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Pattern of asthma medication use among children from a large urban center in Brazil

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Abstract

Purpose Despite the advances in asthma therapeutics, there are few data on the use and determinants of anti-asthmatic drugs in the general population of children. This study describes the use of asthma medications among children in the general population and in children with current asthma, living in a large urban center in Brazil.

Methods A population-based cross-sectional survey, aimed at analyzing asthma determinants, was conducted with 1,382 children aged 4–11 years, between February and May 2006, in Salvador, Brazil. At baseline, an extensive questionnaire was applied, including questions about the use of asthma medications in the last 12 months.

Results In all studied children ($n=1,382$) aged 4–11 years, oral beta2-agonists were the drugs most frequently used (9.8%), followed by short-acting inhaled beta2-agonists (4.3%) and systemic corticosteroids (1.6%). Anti-asthmatic drug use was higher among males than females, and it significantly decreased with age in both genders. A total of 312 children (22.6%) reported current asthma, and 62% of them were not being treated with any anti-asthmatic drugs. Of all those who reported following a certain type of treatment, 20% used oral beta2-agonists alone; 6.1%, short-acting inhaled beta2-agonists alone; and 4.8%, a combination of both drugs. Anti-asthmatic drug use did not differ according to socioeconomic status,

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except for the use of inhaled beta2-agonists and systemic corticosteroids.

Conclusions An overwhelming majority of asthmatic children were not using long-term medications for asthma, in particular inhaled corticosteroids, regardless of the severity of their disease. This result points to the deficiencies of the Brazilian public health system in recognizing this important pharmacological need for child care and thereby limiting the access of these children to a group of efficacious, available, and low risk therapeutic medications.

Keywords Asthma · Pharmacoepidemiology · Asthma · Therapy · Children · Prevalence · Cross-sectional studies · Brazil

Introduction

Asthma is a chronic disease, very frequent in children and adolescents, and its prevalence has increased in recent decades, although with significant differences among countries [1, 2]. Despite therapeutic advances achieved in the last decades, asthma continues to be an important public health problem, and it requires a substantial use of health services [1–3]. Among the factors influencing the elevated morbidity of asthma, the following stand out: genetic predisposition, environmental factors, lifestyle, under-diagnosis, and ineffective treatment, including inadequate management of the disease and the adoption of outdated therapeutic practices [4, 5].

Current international and national guidelines, directives, and consensus recognize that asthma is an inflammatory disease and that inhaled corticosteroids are the most effective therapy available, as they have a prolonged action and have been available for over 30 years. However, recent studies in different populations have shown the under-use of this class of drugs and the great use of other classes of drugs, the short-acting β -agonists [6–8]. Therapy based on the preferred use of these β -agonists results in inadequate control of asthma and may be contributing to a greater number of asthma-related deaths [9]. In the United States, there is evidence that morbidity and mortality from asthma have increased in children who live in unfavorable socioeconomic conditions [10]. One of the probable explanations is that asthma, when treated only during exacerbations with drugs that are effective, yet short-acting, increases the frequency of visits to emergency rooms and the risk of death [11, 12]. Prevalence of asthma in children in Latin America, especially in Brazil, is high [2, 6, 13].

Standard population surveys have been used as the main instrument to estimate the prevalence of asthma in the population [14]. In children aged 6–7 years and 13–14 years, living in five Brazilian regions, prevalence of

wheezing in the last 12 months ranged from 24.3 to 19.0% [15]. Rosário Filho reported an increase in spending on drugs for asthma treatment and in hospitalizations due to this disease [16]. Other studies performed in children with asthma in the public health care facilities in Brazil revealed small proportions of use of anti-inflammatory treatment, ranging from 6.0 to 14.0% [17, 18]. In Brazil, the lack of population-based studies on the use of anti-asthmatics in children, as well as on the reasons for this lack, necessitates such studies, particularly as the use of these drugs is considered an indirect indicator of quality of care provided to asthmatic children. Thus, the objectives of this study were (1) to determine the pattern of consumption of anti-asthmatic drugs and (2) to analyze factors associated with the patterns found, in children living in poorer areas of an urban center of northeastern Brazil.

