



# Impact of asthma control on different age groups in five Latin American countries

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## ABSTRACT

**Background:** Asthma is a chronic airway inflammatory condition of the airway and is classified as controlled, partially controlled, and uncontrolled. Patients with uncontrolled asthma are at greater risk for hospitalizations and visits to emergencies, and the condition has greater impact on their daily lives. The aim of this study was to evaluate asthma control, the use of health resources, and asthma's impact on the activities of daily living of patients with different age groups in 5 Latin American countries.

**Methods:** This was a retrospective analysis of The Latin America Asthma Insights and Management (LA AIM) study carried out in Argentina, Brazil, Mexico, Venezuela, and Puerto Rico. Asthmatics were split into 3 age groups: 12-17, >17-40 and > 40 years old. An interview face to face was carried out and patients answered a questionnaire of 53 questions related to 5 main domains of asthma: symptoms, impact of asthma on daily living activities, patients' perceptions of asthma control, exacerbations, and treatment/medication.

**Results:** A total of 2167 asthmatics were interviewed. There was a low percentage of controlled patients (mean 9%) in all 3 groups with no particular difference among the five countries, but Venezuelan patients had a 71% chance of having uncontrolled asthma ( $p < 0.001$ ).

**Conclusion:** In the 3 age groups, patients experienced poor asthma control, with no significant differences among the countries. Patients who used control medication had a greater chance of controlling their asthma, and those who had emergency health care visits had a greater chance of having uncontrolled asthma.

**Keywords:** Asthma, Age group, Latin America, Medication adherence, Epidemiology

## INTRODUCTION

According to the World Health Organization (WHO), an estimated 235 million people worldwide have asthma,<sup>1</sup> and it affects all age groups.<sup>2</sup> It is well established that asthma is a variable

disease and can vary among individuals, and its progression and symptoms can vary within an individual's experience over time.<sup>3</sup> Worldwide, asthma in children is more common in males

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than in females. However, after puberty, the disease is more prevalent in females.<sup>4</sup>

Asthma is a chronic inflammatory disease, and it is recommended that patients practice self-management and adhere to a regimen of anti-inflammatory controller medication.<sup>5,6</sup> Inhaled corticosteroids (ICS) are considered first line treatment for asthma control. The scarce use of ICS (6%), as revealed in the 2005 Asthma Insights and Reality in Latin America (AIRLA) study was considered to be one of the factors for the low rates of asthma control (2.5%) in this continent.<sup>7</sup> Action plans should be a part of the interactions between health professionals and patients in order to increase treatment adherence.<sup>5</sup> Education should be personalized, and social and psychological aids are often needed to maintain positive behavioral changes.<sup>5</sup>

The Global Initiative for Asthma (GINA) classifies asthma patients as having asthma that is controlled, partially controlled, or uncontrolled on the basis of symptoms, limitations in daily activities, nocturnal awakenings, and rescue medication use; in addition, the GINA states the importance of achieving and maintaining clinical asthma control as a treatment goal and to reduce future risks, including exacerbations, fixed airflow limitation, and adverse effects of medication.<sup>5,8,9</sup> To reach this aim, it is necessary to identify barriers that can compromise asthma control and to determine whether subgroups of patients stratified by age are at an increased risk of poor disease control.<sup>8</sup>

Low adherence to ICS treatment can lead to partially controlled or uncontrolled asthma, and it increases the costs to health care systems. Patients with uncontrolled asthma increase disease-related costs primarily because of emergency department visits and hospitalizations.<sup>8,10</sup> The AIRLA study showed that in addition to the increased use of health resources, asthma causes considerable limitations in daily activities: most adults (79%) and children (68%) have reported that asthma symptoms limit their daily activities in some way.<sup>7</sup>

Data on the impact of asthma on public health are scarce in many Latin American countries. Both the prevalence and morbidity of asthma tend to be

highly variable among Latin American countries.<sup>11</sup> A recent study conducted in Argentina (2018) investigated the burden of asthma only in subjects aged 20–44 years and showed that 51.9% of asthmatics used asthma controller medication on a daily basis and 46.8% only took medication when they had symptoms.<sup>12</sup> However, this study has not looked at the main objective of treating asthmatic patients which is the control level the patients' group has achieved; besides, this study was conducted in only one country. The Latin America Asthma Insights and Management (LA AIM) study<sup>12</sup> looked at asthma control in 5 Latin American countries from ages 12 years old and on, which allows to evaluate asthma control in different age groups. Even though the LA AIM study was published in 2013, it still may give us important information on asthma control across different age groups. This knowledge would give us some insight on how asthma treatments impact patients in different age groups in Latin America and help us to determine appropriate measures for control of the disease in each group.

