstrated in adults (53) and children (54). It has been suggested that increases in obesity may have contributed to the rise in wheezing or asthma. In this study, a report of wheezing in the past 12 months was used as an outcome, as in other population-based studies. While the lack of asthma diagnosis by a physician and medication usage could be interpreted as limitations of the study, the report of symptoms (wheezing) is less dependent on access and quality of health services. However, The ISAAC questionnaire showed good specificity and sensibility for using in worldwide multicenter surveys (55). In Brazil, a validation study showed that wheezing in the past 12 months had high values of sensitivity, specificity, and positive and negative predictive values, reinforcing the concept that this is the key question for the diagnosis of asthma (56). Conversely, the following are the strengths of the study: the control for confounding variables relevant to estimating the association between anthropometric indicators and asthma and the analytical procedures employed to ensure comparability in assessing the explanatory power of anthropometric indices in determining asthma.

CONCLUSION

In summary, we found a statistically significant association between the prevalence of wheezing and multiple measures of body size, confirming previous studies showing excess weight/obesity in the occurrence of wheezing or asthma. Our results suggest that an increase in fat deposits, either in the abdominal region or elsewhere in the body, increases the risk

of wheezing. Because excess weight/obesity is an important public health problem, its control may reduce the occurrence of wheezing and asthma. Studies focusing on the mechanisms involved in the association between obesity and both wheezing and asthma should aim to improve preventive and therapeutic approaches for both illnesses.

NOTES ON CONTRIBUTORS

Rita de Cássia Ribeiro Silva participated in the study design, the data collection, the interpretation of results and in writing the article. Ana Marlúcia Oliveira Assis participated in the interpretation of results and writing the article. Luce Alves da Silva participated in the field work and reviewed the article. Rosemeire Leovigildo Fiaccone designed the work and reviewed the article. Mauricio L Barreto, Elizabete de Jesus Pinto, Marilda Souza Goncalves, Sheila Maria Alvim Matos, and Laura C. Rodrigues participated in the interpretation of results and revision of the article. Neuza Maria Alcantara-Neves participated in the study design and the revision of the article.

DECLARATION OF INTEREST

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