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PEDIATRIC ASTHMA

Factors Associated with Asthma Severity in Children: A Case–Control Study

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Objective. To investigate factors associated with the severity of childhood asthma. *Methods.* We conducted a case–control study in a group of Brazilian children (2–12 years old) with diagnosis of asthma attending the pediatric pulmonology clinic of a teaching hospital. The study sample consisted of cases (children with persistent asthma) and controls (children with intermittent asthma). Data were collected through an interview with the child's parent or caretaker using a standard questionnaire. Association between asthma severity and studied variables was assessed by calculating odds ratios (OR) and 95% confidence interval (95% CI) through logistic regression test. *Results.* 171 children were included in this study, of which 104 (61%) had persistent asthma and 67 (39%) had intermittent asthma. Onset of the disease before 2 years of age, paternal educational level lower than 9 years, and low household income (≤1 minimum wage per month) were independent risk factors for persistent asthma, with adjusted OR (95% CI) of 2.56 (1.01–6.48), 2.49 (1.04–5.99), and 4.36 (1.06–17.87), respectively. Regular consumption of fruits during the last 30 days was inversely associated with the risk of having persistent asthma, with an adjusted OR (95% CI) of 0.19 (0.04–0.97). *Conclusions.* Early onset of the disease, low paternal education, and low household income are independent risk factors for persistent childhood asthma. Regular consumption of fruits appears to be a protective factor against more severe asthma in children.

Keywords asthma severity, childhood, case–control study, odds ratio, risk factor

INTRODUCTION

Asthma is the most common chronic disease of childhood, in both developed and developing countries (1, 2). The prevalence of childhood asthma has been increasing over the last few decades throughout the world, as has its related burden (3, 4).

Asthma is currently classified as either intermittent or persistent according to its severity (1). Persistent asthma warrants daily long-term maintenance therapy and contributes significantly to the burden of childhood asthma. Special attention should be given to this group of children. Therefore, identification of predictors for persistent asthma may have potential impact on reducing the burden of childhood asthma through early preventive measures and interventions in children at high risk of more severe asthma.

A limited number of studies have investigated factors associated with asthma severity in children. Non-Caucasian race, male gender, early onset of the disease, family history of asthma, exposure to tobacco smoke or dust, lack of breastfeeding, lower maternal education, and allergen sensitization were shown to be associated with more severe childhood asthma (5–9). However, most of these factors were investigated only by one or two studies and further studies are needed to confirm these results.

This case–control study aimed to investigate factors associated with asthma severity in a sample of Brazilian children.

METHODS

Study Design

This case–control study has been conducted, between November 2008 and December 2009, at the Pediatric Pulmonary Clinic of a teaching hospital in the municipality of Rio Grande, located in the extreme south of Brazil and with a population of approximately 200,000. Federal University of Rio Grande is the only clinic in the municipality providing subspecialist care for pediatric asthma patients. The research project has been approved by the Health Research Ethics Committee of the University and written informed consent was obtained from parents/guardians of all participants before the recruitment.

Participants

Children aged 2–12 years with diagnosis of asthma were eligible for this study. The diagnosis of asthma was made

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by two senior pediatric pulmonologists based on the following criteria: (1) recurrent episodes (≥3) of wheezing associated or not with cough; (2) symptoms relieved by short-acting bronchodilators associated or not with corticosteroids; (3) presence of precipitating or aggravating factors such as exposure to allergens or irritants, physical activities, emotional stress, or climate change; (4) history of asthma, allergic rhinitis, or atopic eczema among first-degree relatives and/or personal history of atopic eczema or allergic rhinitis.

Two groups of participants were recruited: (1) case group—children with persistent asthma; (2) control group—children with intermittent asthma. Classification of asthma severity was based on the frequency of symptoms and acute exacerbations recommended by the Global Initiative for Asthma (GINA) (10). To be classified as having intermittent asthma, patients should experience daytime symptoms less than once a week, nocturnal symptoms not more than twice a month, and brief exacerbations. Otherwise, patients were classified as having persistent asthma. Clinical data for the assessment of asthma severity were collected by parents/guardians at home using a symptom diary for at least 30 consecutive days. Patients who were receiving regular maintenance medications for asthma at the moment of recruitment or who had been treated previously with regular maintenance medications for at least 30 days were also classified as having persistent asthma.

Children were excluded from this study if they had a history of any significant comorbid disease, such as neonatal chronic lung disease, cystic fibrosis, congenital cardiopulmonary diseases, chronic encephalopathy, or immune deficiency syndrome.