Our study's first hypothesis is that currently patients should have better asthma control than was identified in the 2005 AIRLA study,<sup>7</sup> as it is possible that health care professionals have a better knowledge of asthma management and treatment and the public health system of most of Latin America countries usually provides medication for control of the disease. From the literature it is known that children and adolescents do not follow treatment recommendations given to them by doctors for many reasons.<sup>13</sup> This is a major cause of increased frequency of asthma attacks placing this age group at high risk for life-threatening asthma. However, we hypothesize as they are cared for and supervised by their parents/caregivers, that their level of asthma control should be high in this sample. Therefore, the primary objective of the present study was to evaluate the asthma control of patients who participated in LA AIM Study in 2011, in different age groups in 5 Latin America countries: Argentina, Brazil, Mexico, Venezuela, and Puerto Rico. A secondary objective was to evaluate the impact of asthma control on the use of health resources and physical aspects of

patients in 3 different age groups in these countries.

## METHODS

### Sample

The current study is a retrospective analysis of the LA AIM survey, which was conducted in 2011 in Argentina, Brazil, Mexico, Venezuela, and Puerto Rico to explore and document patients' perceptions of asthma as well as their knowledge of the disease and its treatment.<sup>14</sup> This cross-sectional study used the same method previously applied in the multicenter Asthma Insight and Management (AIM) study in the United States, Europe, Canada, Asia, and the Asia-Pacific region. The survey was developed by Abt SRBI (New York, NY, USA). As it occurred in all other countries where the AIM questionnaire was applied, all questions were originally drafted in English and translated to the local languages of the 5 countries; the translated questions were back-translated to English and compared for meaning against the original English version. The LA AIM study was not subject to formal ethics approval or formal consenting processes in any country. The need for full consideration, and written informed consent, was waived by the Ethics Committee on Clinical Pharmacology at the CIDEA Foundation in Argentina, the Ethics Committee of the Federal University of São Paulo Hospital, São Paulo in Brazil, the Ethics Committee of the Instituto Nacional Enfermedades Respiratorias Ismael Cosío Villegas in Mexico, the Cardio Pulmonary Research Center in Puerto Rico, and the Bioethics Committee for Research at Hospital de Clinicas Caracas in Venezuela.<sup>14</sup>

In the study, 51,208 households were screened, yielding a sample of at least 400 patients in each country/area; the patients were randomly selected using a national probability sampling. The participants were contacted at their residences by a professional interviewer. Asthma patients  $\geq 12$  years old were invited to participate in this study; for patients aged 12-17, invitations to participate were submitted to parents or caregivers.

Patients who agreed to participate in the study were interviewed face-to-face at their homes by a professional interviewer trained to administer the questionnaire. For the adolescent asthmatics aged

12-17 years parents or caregivers were interviewed. To be eligible for inclusion in the study, patients had to have their asthma diagnosed by a physician, have experienced asthma symptoms, and used asthma medication within the past year. If 2 or more persons with asthma lived in the same residence, 1 of them was chosen at random. Patient consent was explicitly obtained before the interview began, and respondents were advised that they could refuse to cooperate at any point during the interview. No identifiable personal information, including names, was collected or maintained in the survey.

To evaluate the asthma control of patients who participated in LA AIM Study in 2011 in different age groups, we divided patients into 3 age groups: 12-17 years, > 17-40 years, and >40 years. This was the greater difference from the master AIM study paper.<sup>13</sup>

The questionnaire consisted of 53 questions covering 5 asthma-related topics: symptoms, impact of asthma on daily living activities, patients' perceptions of asthma control, exacerbations, and asthma treatment/medication. Questions about physical and emotional limitations associated with asthma were included to assess the negative impacts of asthma on the physical and emotional aspects of the patients. The questionnaire included questions of the original LA AIM study regarding socioeconomic level, education level, asthma-related factors, such as smoking, presence of animals in the home, history of rhinitis or allergies, use of asthma controller medication and rescue medication use, prescription of a written action plan, need to visit health-care resources within the last 12 months, and limitations of daily activities due to asthma.<sup>14</sup>