Methods

Study design and population

A population-based cross-sectional study was performed in a cohort of children in the urban area of the city of Salvador (northeastern Brazil) between February and May 2006. The methods of the longitudinal study are described in detail elsewhere [19]. In brief, the sample was selected randomly from 24 areas, representative of the population living in areas of Salvador that had no sanitation at the time of the cohort recruitment. The original sample had 1,445 children. This is a cross-sectional study of these children, and 1,382 had complete data to participate in this specific analysis.

Data collection

A structured pre-coded questionnaire was used. It included a specific component on the use of medications for respiratory diseases, and another, involving demographic and socioeconomic variables, health conditions and questions about asthma-related symptoms based on the Brazilian Portuguese version of the International Study of Allergies and Asthma in Children (ISAAC) Questionnaire [14]. Table 1 gives further details of the questions used in this study. This instrument was submitted to a pre-pilot evaluation to test the comprehensibility of the questions. After the necessary corrections were made, a pilot study was performed with 10% of the source population for the final test of the questionnaire, development of the manual of instructions, and training of interviewers. Questionnaires were applied using home interviews, conducted with the mothers or adults responsible for the children. In case of absence of interviewees or refusal, interviewers would return to these homes at least two more times.

Table 1 Questions on asthma medication use and other factors together with the answer alternatives presented to children from a large urban center in Brazil

Administered questions	Answer alternatives
Health conditions	
In general, how has the health of your child been in the last 15 days?	Excellent, very good, good, poor, very poor
Exposure to cigarette smoke	
Does your child's mother smoke cigarettes?	No, yes
Are there other people living in the house who smoke cigarettes, including parents?	No, yes
Questions on wheezing and asthma	
Has your child ever had wheezing or whistling in the chest at any time in the past?	No, yes
Has your child had wheezing or whistling in the chest in the last 12 months?	No, yes
How many attacks of wheezing has your child had in the last 12 months?	None, 1–3, 4–12, more than 12
In the last 12 months, how often, on average, has your child's sleep been disturbed due to wheezing?	Never woken with wheezing, less than one night per week, one or more nights per week
In the last 12 months, has wheezing ever been severe enough to limit your child's speech to only one or two words at a time between breaths?	No, yes
Has your child ever had asthma?	No, yes
In the last 12 months, has your child's chest sounded wheezy during or after exercise?	No, yes
In the last 12 months, has your child had a dry cough at night, apart from a cough associated with a cold or chest infection?	No, yes
Asthma management	
In the last 12 months, has your child used any medicines, pills, puffers, or other medication for wheezing or asthma?	No, yes
Medicines	
How often?	If you answered "yes," please name the medication(s) When wheezy; regularly (i.e., every day for at least 2 months of the year)
In the past 12 months, how many visits has your child made to any of the following health professionals for wheezing or asthma?	
Doctor	None, 1–3, 4–12, >12
Hospital emergency department	None, 1–3, 4–12, >12
In the past 12 months, how many times has your child been admitted to hospital because of wheezing or asthma?	None, 1, 2, >2

Asthma definition

Asthma was defined as the occurrence of wheezing in the 12 months preceding the application of the questionnaire, associated with at least one of the following criteria: diagnosis of asthma some time in life, at least four episodes of wheezing in the chest in the last year, history of wheezing in the chest during or after physical exercises, or having woken up at least one night per week due to wheezing in the last 12 months. Children who met these criteria and had taken β -agonists daily or reported their use during hospitalizations due to acute asthma in the last 12 months comprised the group classified with the diagnosis of severe asthma.

Asthma medication use

The use of asthma medication in the 12 months preceding the interview was measured by answering the following

question: "In the last 12 months, did your child use any medication (pills, syrups, nebulizers, or pressurized metered dose inhalers) for wheezing, whistling, or asthma?" Based on the responses to these questions, the medicines for asthma taken by children and reported by mothers were classified as follows: (1) quick-relief medications to treat acute symptoms and exacerbations (short-acting β -agonists, ipratropium bromide, and systemic corticosteroids) and (2) long-term control medications or "controllers" (inhaled corticosteroids, prolonged-release theophylline, long-acting β -agonists, systemic corticosteroids, and antileukotrienes).

