

Distribution of severity of asthma in childhood

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Abstract

Objective: To estimate the distribution of asthma severity in a population-based sample of children from Salvador, Brazil.

Methods: An epidemiologically oriented questionnaire (International Study of Asthma and Allergies in Childhood, ISAAC) and a questionnaire based on criteria used in clinical practice (The Global Initiative for Asthma, GINA) were administered simultaneously to 417 children aged 5 to 12 years who reported symptoms of asthma in the past 12 months. According to the ISAAC instrument, children were classified into severe and non-severe asthma, whereas GINA clinical criteria produced four categories of severity: intermittent, mild persistent, moderate persistent and severe asthma.

Results: Ninety children reported symptoms indicative of severity according to the ISAAC questionnaire. According to GINA criteria, 143 children had intermittent asthma, 160 mild persistent, 51 moderate and 43 severe asthma. Agreement between the two instruments was 81.3% ($\kappa = 0.5$).

Conclusions: Most asthmatic children in the Salvador urban area have persistent asthma. Agreement between epidemiological and clinical classifications of asthma severity was satisfactory.

J Pediatr (Rio J). 2010;86(5):417-423: Asthma, severity, questionnaire, child.

Introduction

The prevalence of asthma has been on the rise in recent decades, and the disease is now considered one of the foremost chronic illnesses worldwide.¹ Administration of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire in some Brazilian municipalities in 1995 showed that Salvador, state of Bahia, had one of the highest prevalence rates of wheezing among children aged 13 to 14 years (27.1%) for the 12 months prior to the

study.² A 2002 survey conducted in the city found asthma symptom prevalence rates of 17.2 and 24.6% in children aged 6 to 7 and 13 to 14 years respectively.³ These data show that asthma can be considered a public health issue in Salvador.

Childhood asthma is a major cause of morbidity hampering activities of daily living and leading to missed school or classroom time. It is also the chronic childhood

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disease most associated with need for emergency care and hospitalization.⁴

The Global Initiative for Asthma⁵ (GINA) recommends that cases of asthma be classified into four levels of clinical severity, based on symptom frequency (dyspnea with wheezing and/or cough) and pulmonary function (forced expiratory volume in the first second, FEV₁): intermittent and mild, moderate, or persistent asthma. Around 60% of cases are estimated to meet criteria for intermittent or mild persistent asthma, 25 to 30% as moderate asthma, and 5 to 10% are severe.⁶ Patients with severe asthma are a minority, but they account for the majority of utilization of health services, morbidity and mortality, and healthcare costs.

The prevalence of asthma and indicators of asthma severity have been estimated worldwide through epidemiological surveys based on the ISAAC protocol, without taking clinical criteria or pulmonary function resting into account for a more accurate classification of disease severity.^{7,8} In addition to being subject to differences inherent to each population, these studies have used different criteria for asthma severity, leading to divergent and difficult-to-compare results. The epidemiological classification of asthma obtained by administration of the ISAAC questionnaire has never been compared with the clinical classification adopted worldwide as recommended by GINA.

The frequency of symptoms and severity of asthma are associated with lung function involvement and persistence of asthma symptoms in adulthood. A cohort study conducted in Australia estimated that 30% of children with asthma experience remission of symptoms in adulthood, 45% grow to have occasional attacks only and 25% will have persistent asthma.⁹

Severity-based information of the distribution of asthma cases allows planning of public strategies for asthma care. To date, no studies have described this distribution in Salvador. This study sought to ascertain the severity of asthma in children in the city by comparison of results obtained from a symptom-based questionnaire used in epidemiological research (the ISAAC questionnaire) and from another instrument developed with an internationally accepted clinical classification of asthma severity (GINA) as its basis.