Asthma control was defined as controlled, partially controlled, and uncontrolled asthma, according to GINA. To assess asthma control as recommended by GINA, patients were asked about the following in the past 4 weeks: frequency of asthma symptoms, any night waking due to asthma, limitations of activity due to asthma, and frequency of reliever use for relief of symptoms.<sup>5</sup>

### Statistical analysis

In the statistical analysis, categorical variables were presented as absolute numbers and

N (%)	Argentina 433 (19.9)	Brazil 401 (18.6)	Mexico 532 (24.5)	Puerto Rico 401 (18.6)	Venezuela 400 (18.4)	P*
Gender (female)						
12-17yr	31 (50)	18 (43.9)	53 (42.4)	21 (36.2)	36 (53.7)	0.302
>17-40yr	107 (64.8)	130 (69.1)	135 (63.1)	89 (63.6)	124 (61.7)	0.607
>40yr	147 (71.4)	125 (72.7)	144 (74.6)	147 (72.4)	98 (74.2)	0.954
Pets in the household						
12-17yr	35 (56.5)	23 (56.1)	71 (56.8)	32 (55.2)	34 (50.7)	0.394
>17-4yr	84 (50.9)	88 (47.1)	111 (51.9)	81 (57.9)	111 (55.2)	0.159
>40yr	119 (57.8)	89 (52.0)	108 (56.0)	109 (53.7)	74 (56.1)	0.820
Smokers in the household						
12-17yr	26 (41.9)	23 (56.1)	52 (41.6)	17 (29.3)	35 (52.2)	0.036
>17-40yr	76 (46.1)	83 (44.1)	96 (44.9)	36 (25.7)	108 (53.7)	<0.001
>40yr	81 (39.3)	66 (38.4)	73 (37.8)	47 (23.2)	53 (40.2)	0.002
History of rhinitis or allergy						
12-17yr	34 (54.8)	32 (78.0)	58 (46.4)	45 (77.6)	24 (35.8)	<0.001
>17-40yr	81 (49.1)	146 (77.7)	84 (39.3)	109 (77.9)	109 (54.2)	<0.001
>40yr	91 (44.2)	126 (73.3)	82 (42.5)	132 (65.0)	66 (50.0)	<0.001
Active smokers						
12-17yr	13 (21.0)	16 (39.0)	23 (18.4)	3 (5.2)	7 (10.4)	0.001
>17-40yr	32 (19.4)	47 (25.0)	17 (7.9)	17 (12.1)	19 (9.5)	<0.001
>40yr	29 (14.1)	33 (19.2)	13 (6.7)	17 (8.4)	18 (13.6)	<0.001
Ex smokers						
12-17yr	8 (12.9)	9 (22.0)	17 (13.6)	6 (10.3)	9 (13.4)	0.001
>17-40yr	37 (22.4)	31 (16.5)	47 (22.0)	14 (10.0)	35 (17.4)	<0.001
>40yr	59 (28.6)	64 (37.2)	65 (33.7)	43 (21.2)	35 (26.5)	<0.001
Non smokers						
12-17yr	39 (62.9)	16 (39.0)	84 (67.2)	45 (77.6)	51 (76.1)	0.001
>17-40yr	92 (55.8)	109 (58.0)	149 (69.6)	107 (76.4)	147 (73.1)	<0.001
>40yr	114 (55.3)	75 (43.6)	115 (59.6)	143 (70.4)	78 (59.1)	<0.001
Complete high school						
12-17yr	24 (38.7)	19 (46.3)	36 (28.8)	27 (46.6)	43 (64.2)	<0.001
>17-40yr	77 (46.7)	123 (65.4)	88 (41.1)	43 (30.7)	95 (47.3)	<0.001
>40yr	54 (26.2)	82 (47.7)	31 (16.1)	99 (48.8)	66 (50.0)	<0.001