Covariables

A total of five sets of variables were considered: demographic, socioeconomic, health conditions, life habits, and severity of asthma. The following were considered as socioeconomic and demographic variables: child's age and sex; mother's age, ethnicity (white or black), and level of

education; and monthly household income (<1, 1–2, 3–5× minimum wage). The national minimum wage at the time of the survey corresponded to US\$100. Child health conditions (excellent/very good, good, poor/very poor) were established by the mother's self-perception of health. Exposure to cigarette smoke was defined by current maternal smoking (yes/no) and presence of other smokers in the household (yes/no). Information about the severity of asthma in the last 12 months consisted of the number of episodes of wheezing (none, 1–3, and ≥ 4); frequency of awakenings at night due to wheezing (has never woken up with wheezing, less than one night per week, one or more nights per week); difficulty in pronouncing two consecutive words during exacerbations (yes/no); perception of wheezing during or after exercising (yes/no); visits to the doctor while having exacerbations (none, 1–3, ≥ 4 times); visits to emergency services due to exacerbations (none, one or more times) and hospitalizations due to asthma (none, one or more times).

Data analysis

Prevalence of asthma medication use according to sex and age group was calculated by the proportion of children who had taken at least one of these medicines in the last 12 months, divided by the total number of children in each age group per sex. In the bivariate analysis, chi-squared test was used to compare proportions (Mantel-Haenszel) and the linear trend test for ordinal variables. In the present study, analysis was performed by comparing children who had used asthma medication with those who had taken other types of medicines or not, according to maternal information. A *P* value <0.05 was considered significant. Data analysis was performed using Stata software, version 9.0 (StataCorp, College Station, TX).

Ethical approval

Approval was obtained from the Brazilian Research Ethics Committee. Written informed consent was obtained from the legal guardian of each child studied.

Results

The 1,382 children studied represent 95.6% of the cohort (1,445 individuals). Of all children, 63 were excluded from this analysis: 26 because they were not found as a result of change of address and 37 because complete information, provided by the mothers and obtained in previous survey, was not available. Of the 1,382 studied children, 12.3% had taken asthma medication specifically (R03) and 219 children (15.8%) had taken medicines for

respiratory problems in the last 12 months, as reported by their mothers. The use of medication for asthma was similar between boys and girls, at 13 and 12%, respectively. The prevalence of use of medicines decreased significantly with age ($P < 0.001$) in both sexes; in the extremes of age groups into which the study population was categorized, 4–5 and 9–11 years, the prevalence decreased from 17.2 to 8.0% in females ($P = 0.005$) and from 20.3 to 8.8% in males ($P = 0.001$) (Table 2).

Oral β -agonists as monotherapy were the therapeutic regimen most frequently reported by mothers, with inhaled β -agonists following far behind (Fig. 1). The oral β -agonists most frequently used in syrup formulation were salbutamol (87.2%) and fenoterol (9.5%), whose consumption was reported by 138 children, of which 88 (64%) used them intermittently. Inhaled β -agonists were consumed by 59 children, of which 21 (36%) did so on a daily basis. In contrast to the oral β -agonists, the inhaled β -agonist most frequently used was nebulized fenoterol (93.1%). Systemic corticosteroids, especially prednisone and prednisolone, were used by 22 (1.6%) children, of which 14 (64%) used these intermittently (data not show).

Of the 312 children with asthma, 37.2% had taken medications for asthma (R03) in the last 12 months. Medications for asthma were equally used by girls and boys, at 38 and 36%, respectively (Table 2). The frequency of medication did not increase with age ($P = 0.886$). A perception of the child's health reported by the mother as being poorest was associated with greater consumption of medication ($P < 0.001$). With regard to the severity of asthma in the last 12 months, consumption of medication was greater in children with difficulty in pronouncing two consecutive complete words during exacerbations (52%), those wheezing during or after exercising (46%), and those who experienced one or more hospitalizations due to exacerbations of asthma in the last year (51%). Oral β -agonist as monotherapy was the therapeutic regimen most frequently reported (19.9%), followed by inhaled β -agonists (6.1%), with 15 (4.8%) children receiving both (Fig. 1). Oral β -agonists (salbutamol and fenoterol were the most frequently used) were used by 91 children and, of these, 59 (64.8%) consumed them intermittently. A total of 40 children reported the use of inhaled β -agonists, especially salbutamol and fenoterol, of which 16 (40.0%) used daily. Systemic corticosteroids (especially prednisone and prednisolone) were used by 17 (5.4%) children, of which 70.1% reported occasional use (data not show).