Data Collection and Study Variables

Data collection was performed through an interview with the child's parent or caretaker by one of the four trained investigators using a standard questionnaire. All four investigators were blind to asthma severity.

The dependent variable in this study was asthma severity, categorized as persistent or intermittent asthma. The independent variables were as follows: demographic and socioeconomic factors (patient's gender, age and race, parental education levels, and monthly household income—number of minimum wage that is currently equal to US$300), family history (first-degree relatives) of asthma, personal history of atopy (allergic rhinitis or atopic eczema), premature birth (gestational age <37 weeks), low birth weight (<2500 g), use of mechanical ventilation during the neonatal period, history of bronchiolitis, age at onset of the disease, need for hospital admission at the first episode of wheezing, presence of household pets, exposure to passive smoking, and dietary and nutritional factors (duration of exclusive breastfeeding, child's weight, height and body mass index, and type of foods regularly consumed in the last 30 days).

Statistical Analysis

The sample size was calculated based on the estimated prevalence of the main study variables in the case group (varied from 25% for obesity defined as body mass index >95th percentile to 80% for family history of asthma) and estimated odds ratios (OR) for persistent asthma ranging from 1.5 to 6. We selected the largest estimated sample size as the final sample size of this study; then at least 58 participants were needed to be recruited in each group (alpha level 0.05, power 80%).

Data were entered into the Epi-Info version 6.4 database (Centers for Disease Control and Prevention, Atlanta, GA, USA). Statistical analysis was performed using the Stata version 9.2 program (Stata Corporation, College Station, Texas, USA). A descriptive analysis was initially performed to calculate the prevalence of each variable in both groups. Second, a bivariate analysis was conducted to estimate the association between the dependent variable (asthma severity) and each of the independent variables by calculating OR and its 95% confidence interval (95% CI). Finally, a multivariate backward stepwise logistic regression was performed to control the effects of confounders. All variables with p-value <.2 in bivariate analysis were entered into the logistic regression model. We also selected some potentially relevant variables to be entered into the model based on previous reports (5–8) and clinical judgment, such as race, gender, maternal education, presence of household pets, family history of asthma, personal history of atopy, maternal smoking, breastfeeding, obesity, and regular consumption of fish, eggs, vegetables, and fruits in the last 30 days. A Hosmer–Lemeshow test was used to assess the goodness of fit of the final model (11). A two-tailed p-value of <.05 was considered statistically significant.

RESULTS

Of the 171 included patients, 104 (61%) had persistent asthma (case group) and 67 (39%) had intermittent asthma (control group). Table 1 shows the results of bivariate analysis of factors associated with asthma severity. Among the 26 study variables, only lower level of paternal education (<9 years of schooling) was significantly associated with persistent asthma (OR = 2.18; 95% CI = 1.06–4.50).

Multivariate logistic regression showed that onset of the disease before 2 years of age, paternal education level less than 9 years, and low household income (≤1 minimum wage per month) were independent risk factors for persistent asthma, with adjusted OR (95% CI) of 2.56 (1.01–6.48), 2.49 (1.04–5.99), and 4.36 (1.06–17.87), respectively (Table 2). An inverse linear association between household income and risk of persistent asthma was observed, that is, the lower the household income, the higher the risk of persistent asthma. Regular consumption of fruits in the last 30 days was associated with lower risk of having persistent asthma, with an adjusted OR of 0.19 (95% CI = 0.04–0.97).

DISCUSSION

This study demonstrates that early onset of the disease, lower paternal education, and lower household income are

TABLE 1.—Factors associated with persistent asthma—bivariate analysis.