Methods

The present study was performed on a cohort of children from Salvador, the capital of the state of Bahia, initially enrolled to assess the impact of a public sanitation program and later used in a study of risk factors for asthma. The cohort comprised 1,445 children aged 4 to 11 years (as of 2005) from 24 areas throughout the city. The study methods have been previously described in detail.¹⁰

Classification of asthma

Classification of asthma was accomplished through administration of two questionnaires:

a) Respiratory module of the ISAAC questionnaire.¹¹ The main question determining a diagnosis of asthma (or wheezing) in the instrument was: "has your child had wheezing or whistling in the chest in the past 12 months?" Severe asthma was defined as cases with wheezing in the past 12 months and a positive response to one or more of the following questions: wheezing severe enough to limit the child's speech to only one or two words at a time between breaths, more than 12 attacks in the past 12 months, or child's sleep disturbed due to wheezing more than one night per week.

b) A questionnaire based on the Global Initiative for Asthma (GINA) criteria, which seeks to classify asthma according to clinical severity.⁵ Questions were based on frequency of symptoms¹²; pulmonary function parameters are not considered. As in the ISAAC questionnaire, the first question inquired as to the number of episodes in the past year, but, unlike ISAAC, used other terms in addition to "wheezing" (cough, shortness of breath, and chest tightness). The remaining questions were based on the frequency of symptoms throughout the week in the month in which symptoms occurred. The instrument also inquired into imitation of daily activities. Based on the data obtained from the questionnaire, asthmatic children were classified into four groups depending on clinical severity, according to the GINA classification: 1 = intermittent asthma; 2 = mild persistent asthma; 3 = moderate persistent asthma; and 4 = severe persistent asthma. The presence of at least one indicator of severity was defined as sufficient to place the child into the category of greatest severity, as recommended in the GINA classification (Table 1).

The first survey was conducted between May and October 2005, and consisted of administration of the ISAAC questionnaire alone. All children with a history of wheezing over the past 12 months were selected, and became the sample of a second survey conducted between June 2006 and February 2007. The questionnaire for this second survey consisted of the eight ISAAC respiratory module questions, plus four questions that concerned GINA criteria. In both surveys, questions were asked by trained interviewers at home visits and answered by the participants' guardians. Visits for the second survey followed the same order of neighborhoods used the first time.

For analysis of agreement between both questionnaires (second survey ISAAC and GINA), responses were compared by means of the kappa statistic and overall agreement rate for positive and negative diagnosis of severe asthma.¹⁰ For purposes of agreement analysis, the moderate and severe asthma categories of the GINA questionnaire were collated into a single "severe" category, whereas intermittent and

Table 1 - Symptom-based classification of asthma severity according to modified Global Initiative for Asthma (GINA) criteria^{1,11}

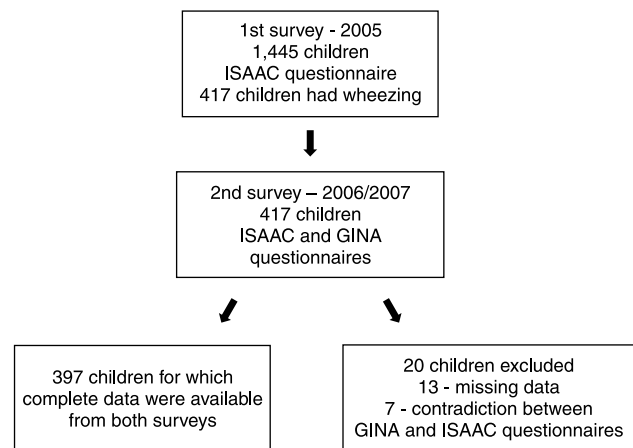
Severity of asthma	Symptoms
Intermittent	1-3 exacerbations over past 12 months Symptoms ≤ 1 time a week Waking at night < 2 times a month No limitation of activities
Mild persistent	4-12 exacerbations over past 12 months Symptoms several times a week, no more than 1 attack per day Waking at night ≥ 2 times a month Sometimes affects activities of daily living
Moderate persistent	>12 exacerbations over past 12 months Daily symptoms, with occasional improvement Waking at night 1-2 times a week Sometimes affects activities of daily living
Severe persistent	>12 exacerbations over past 12 months Continuous symptoms (daily, no improvement) Waking at night > 2 times a week Always affects activities of daily living

mild persistent asthma were combined into a "non-severe" group, to allow comparison with the two epidemiological severity categories provided for in ISAAC. Analyses were performed with the Stata[®] 8 for Windows software package (Stata, USA).