As shown in Table 3, the use of medication for asthma in children did not differ significantly according to monthly household income, except for the use of inhaled β -agonists and systemic corticosteroids, whose use was more frequent in children from families with a monthly income above the minimum wage. The use of oral β -agonists was signifi-

Table 2 The number and percentage of children using asthma medication in a population-based sample from an urban center in Brazil in relation to social, environmental, demographic, and health characteristics

Characteristics	Children with asthma (<i>n</i> =312)	Total sample of children (<i>n</i> =1,382)
Total using any medication for asthma	116 (37)	170 (12)
Demographics		
Age (years)		
4–5	36 (37)	50 (19)*
6	27 (38)	41 (13)
7–8	31 (35)	50 (11)
9–11	22 (42)	29 (8)
Sex		
Male	62 (36)	94 (13)
Female	54 (38)	76 (12)
Socioeconomic		
Maternal ethnicity		
White	12 (44)	19 (14)
Black	104 (36)	151 (12)
Monthly household income (minimum wages)		
<1× MW	65 (37)	95 (13)
1–2× MW	33 (38)	46 (11)
3–5× MW	18 (37)	29 (12)
Maternal level of education (years)		
0–4	29 (36)	39 (13)
5–8	37 (40)	53 (12)
9 or more	49 (36)	76 (12)
Maternal age (years)		
10–29	50 (37)	84 (15)*
30–39	48 (37)	61 (11)
40–80	18 (38)	25 (10)
Health conditions		
Perception of health of the child reported by mother		
Excellent	8 (35)*	15 (7)**
Good	65 (31)	102 (11)
Poor	43 (53)	53 (26)
Exposure to cigarette smoke		
Current maternal smoking		
No	101 (38)	153 (13)
Yes	14 (33)	16 (9)
Presence of other smokers in the household		
No	85 (36)	131 (12)
Yes	31 (40)	39 (13)
Severity of asthma in the last 12 months		
Number of exacerbations of wheezing		
None	3 (18)	4 (1)**
1–3	75 (34)	91 (31)
≥4	38 (53)	38 (53)
Awakenings at night due to wheezing		
Never woke up	12 (40)	29 (3)

Table 2 (continued)

Characteristics	Children with asthma (<i>n</i> =312)	Total sample of children (<i>n</i> =1,382)
Less than one night per week	52 (31)	52 (31)
One or more nights per week	52 (45)	52 (45)
Difficulties in pronouncing two consecutive words during exacerbations		
No	72 (32)**	88 (7)**
Yes	44 (52)	45 (51)
Wheezing during or after exercising		
No	64 (32)*	117 (9)**
Yes	52 (46)	53 (39)
Visits to the doctor		
None	44 (34)	73 (7)**
1–3	52 (37)	62 (26)
≥4	19 (44)	20 (41)
Visits to emergency services		
None	105 (36)	145 (11)*
One or more	11 (52)	11 (33)
Hospitalizations		
None	74 (32)*	114 (9)**
One or more	42 (51)	42 (42)

P* <0.05; *P* <0.001

cantly more frequent in children who met certain characteristics related to the severity of asthma in the last 12 months. In Table 4, characteristics of children who were categorized as having severe asthma (*n*=110; 35.3%) compared with those with nonsevere asthma (*n*=202; 64.7%) are presented. Social and demographic differences were not observed between the two groups, but as expected the severe cases present a great frequency of severe symptoms and more frequent use of systemic corticosteroids.

Discussion

In this population-based study conducted among children living in poor neighborhoods from a large urban center in Brazil, a significant underuse of long-term control medications was found among those reported with asthma. In addition, 62.8% of the 312 children classified as asthmatic reported no use of any specific medication. Studies show that underuse of medication by certain children results mainly from their families' low socioeconomic level, thus hindering drug acquisition; characteristics of the health system; and professional practices [7, 20].