Variables	Persistent asthma, *n* (%)	Intermittent asthma, *n* (%)	OR (95% CI)	*P*-value
Age, years				
>6	58 (55.8)	42 (62.7)	1	
≤6	46 (44.2)	25 (37.3)	1.33 (0.71–2.49)	.37
Gender				
Female	54 (51.9)	34 (50.7)	1	
Male	50 (48.1)	25 (49.3)	0.95 (0.52–1.76)	.88
Race				
White	79 (76.0)	52 (77.6)	1	
Non-White	25 (24.0)	15 (22.4)	1.09 (0.53–2.28)	.8
Monthly household income				
>3MW	11 (10.9)	12 (19.0)	1	
1.1–3MW	73 (72.3)	43 (66.7)	1.90 (0.77–4.67)	.16
≤1MW	17 (16.8)	9 (14.3)	2.06 (0.65–6.51)	.2
Maternal education, years				
≥9	29 (29.0)	20 (29.9)	1	
0–8	71 (71.0)	47 (70.1)	1.04 (0.53–2.05)	.91
Paternal education, years				
≥9	20 (20.2)	21 (35.6)	1	
0–8	79 (79.8)	38 (64.4)	2.18 (1.06–4.50)	.03
Prematurity, <37 weeks				
No	85 (81.7)	50 (74.6)	1	
Yes	19 (18.3)	17 (25.4)	0.66 (0.31–1.38)	.26
Low birth weight, <2500 g				
No	88 (87.2)	53 (79.1)	1	
Yes	13 (12.8)	10 (20.9)	0.78 (0.32–1.91)	.59
Maternal smoking during pregnancy				
No	81 (77.9)	53 (81.5)	1	
Yes	23 (22.1)	12 (18.5)	1.25 (0.58–2.73)	.56
Family history of asthma				
No	39 (37.5)	30 (44.8)	1	
Yes	65 (62.5)	37 (55.2)	1.35 (0.72–2.52)	.34
Personal history of allergic rhinitis				
No	26 (25.0)	18 (26.9)	1	
Yes	78 (75.0)	49 (73.1)	1.10 (0.55–2.21)	.78
Personal history of atopic eczema				
No	58 (56.3)	32 (47.8)	1	
Yes	45 (43.7)	35 (52.2)	0.71 (0.38–1.32)	.27
Mechanical ventilation during neonatal period				
No	91 (89.2)	54 (81.8)	1	
Yes	11 (10.8)	12 (18.2)	0.54 (0.22–1.32)	.18
Previous diagnosis of bronchiolitis				
No	60 (58.8)	35 (52.2)	1	
Yes	42 (41.2)	32 (47.8)	0.77 (0.41–1.42)	.39
Age at onset of the disease				
≥ 2 years old	70 (72.9)	51 (82.3)	1	
< 2 years old	26 (27.1)	10 (17.7)	1.89 (0.84–4.27)	.12

(continued)

TABLE 1.—(continued)

Variables	Persistent asthma, *n* (%)	Intermittent asthma, *n* (%)	OR (95% CI)	*P*-value
Hospital admission for the first episode of wheezing				
No	30 (28.8)	21 (31.8)	1	
Yes	74 (71.2)	45 (68.2)	1.15 (0.59–2.25)	.68
Presence of cat in household				
No	77 (74.0)	52 (77.6)	1	
Yes	27 (26.0)	15 (22.4)	1.22 (0.59–2.50)	.59
Presence of dog in household				
No	66 (63.5)	41 (61.2)	1	
Yes	38 (36.5)	26 (38.8)	0.91 (0.48–1.71)	.76
Current maternal smoking				
No	79 (76.0)	54 (80.6)	1	
Yes	25 (24.0)	13 (19.4)	1.31 (0.62–2.80)	.48
Duration of exclusive breastfeeding				
≥4 months	58 (55.8)	36 (53.7)	1	
<4 months	46 (44.2)	31 (46.3)	0.92 (0.49–1.71)	.79
Regular consumption of fish in the last 30 days				
No	54 (52.4)	37 (55.2)	1	
Yes	49 (47.6)	30 (44.8)	1.12 (0.60–2.08)	.72
Regular consumption of eggs in the last 30 days				
No	39 (37.9)	20 (30.0)	1	
Yes	64 (62.1)	47 (70.0)	0.69 (0.36–1.35)	.28
Regular consumption of fruits in the last 30 days				
No	13 (12.6)	6 (9.0)	1	
Yes	90 (87.4)	61 (91.0)	0.68 (0.25–1.89)	.46
Regular consumption of vegetables in the last 30 days				
No	35 (34.0)	28 (41.8)	1	
Yes	68 (66.0)	39 (58.2)	1.39 (0.74–2.63)	.30
Obesity (body mass index >95th percentile)				
No	81 (79.4)	57 (85.1)	1	
Yes	21 (20.6)	10 (14.9)	1.48 (0.65–3.37)	.35

Note: MW, minimum wage that is currently equal to US$300.

independent risk factors for persistent childhood asthma. In contrast, regular consumption of fruits in the last 30 days is inversely associated with the risk of having more severe asthma.