**Table 1.** Demographic and clinical characteristics of asthmatic patients from 5 Latin American countries in different age groups. Values expressed in n (%). \* Chi-square test,  $p < 0.05$

percentages, and continuous variables were presented as mean and standard deviations. The chi-square test was used to compare categorical variables among the age groups studied (12-17 years, > 17-40 years, and >40 years), and the level of significance was set at  $p < 0.05$ . The significant variables in the chi-square test were included in the logistic regression model, with controlled asthma being considered as the dependent variable. The group of patients with uncontrolled

asthma consisted of all asthmatics with partially controlled or uncontrolled asthma. Mexico was chosen as a reference because it is the country whose patients were observed to have the best level of asthma control (9.4%), and the age category of 12-17 years old was chosen as a reference due to our initial hypothesis. Data analysis was performed with the Statistical Package for the Social Sciences, version 18.0 (SPSS Inc., Chicago, IL, United States).

## RESULTS

Interviews with 2167 asthmatics aged  $\geq 12$  years from a sample of 51,208 households in 5 Latin American countries, including Argentina (19.9%), Brazil (18.6%), Mexico (24.5%), Puerto Rico (18.6%), and Venezuela (18.4%) were performed.

Table 1 shows the demographic and clinical characteristics of asthmatic patients from different age groups in the 5 Latin American countries. There were no differences in relation to gender between the 3 age groups in the 5 countries studied; however, there were progressive increases in the proportion of asthmatic women with the increase in age. The allergic rhinitis prevalence in patients with asthma was higher in Brazil and Puerto Rico (between 70% and 80%) in the 3 age groups. Brazil was the country that presented the highest number of active smokers, and Puerto Rico and Venezuela presented the lowest number of active smokers, in the 3 age groups.

Regarding the level of asthma control in the 5 countries, the majority of patients had partially controlled or uncontrolled asthma in all 3 age groups. In addition, we verified that of the 5 countries studied, Argentina had the highest percentage of uncontrolled asthma in the 3 age groups (Fig. 1).

An assessment of 3 aspects of asthma treatment revealed that Argentina was the country in which prescribed treatment plans for asthma and rescue medication were most often used in the 3 age groups (Table 2).

In all 3 age groups, asthmatics in Argentina used oral corticosteroids more often than patients in the other countries studied (12-17 years old:  $p < 0.001$ ;  $>17-10$  years old:  $p < 0.001$  and  $> 40$  years old:  $p = 0.001$ ).

Regarding the impact of asthma on patients needing emergency visits and hospitalizations, Argentina presented the highest frequency of emergency visits to doctors' offices, hospitals, or outpatient clinics in the age group 12-17 years (67.7%,  $p = 0.002$ ), and in the age groups  $> 17-40$  years and  $>40$  years Puerto Rico had the highest prevalence (57.1%,  $p < 0.001$  and 59.6%,  $p < 0.001$ , respectively). With respect to hospital admissions, Brazil was the country with the highest

number of hospitalizations in the age group  $>17-40$  years (28.7%,  $p < 0.001$ ), while Puerto Rico had the highest frequency of hospitalizations for the age group  $> 40$  years (25.1%,  $p = 0.040$ ) (Table 3).

Regarding the impact of asthma on daily living activities, more than 70% of asthmatics in the 5 countries and in the 3 age groups presented some limitations in sports and recreation, with a significant difference only in the age group  $>17-40$  years