In Brazil, asthma is responsible for around 350,000 hospitalizations annually and represents the fourth cause of hospitalizations (2.3% of the total) in the SUS (Unified Health System) and the third cause of hospitalizations among children and

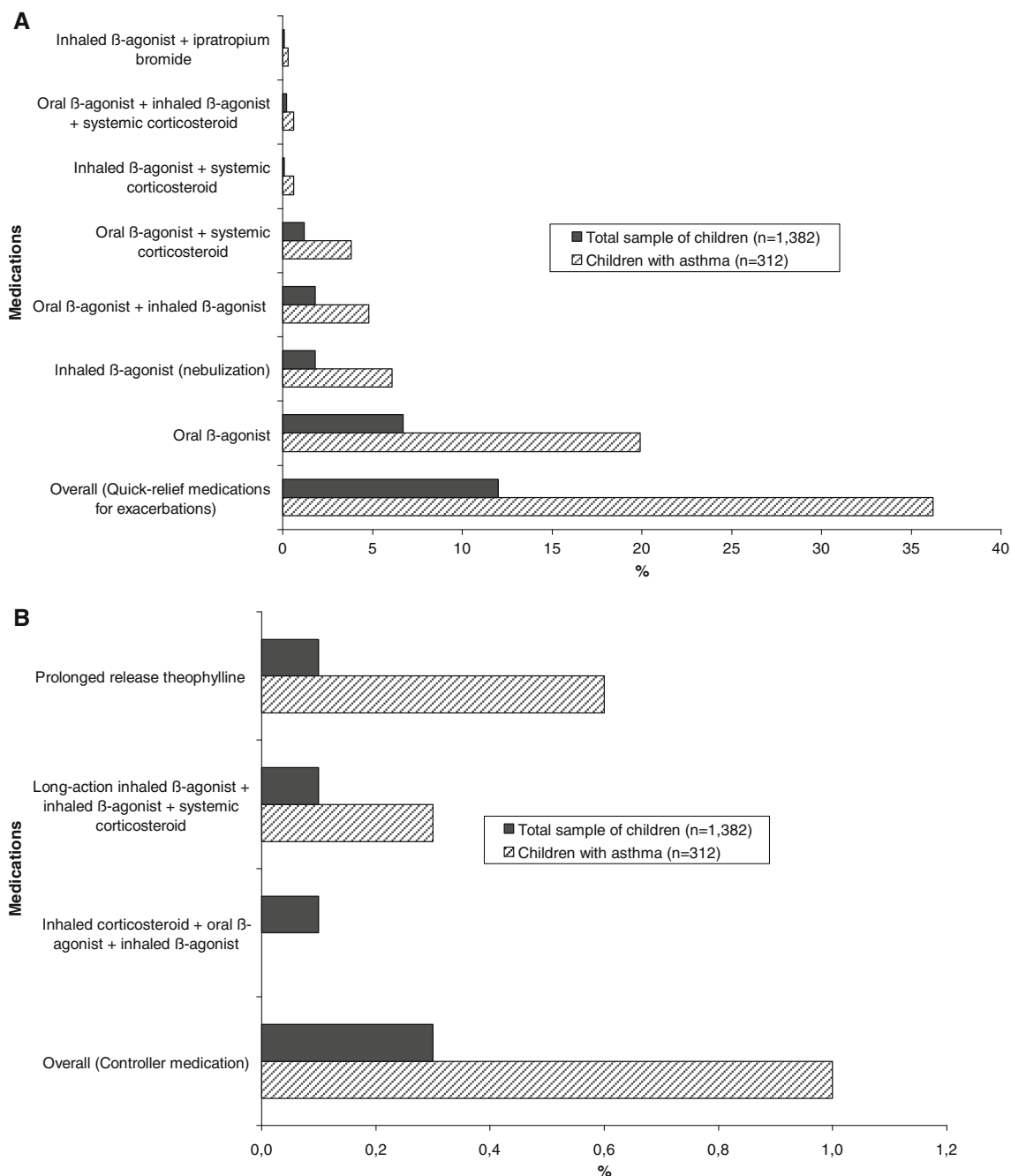


Fig. 1a, b Use of medications for asthma in monotherapy or in combination, in the last 12 months, among children in Salvador, Brazil. **a** Quick-relief medications for exacerbations, **b** controller medication

young adults. In 1996, SUS spent US\$43 million on hospitalizations due to asthma, 2.8% of the total annual spending and the third highest value spent on a specific disease [21–23].