Patients in whom the disease started before 2 years of age are more likely to have persistent asthma. Early onset of the disease as the predicator of more severe childhood asthma has been shown by one (6) but not the other previous study (7). The first 2 years of life is a critical period for lung development and the lungs are more susceptible to both internal and external injuries (12). This may explain the association between early onset of asthma and increased severity of the disease.

With regard to parental education, this study shows that paternal but not maternal educational levels are significantly associated with asthma severity in children. Patients whose fathers have less than a high school education (<9 years of schooling) are more likely to have persistent asthma. In contrast, one study in Columbian children demonstrated that lower maternal education was an independent predictor of severe asthma (7). Paternal educational level was not investigated by that study. Association between parental education and child health outcomes has been well recognized (13–15). The pathways through which parental education positively impacts child health remains to be clarified; however, two

TABLE 2.—Factors associated with persistent asthma—multivariate analysis.

Variables	Adjusted OR (95% CI)	*P*-value
Age at onset of the disease		
≥2 years old	1	
<2 years old	2.56 (1.01–6.48)	.047
Paternal education, years		
≥9	1	
0–8	2.49 (1.04–5.99)	.041
Monthly household income		
>3MW	1	
1.1–3MW	2.44 (0.86–6.94)	
≤1MW	4.36 (1.06–17.87)	.04**
Regular consumption of fruits in the last 30 days		
No	1	
Yes	0.19 (0.04–0.97)	.046

Notes: The following variables were entered into the initial model of multivariate logistic regression model: race, gender, mechanical ventilation during neonatal period, age at onset of the disease, parental education, household income, presence of household pets, family history of asthma, personal history of allergic rhinitis, exposure to maternal smoking, exclusive breastfeeding, obesity, and regular consumption of fish, eggs, vegetables, and fruits in the last 30 days.
$p = .3$ for Hosmer–Lemeshow test.
**Test for linear trend.

hypotheses have been proposed (13). First, more educated parents may be more efficient "producers" of child health from given health inputs because they are more likely to adhere to medical advice and to adopt better child care practice or higher hygiene standards (productive efficacy). Alternatively, more educated parents may choose better health input mixes that generate more health outputs (allocative efficacy). It is generally believed that maternal education is the more critical determinant of child health (16, 17); however, the relative roles of mother's and father's education on child health outcomes vary substantially across countries with different social and cultural background (13). This may explain the difference between this study and the study from Colombia regarding parental education and asthma severity in children.

This study shows an inverse linear association between household income and risk of persistent childhood asthma in a developing country. The link between low household income and occurrence of persistent asthma in children has also been reported in developed countries (18). Children living in low income households generally have limited access to health care and poorer living conditions that may negatively impact the asthma morbidity.

Parental education and household income are the key markers of a child's socioeconomic status. Identification of lower socioeconomic status as the risk factor of more severe asthma in children may provide new insights into the reasons for global increase in the burden of childhood asthma.

This study shows that regular consumption of fruits during the last 30 days is inversely associated with the risk of having persistent asthma. Despite a growing body of evidence suggesting an inverse association between intake of fruits and risk of asthma (19–21), to the best of our knowledge, this is the first study to report a protective effect of regular consumption of fruits against more severe childhood asthma. Fruits are the main sources of dietary vitamins, especially vitamin C that is believed to reduce airway inflammation in patients with asthma (22).

There are some methodological limitations in this study that needed to be addressed. First, diagnosis and classification of asthma was based on only clinical history without lung function measures because a considerable proportion of patients were younger than 6 years. However, we excluded children younger than 2 years of age in which diagnosis of asthma is more challengeable. We also used relatively robust clinical parameters for the diagnosis of asthma, based on the recommendations of GINA (10). Second, this study may have low power to investigate the association between asthma severity and some independent variables, such as patient's age, exposure to maternal smoking, family history of asthma, exposure to household pets, regular consumption of vegetables, and obesity. Third, in the dietary survey, we did not collect detailed data regarding frequency, quantity, and type of regularly consumed fruits or vegetables. Moreover, we obtained dietary data only during the last 30 days to minimize memory biases. However, dietary style in this short period may not necessarily represent patient's long-term dietary habits. Finally, the results of this hospital-based study may not be applicable to community-based patients with asthma. Further large-scale, population-based prospective surveys are needed to investigate factors associated with the severity of childhood asthma.

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Declaration of Interest

The authors report no competing interests. The authors alone are responsible for the content and writing of this paper.

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