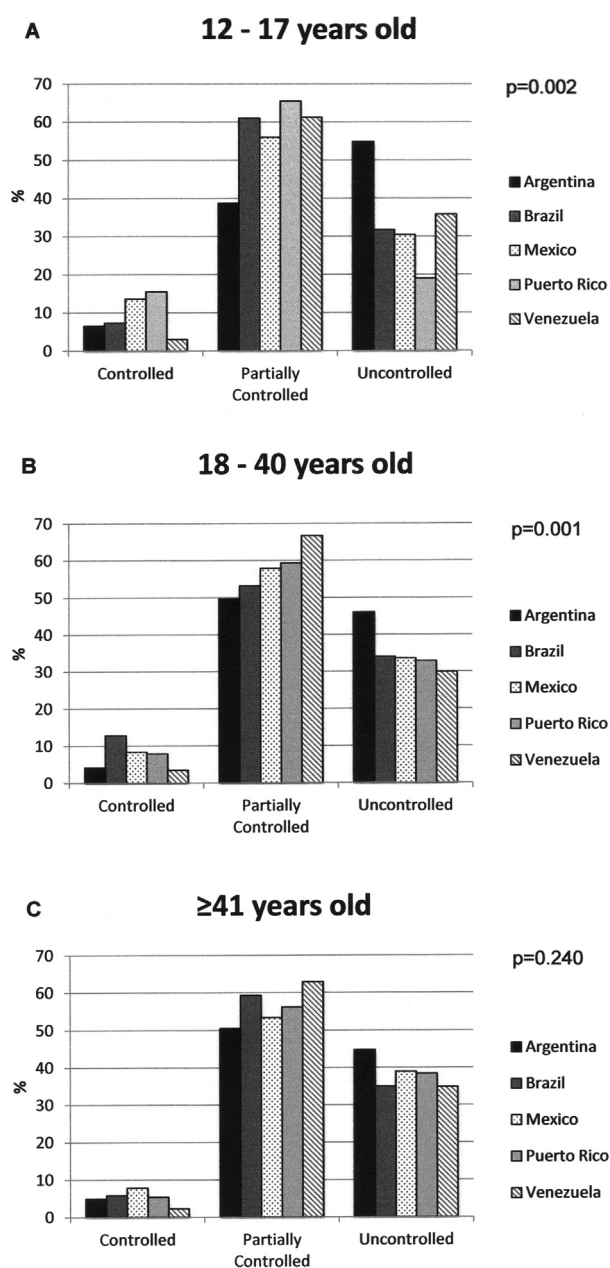


Fig. 1 Level of asthma control in 5 Latin American countries in different age groups. 1A. Patients with 12-17 years old; 1B. Patients with 18-40 years old; 1C. Patients with  $\geq 41$  years old

N (%)	Argentina 433 (19.9)	Brazil 401 (18.6)	Mexico 532 (24.5)	Puerto Rico 401 (18.6)	Venezuela 400 (18.4)	P*
Had a written action plan for the asthma management						
12-17yr	41 (66.1)	18 (43.9)	45 (36.0)	31 (53.4)	28 (41.8)	0.004
>17-40yr	83 (50.3)	77 (41.0)	55 (25.7)	65 (46.4)	97 (48.3)	<0.001
>40yr	115 (55.8)	74 (43.0)	73 (37.8)	109 (53.7)	61 (46.2)	<0.001
Used asthma control medication in the last 4 weeks						
12-17yr	33 (53.2)	12 (29.3)	14 (11.2)	16 (27.6)	8 (11.9)	<0.001
>17-40yr	71 (43.0)	41 (21.8)	27 (12.6)	71 (50.7)	44 (21.9)	<0.001
>40yr	106 (51.5)	52 (30.2)	28 (14.5)	138 (68.0)	29 (22.0)	<0.001
Used relief medication in the last 4 weeks						
12-17yr	48 (77.4)	24 (58.5)	57 (46.0)	22 (38.6)	28 (42.4)	<0.001
>17-40yr	115 (70.1)	104 (55.6)	121 (56.8)	69 (49.6)	111 (55.8)	0.005
>40yr	153 (74.3)	95 (55.2)	126 (66.7)	131 (64.9)	85 (64.4)	0.004

**Table 2.** Questions regarding asthma treatment in 5 Latin American countries in different age groups including action plan and control and relief medication use. Values expressed in n (%). \* Chi-square test,  $p < 0.05$

among asthmatics in Venezuela (87.4%) and Brazil (70.7%) ( $p < 0.001$ ) (Table 4).

Table 5 presents the logistic regression model of the variables with statistical significance in terms of asthma treatment, use of health resources, and physical limitations to evaluate controlled asthma as an outcome. There was no relation between the studied age groups and asthma control, with the age group 12-17 years as a reference. Considering Mexico as a reference, as it was the country with the highest percentage of patients with controlled asthma, Venezuela had a 71% chance of having uncontrolled asthma ( $p < 0.001$ ). Patients who used asthma controller medication were 3 times more likely to have controlled asthma ( $p < 0.001$ ), and patients who had emergency visits to a physician's office, hospital, or clinic had a 59% chance of having uncontrolled asthma ( $p < 0.001$ ).