Only 37% of asthmatic children had used medication for asthma in the 12 months prior to the survey. The most frequently used medicines by pharmacological group were, in decreasing order: oral β -agonists, inhaled β -agonists, and systemic corticosteroids. The distribution by age showed a more frequent use of inhaled β -agonists by older children

and of systemic corticosteroids by younger ones. This is probably a result of the difficulties in teaching younger children how to use an inhaler, according to similar findings among German asthmatic children [24]. Of the asthmatic children, 12.7% had used systemic corticosteroids alone or in association with other anti-asthmatic medications. However, this group of drugs is not recommended for asthma treatment, due to an increased risk of bone fractures in children even when used for short periods of time [25, 26].

Table 3 Type of asthma medication used by children with reported wheezing in a population-based sample from an urban center in Brazil

	Numbers	Oral β -agonists (%)	Inhaled β -agonists (%)	Systemic corticosteroids (%)	No medicine (%)
Overall	312				
Sex					
Male	171	27.5	11.7	7.0	57.3
Female	141	31.2	14.2	3.5	56.7
Age (years)					
4–5	98	26.5	14.3	8.2	55.1
6	72	33.3	12.5	2.8	55.6
7–8	89	28.1	10.1	4.5	62.9
9–11	53	30.2	15.1	5.7	52.8
Maternal ethnicity					
White	27	33.3	22.2	7.4	51.8
Black	285	28.8	11.9	5.3	42.1
Monthly household income (minimum wages)					
<1× MW	175	30.9	8.6*	2.3*	41.1
1–5× MW	137	27.0	18.3	9.5	45.3
Indicators of severity of asthma in the last 12 months					
Number of exacerbations of wheezing					
None	17	17.7*	5.9	0.0	82.4*
1–3	223	25.1	13.5	4.5	59.2
≥ 4	72	44.4	12.5	9.7	44.4
Awakenings at night due to wheezing					
Never woke up	30	30.0	16.7	3.3	56.7
Less than one night per week	167	24.6	9.6	4.8	62.3
One or more nights per week	115	35.7	16.5	7.0	49.6
Difficulty in pronouncing two consecutive words during exacerbations					
No	227	23.8*	11.9	4.4	61.2*
Yes	85	43.5	15.3	8.2	45.9
Wheezing during or after exercising					
No	198	23.7*	12.1	2.5*	60.6
Yes	114	38.6	14.0	10.5	50.9
Visits to the doctor					
None	129	29.5	8.5*	4.7	58.9
1–3	139	28.1	13.7	6.5	56.8
≥ 4	43	30.2	23.3	4.7	53.5
Visits to emergency services					
None	291	28.2	12.7	5.2	57.7
One or more	21	42.9	14.3	9.5	47.6
Hospitalizations					
None	229	24.9*	11.4	2.2*	60.7*
One or more	83	41.0	16.9	14.5	47.0

* $P < 0.05$

In this studied population, it has already been shown that the use of medicine, in general, is irrational for some pharmacological groups, in particular antibiotics and analgesics/antipyretics [27]. In the present study we showed that the patterns of use of medications for asthma are in great divergence with the recommendations established in

guidelines that emphasize the need to use daily preventive anti-inflammatory drugs in children with asthma, be it mild, moderate, or severe [28]. Inhaled corticosteroids, the main pharmacological choice for control of this disease, were reported to have been used by only one child in this population. Other studies conducted in Brazil, although

Table 4 Characteristics of children classified as having severe asthma compared with children with nonsevere asthma