The study was approved by the UFBA Collective Health Institute Human Subjects Research Ethics Committee (CEP/ISC 003-05) and by the National Research Ethics Committee (CONEP 11616).

Results

Of the original sample of 1,445 children, 417 (28.9%) reported a history of wheezing in the past 12 months in the first survey, and were therefore selected for review in the second survey. Answers were incomplete for 13 of these 417, and 7 provided contradictory responses to questions in both instruments. A total of 397 children had complete, valid information for both surveys (Figure 1) and thus made up the final sample of the study. Of these, 209 were male (52.6%) and 188 female (47.4%); age ranged from 5 to 12 years. Comparison of both ISAAC surveys, carried out in 2005 and 2006/2007, showed that 191 (48.1%) children answered "yes" to the question on wheezing in the past 12 months in both, whereas 206 (51.9%) denied the presence of wheezing in the second survey. Of these 206, 61 answered "yes" to the corresponding question

**Figure 1** - Flowchart outlining study progression over both surveys

in the GINA questionnaire, which employed other terms to describe the manifestations of asthma, in addition to wheezing. Of these 61 children, 31 reported nightly cough unrelated to upper respiratory infection (a 2006/2007 ISAAC question). The 145 remaining children were asymptomatic at the time of the second survey. Of these, 134 reported having had wheezing at least once, but only 12 had a past diagnosis of asthma reported in the "have you ever had

asthma question" of the ISAAC questionnaire administered during the second survey.

Based on the modified GINA criteria, of the 397 children in the sample, 143 (36%) had intermittent asthma; 160 (40%) had mild persistent asthma; 51 (12.8%) had moderate persistent asthma; and 43 (10.8%) had severe persistent asthma. In 60 children, occasional limitation of daily activities was the indicator of greatest severity. Taking into account that responses to the remaining questions were not related to more severe asthma, a decision for more conservative categorization was made, and these children were classified as having mild persistent asthma. Based on the ISAAC questionnaire, 90 of the 397 children (22.3%) provided positive responses to questions assessing symptom severity, whereas 307 (77.3%) replied in the negative.

Comparison of both asthma severity criteria according to data from the second survey (Table 2) shows that, the greater the severity of the disease according to GINA criteria, the greater the proportion of children with more severe symptoms as assessed by ISAAC. No children categorized as having mild intermittent asthma were classified as having severe asthma according to ISAAC. On the other hand, approximately 35% of children with severe asthma according to GINA criteria were not diagnosed as having severe asthma according to the ISAAC questionnaire.

A total of 89 children reported wheezing on exertion in the 2006/2007 ISAAC questionnaire. The distribution of asthma severity in these children was as follows: 43 children with mild asthma, of which 5 (5.6%) had intermittent asthma and 38 (42.7%) had mild persistent asthma; 21 (23.6%) children with moderate asthma; and 25 (28.1%) children with severe asthma.

A statistically significant association was found between frequency of emergency room visits due to asthma exacerbation, as well as number of missed school days, and severity of asthma (Table 3). The percentage of children who

sought emergency care was: 13.2% (40/303) of those with intermittent and mild persistent asthma; 31.4% (16/51) of those with moderate persistent asthma; e 55.8% (24/43) of those with severe asthma (chi-square for trend = 46,7; $p < 0.001$). The percentage of children who missed school was: 25.7% (78/303) for children with intermittent or mild persistent asthma; 68.6% (35/51) for those with moderate persistent asthma; and 88.4% (38/43) for those with severe asthma (chi-square for trend = 85.5; $p < 0.001$).