## DISCUSSION

This study has shown that there is a large prevalence of asthmatic patients in the partially and uncontrolled asthma groups in detriment of asthma controlled patients in the 3 age groups evaluated. Of the 5 Latin American countries

studied, Venezuela was the country whose patients were most likely to have partially controlled and uncontrolled asthma. In addition, it was found that patients who had emergency visits to physicians' offices, hospitals, or clinics had a greater chance of having uncontrolled asthma, and those who used asthma controller medication were more likely to have controlled asthma. The outcomes of this study could have been influenced by the possibility of different characteristics of the health system of the 5 countries, including the availability of medications intended for control of asthma. However, in general, all 5 countries, in different ways, provide asthma controller medication; and when all aspects are looked over, the mean results are very similar, meaning that overall the asthma scenario in Latin America is not too different among the countries.

The fact that there were more patients with partially controlled and uncontrolled asthma diverges from the first hypothesis of the study that had suggested there should be more patients with better asthma control. The AIM study conducted in the United States, Canada, Europe, and Asia-Pacific countries also demonstrated poor asthma control and poor patient perceptions of the level of asthma control.<sup>15-21</sup> Similarly, a study conducted by Price et al. (2014) in 11 European

N (%)	Argentina 433 (19.9)	Brazil 401 (18.6)	Mexico 532 (24.5)	Puerto Rico 401 (18.6)	Venezuela 400 (18.4)	P*
Emergency visit to physician's office, hospital or a clinic						
12-17yr	42 (67.7)	21 (51.2)	52 (41.6)	26 (44.8)	23 (34.3)	0.002
>17-40yr	62 (37.6)	87 (46.3)	78 (36.4)	80 (57.1)	70 (34.8)	<0.001
>40yr	81 (39.3)	80 (46.5)	68 (35.2)	121 (59.6)	53 (40.2)	<0.001
Hospital admission						
12-17yr	17 (27.4)	13 (31.7)	23 (18.4)	10 (17.2)	11 (16.4)	0.182
>17-40yr	22 (13.3)	54 (28.7)	32 (15.0)	20 (14.3)	26 (12.9)	<0.001
>40yr	34 (16.5)	42 (24.4)	35 (18.1)	51 (25.1)	19 (14.4)	0.040
ICU <sup>a</sup> admission						
12-17yr	12 (19.4)	2 (4.9)	23 (18.4)	3 (5.2)	12 (17.9)	0.082
>17-40yr	26 (15.8)	10 (5.3)	21 (9.8)	9 (6.4)	42 (20.9)	<0.001
>40yr	49 (23.8)	14 (8.1)	37 (19.2)	20 (9.9)	31 (23.5)	<0.001

**Table 3.** Use of health resources during asthma attacks requiring unscheduled emergency visit, hospital admission and ICU admission in asthmatic patients from 5 Latin American countries stratified by age groups. \* Chi-square test,  $p < 0.05$ . a. ICU: Intensive Care Unit. Values expressed in n (%)

countries concluded that levels of asthma control remain low and that disease symptoms and exacerbations are common.<sup>22</sup> Likewise, a 2015

study conducted in Australia found that patients had poor perceptions of disease control.<sup>23</sup> In addition to these findings, the AIM study

N (%)	Argentina 433 (19.9)	Brazil 401 (18.6)	Mexico 532 (24.5)	Puerto Rico 401 (18.6)	Venezuela 400 (18.4)	P*
Sports and recreation						
12-17yr	49 (79.0)	31 (77.5)	101 (81.5)	42 (72.4)	56 (83.6)	0.580
>17-40yr	138 (85.7)	130 (70.7)	164 (76.6)	108 (78.3)	173 (87.4)	<0.001
>40yr	162 (82.2)	119 (73.9)	142 (74.0)	143 (74.1)	103 (78.6)	0.211
Normal Physical exertion						
12-17yr	45 (72.6)	30 (73.2)	76 (60.8)	33 (57.9)	55 (82.1)	0.012
>17-40yr	124 (75.6)	139 (74.3)	144 (67.3)	105 (75.5)	170 (85.0)	0.001
>40yr	162 (81.0)	145 (84.8)	159 (82.4)	171 (84.7)	111 (84.1)	0.831
Social activities						
12-17yr	33 (53.2)	19 (46.3)	42 (33.6)	24 (41.4)	43 (64.2)	0.001
>17-40yr	80 (48.5)	92 (49.5)	95 (44.6)	84 (60.9)	132 (65.7)	<0.001
>40yr	127 (61.7)	111 (64.9)	121 (63.0)	139 (70.2)	93 (71.0)	0.234
Sleep						
12-17yr	51 (82.3)	36 (87.8)	72 (57.6)	34 (58.6)	57 (85.1)	<0.001
>17-40yr	123 (75.0)	141 (75.0)	162 (75.7)	111 (79.9)	170 (84.6)	0.097
> 40yr	158 (77.1)	143 (83.1)	138 (72.3)	167 (82.7)	115 (87.1)	0.006
Daily activities						
12-17yr	44 (71.0)	30 (73.2)	58 (46.4)	31 (53.4)	49 (73.1)	<0.001
>17-40yr	97 (58.8)	111 (59.0)	130 (61.3)	105 (75.5)	148 (73.6)	<0.001
>40yr	158 (76.7)	128 (74.4)	137 (71.0)	170 (84.2)	100 (75.8)	0.035