Characteristics	Number	Severe asthma (<i>n</i> =110) (%)	Nonsevere asthma (<i>n</i> =202) (%)	<i>P</i> -value
Black mother	285	88.2	93.1	0.142
Male	171	59.1	52.5	0.262
7–8 years of age	89	35.5	24.8	0.174
Household income less than minimum wage	175	57.3	55.4	0.756
Severity of asthma in the last 12 months				
1–3 exacerbations of wheezing	223	65.5	74.8	0.012
Less than one awakening at night per week due to wheezing	167	53.6	53.5	0.313
Difficulty in pronouncing two consecutive words during exacerbations	85	44.6	17.8	<0.001
Wheezing during or after exercising	114	49.1	29.7	0.001
One or more visits to the doctor	182	68.8	53.0	0.007
Visits to the emergency room	21	10.9	4.5	0.030
Use of corticosteroids in the last 12 months				
Systemic	17	12.7	1.5	<0.001
Inhaled	1	0.9	0	

focused on children cared for in health units, found frequencies of use of inhaled corticosteroids between 2 and 6% [18, 29].

The reasons for underuse of inhaled corticosteroids in our context and the fact that well established recommendations are not followed reflect flaws in public health policies aimed at asthma, including the complete absence of strategies to increase prescribers' adherence to the asthma program recommendations, drug availability and affordability flaws, and lack of continuing education for families [6, 17]. Inhaled corticosteroids are listed by the World Health Organization as essential medications, but they cost more than what low-income families can afford, thus emphasizing the need for these to be available in SUS primary health care units through the establishment of a broad public program for asthma control [29].

There were no significant associations between overall use of asthma medication and monthly household income, a result that is similar to those observed in other studies [24, 30]. However, inhaled β -agonists and systemic corticosteroids were used more frequently in children whose monthly household income was higher than the minimum wage. A similar finding was observed in a study among asthmatic German children where the use of systemic corticosteroids was more frequent in the richest ones [24]. In a study performed with a group of low-income asthmatic children in New York City, it was observed that many families understood asthma as an episodic disease, thus giving priority to symptomatic rather than preventive therapies [31, 32].

Inadequate treatment of asthma leads to the frequent use of emergency services and hospitalizations due to exacerbations and leads to a higher risk of complications [33, 34]. For the low-income population in Brazil, the emergency room is often the access to health services. In the case of

asthma, children visit the emergency room motivated by exacerbations of a disease that is not controlled properly [29]. The present study demonstrated this situation. None of the 21 asthmatic children who frequently visited the emergency rooms used long-term control medications for asthma (inhaled corticosteroids, antileukotrienes, or prolonged-release theophylline). Constant visits to emergency units, motivated by exacerbations of asthma, are the best indicator of inadequate treatment [33].

The low quality of care provided to children with asthma was best evidenced in this study by the fact that half of the children classified as having severe asthma had not used any class of medication against asthma in the last 12 months. Moreover, of the 312 children who had asthma, 83 (28%) had had at least one episode of hospitalization in the last 12 months, and 51% were treated only with quick-relief medication (41% oral β -agonist and 16.9% inhaled β -agonist). In population-based studies, the rates of hospitalizations for asthmatic patients represent the joint effect of the prevalence and severity of the disease and the quality of health care provided. Studies have shown that intervention with inhaled corticosteroids contributes to decreased morbidity and mortality [35, 36] and hospitalizations [21] due to asthma.

Childhood asthma was highly prevalent in the studied population in this low-income urban community setting in Brazil [13], but an overwhelming majority of asthmatic children did not use long-term medications for asthma, in particular inhaled corticosteroids, regardless of the severity of their disease. Brazil has a comprehensive health system [37], but this result points to deficiencies in recognizing this important pharmacological need for child care, and thereby the access of these children to a group of efficacious and

low risk therapeutic medications is limited. The lack of access to proper treatment with inhaled corticosteroids has put children at risk through their use of systemic corticosteroids. They may have been well prescribed to treat exacerbations that could have been avoided with the use of inhaled corticosteroids, which have an insignificant rate of systemic side effects. But, for an asthma control program to be effective—in addition to ensuring the availability of adequate pharmacological treatments—the program must be integrated with public education aimed at asthma patients and all health professionals, rather than prescribers only.

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