Comparison between cases classified as "severe asthma" according to ISAAC and those classified as "severe asthma" according to GINA criteria (moderate and severe persistent asthma) showed an overall agreement rate of 81.3%, with a kappa of 0.5 (SD = 0.05; $p < 0.001$).

Discussion

The main findings of the present study were: (i) most children were classified as having persistent asthma (40% mild, 12.8% moderate, 10.8%, severe), according to GINA criteria; (ii) 22.3% of children with asthma had one or more symptoms indicative of severity according to the ISAAC questionnaire; (iii) there was fair agreement (81.3%) between both questionnaires for estimating severe asthma, with a kappa of 0.5; (iv) use of ISAAC questions on asthma severity allows estimation of the frequency of moderate and severe asthma according to the GINA classification; (v) 22.4% of children in the sample reported wheezing on exertion.

The distribution of asthma severity in the pediatric population of Salvador is consistent with the pattern reported in several countries. Studies conducted on adult and pediatric populations in other countries, such as China and France, have shown rates of intermittent asthma between 13 and 83%; mild persistent asthma, 11 to 27%; moderate disease in 6 to 36% of asthmatics; and severe illness in 0 to 25%

Table 2 - Frequency of severe asthma according to ISAAC epidemiological classification* and GINA clinical criteria

GINA (n/%)	ISAAC (n/%)		Total (n)
	Severe	Non-severe	
Intermittent	0 (0)	143 (100)	143
Mild persistent	35 (21.8)	125 (78.2)	160
Moderate persistent	27 (52.9)	24 (46.9)	51
Severe persistent	28 (65.1)	15 (34.9)	43
Total	90	307	397

* All data collected in 2006/2007 survey.

Table 3 - Frequency of emergency services use and missed school days in asthmatic children

	GINA classification of asthma				Total (%)
	Intermittent (%)	Mild persistent (%)	Moderate persistent (%)	Severe persistent (%)	
Emergency care facility visits (per 12 months)					
0	142 (99.3)	121 (75.6)	35 (68.6)	19 (44.2)	317 (80.0)
1-3	1 (0.7)	34 (21.2)	11 (21.6)	13 (30.2)	59 (14.8)
4-2	0	4 (2.5)	4 (7.8)	8 (18.6)	16 (4.0)
>12	0	1 (0.6)	1 (1.9)	3 (7.0)	5 (1.2)
Missed school days					
0	143 (100)	82 (51.2)	16 (31.4)	5 (11.6)	246 (62.0)
1-5	0	67 (41.9)	21 (41.2)	20 (46.5)	108 (27.2)
6-10	0	8 (5.00)	12 (23.5)	6 (13.9)	26 (6.5)
>10	0	3 (1.9)	2 (3.9)	12 (27.9)	17 (4.3)
Total	143	160	51	43	397

of cases.^{12,13} Unlike the present study, however, most of these investigations considered pulmonary function criteria in combination with symptoms for classification of asthma severity. A large population-based study conducted in 29 countries in the Americas, Europe, and Asia estimated asthma severity on the basis of GINA clinical criteria and found that the frequency of severe asthma varied by region, ranging from 11 to 32%.¹⁴ Our study showed mild persistent asthma rates (40%) higher than those reported in the past.¹²⁻¹⁴ This finding is likely due to inadequate treatment, as inhaled corticosteroids have yet to gain wide use in low-income Brazilian populations, such as this sample of children from Salvador.¹⁵

The present study showed a frequency of severe asthma of 22.4% as assessed with the ISAAC questionnaire. Other published studies have analyzed the frequency of asthmatic patients providing positive responses to each question in the instrument as an indicator of greater severity. The few prior studies that defined a single criterion of severity by combining ISAAC questions, as the present study did, reported rates of "severe asthma" in the range of 24.7 to 30%.^{8,16} However, unlike the present investigation, these studies considered the presence of more than four exacerbations of asthma in the past year as an indicator of severity. Our study used ISAAC responses indicative of more severe asthma symptoms – that is, maximum number of yearly exacerbations (more than 12) and nights per week

in which the child was awakened by symptoms (more than once), as well as difficulty uttering complete words during attacks – as criteria of "epidemiological severity".