**Table 4.** Impact of asthma on activities of daily living in 5 Latin American countries in different age groups. Values expressed in n (%). \* Chi-square test,  $p < 0.05$

	Exp(B)	95% CI <sup>b</sup> to EXP(B) <sup>c</sup>		p
		Minimum	Maximum	
<b>Countries</b>				
Mexico (reference)				
Argentina	0.651	0.354	1.199	0.168
Brazil	1.261	0.763	2.085	0.365
Puerto Rico	1.407	0.827	2.395	0.208
Venezuela	0.290	0.147	0.573	<0.001
<b>Stratified age</b>				
12-17 years old (reference)				
>17-40 years old	0.717	0.444	1.159	0.175
>40 years old	0.602	0.361	1.003	0.051
<b>Gender</b>				
Female (reference)				
Male	1.133	0.779	1.647	0.513
<b>Smokers in the household Tabagism</b>				
Non smoker (reference)	0.769	0.528	1.121	0.173
Active Smoker	0.911	0.524	1.584	0.741
Ex-smoker	1.025	0.656	1.601	0.914
<b>History of rhinitis or allergy</b>				
	0.880	0.600	1.291	0.513
<b>Asthma control medication use</b>				
	3.377	1.893	6.023	<0.001
<b>Written action plan for asthma management</b>				
	0.892	0.609	1.306	0.556
<b>Emergency visit to a physician's office, hospital or a clinic</b>				
	0.414	0.256	0.669	<0.001
<b>Episode of severe asthma requiring hospital admission</b>				
	0.624	0.295	1.320	0.217
<b>Episode of severe asthma requiring ICU<sup>a</sup> admission</b>				
	0.937	0.489	1.796	0.845
<b>Oral corticosteroids need</b>				
	0.799	0.525	1.215	0.294
Constant	196.071			<0.001

**Table 5.** Logistic regression to evaluate the outcome of controlled asthma.  $p < 0.05$ . a. ICU: Intensive Care Unit. b. CI: confidence interval. c. Exp (B): exponential beta

conducted in Brazil concluded that the vast majority of asthmatics had uncontrolled asthma and that asthma controller medications were underused.<sup>24</sup>

It is known that the use of low doses of ICS reduces asthma symptoms, improves lung function and quality of life, and reduces the risk of exacerbations and hospitalizations.<sup>25-28</sup> In the present study, it was observed that patients who used asthma controller medication were 3 times more likely to have controlled asthma ( $p < 0.001$ ). When comparing the 3 age groups in all 5 countries, it was found that patients in Mexico (11.2%-14.5%) and Venezuela (11.9%-22.0%) had

the least use of asthma controller medication and that patients in Argentina (43.0%-53.2%) and Puerto Rico (27.6%-68.0%) used it the most; however, even in these countries, the rates of use were lower than expected. The frequency of asthma controller medication use was also lower than expected in the AIM Study conducted in Europe and Canada (52%),<sup>16</sup> India (36%),<sup>17</sup> Thailand (54%), and the Asia Pacific region (13.6%).<sup>19</sup> Likewise, in the Australian study, only 60.8% of the participants used asthma controller medication.<sup>23</sup> In the ADERE (Adherence to Asthma Maintenance Treatment) study, which assessed adherence to preventive asthma treatment in 15 Brazilian states, the frequency



was 51.9%.<sup>29</sup> As it may be seen, the use of asthma controller medication in all these countries was never over 60%.