The second survey component of this study was administered approximately one year after the first epidemiological survey, which was conducted in 2005. The 12-month period to which the instrument's questions referred was therefore different from one survey to the next. We found substantial variation in responses to ISAAC questions, particularly with regard to wheezing in the past year. Approximately 50% of children who reported wheezing in the 12 months prior to the first survey (2005) did not report the symptom in the second survey (2006/2007). Many replied in the affirmative to questions that used terms other than "wheezing" or "whistling" to refer to symptoms, however. These findings may be due to an improvement in asthma symptoms experienced by some children as they grow, the so-called remission period of asthma,¹⁷ as reported in some longitudinal studies.^{18,19} Another possible explanation is a change in wheezing perception, which may occur in milder asthma,²⁰ or cases of atypical asthma, such as the cough variant, which constitutes a subgroup of asthmatic patients who do not present with wheezing.^{21,22}

Approximately 22.4% of children with asthma reported wheezing on exertion in the second survey, most of whom (94.4%) were classified as having mild, moderate, or severe persistent asthma. Only five (5.6%) children with

intermittent asthma complained of symptoms during physical activity. These children may have exercise-induced asthma²³ or may simply have dyspnea on exertion revealed by physical exercise.²⁴ It is believed that 50 to 60% of asthmatics have transient obstruction of the airways triggered by vigorous exercise.²³ A higher frequency of exercise limitation is to be expected in patients with more severe asthma.⁵ The present study, however, found that most asthmatics with exercise-emergent wheezing had mild persistent asthma. Some possible explanations for these findings include: 1) patients with severe asthma tend to avoid physical exertion due to limited lung function; 2) some children may overestimate exercise-related symptoms and believe them to be asthma-related; 3) some of the caregivers who responded on their children's behalf may have underestimated exercise-related symptoms. Indeed, Solé et al.²⁵ found the ISAAC question on wheezing on exertion to have the highest disparity between responses provided by adolescents and those provided by their guardians.

Estimation of asthma severity in the present study was based on a combination of questions from two questionnaires, one standardized and validated worldwide and the other novel and as yet non-validated. We therefore accept that some study limitations are present, as these estimates are subject to error due to varying knowledge of asthma and its symptoms²⁶ or by the absence of clinical examination and complementary testing to increase accuracy of the diagnosis and of severity assessment.⁵ As it had not been validated, the GINA-based instrument was compared to the ISAAC questionnaire by simultaneous administration to the study sample. There was reasonable agreement between both instruments (> 80%) in more severe asthma. Furthermore, the results of the GINA-based questionnaire correlated with other indicators of greater asthma severity, such as number of emergency room visits and number of school days missed due to asthma exacerbations. A longitudinal study conducted in Cleveland, Ohio, showed that most patients seeking emergency care for asthma are inadequately treated, and that suboptimal care persists even after hospital discharge.²⁷ In our study population, few patients used control medications; most had rescue bronchodilators for use during exacerbations as their only treatment.

This was the first study to compare the two available methods for assessment of asthma severity – a questionnaire meant for use in population-based research and an instrument used in identifying asthma severity in the clinical setting – and revealed good overall agreement. Greater severity of asthma as detected by the epidemiologically oriented ISAAC questionnaire correlates with moderate-to-severe persistent asthma as defined by the GINA clinical classification.

Most asthmatic children in the city of Salvador have persistent asthma and require antiasthmatic agents for

disease control. Determination of the frequency distribution of the various patterns of asthma severity in a representative sample of the city's pediatric population will provide key inputs for forecasting the need for essential antiasthmatic medicines in the study age range. Although we cannot speak to the external validity of our data beyond children from Salvador, in the absence of available information, our findings may contribute to the calculation of estimates in comparable Brazilian municipalities until local population-based studies can be conducted.

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