The ultimate objective of asthma treatment is to keep the patient's disease under control. We observed that in the 3 studied age groups, there were low levels of asthma control in all countries (below 20%), which contradicts the second hypothesis of this study, which stated that patients aged 12-17 years are cared for and supervised by their parents/caregivers, therefore their level of asthma control should be high in this sample. A low controlled asthma frequency was also found in other study where AIM Study was conducted: Germany (10%), Spain (12%), Canada (16%), Italia (17%), UK (24%).<sup>16</sup> The negative impact of asthma in patients aged 12-17 years, 18-40 years, and >40 years was separately evaluated in Brazil, and it was found that there was a higher negative impact of asthma on the youngest patients (12-17 years old) than on adults, what was attributed to a low level of adherence to control treatment in the youngest age group.<sup>30</sup>

Ponte et al. (2014)<sup>31</sup> conducted a study in Salvador (Brazil) and evaluated the association between age and level of asthma control. The subjects were divided into 2 groups (<55 years and  $\geq$ 55 years), and the results demonstrated that age was not a predictor of a low level of asthma control when treatment was appropriate. The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR study), conducted in the United States in a multicenter, observational, and prospective protocol, aimed to achieve a better understanding of the natural history of patients with severe asthma who had a low level of control, showed that older patients were treated more aggressively than younger patients and therefore had better asthma control and better quality of life.<sup>8</sup> A Chinese study, whose aim was to evaluate treatment adherence and causes of non-adherence, showed that subjects in the 30-39 year age group had the worst treatment adherence (27.3%).<sup>32</sup> In contrast, a study conducted in the United States has concluded that elderly asthmatic patients have worse short and long-term asthma control compared with the young adult population.<sup>33</sup>

Compared to Mexico, the country in which patients had the best asthma control, Venezuelan patients had a 71% chance of having uncontrolled asthma ( $p < 0.001$ ). Asthma in Venezuela is an example of the difficulties for asthma control in many Latin American countries. Health statistics confirm that asthma is the second cause, after viral syndromes, for consultation in the outpatient clinics of the Ministry of Health and Social Development of Venezuela.<sup>34</sup> This country faces a socioeconomic crisis that has lasted for several years, making it difficult for the population to obtain good health care;<sup>35</sup> this may be one of the factors associated with the present study's finding that patients in Venezuela have a low level of asthma control. In a survey in a low social income community of Caracas that evaluated asthmatic patients in this context, which has been served over the years by a National Asthma Control Program, the authors concluded that the high impact of asthma found in this slum underscores the realities of Venezuela's impoverished urban majority.<sup>36</sup> A pilot study carried out to test the efficacy of a single daily dose of budesonide in aerosol 400  $\mu$ g for control of persistent pediatric asthma in a hospital attending low-income patients from the metropolitan area of Caracas, concluded that this controller medication administered once a day seems effective. Patients are more familiar with its use, and it has some advantages in terms of cost, so it can be an alternative to treat these asthmatic children.<sup>37</sup> Studies have shown an increase in hospital admissions due to asthma and in the severity of asthma in low social classes.<sup>38</sup> Therefore, communities characterized by low social status or poverty can be affected by the severity of asthma as well as the number of people affected.

In the present study, patients with high frequency of admission at the ICU were those >40 years of age ( $p = 0.015$ ); the countries with the highest frequency of ICU admissions were Argentina (age groups 12-17 years and >40 years, 19.4% and 23.8%, respectively), and Venezuela (age group > 17-40 years, 20.9%). It is interesting that a study carried out in France in 2001 found that only 7% of asthma patients who visited emergency departments needed ICU admission.<sup>39</sup> A 2004 study conducted in the United States with

215 hospitals and 29,430 patients who were admitted for asthma, found an ICU admission rate of 10.1%.<sup>40</sup> These 2 studies, in which data were obtained a few years before the AIM study, indicate that the high percentage of ICU admissions in Argentina and Venezuela may be attributed to the infrequent use of asthma controller medication and, consequently, to the poor asthma control observed in the current study.

Some studies have shown that patients with uncontrolled asthma presented a higher risk for hospitalizations and emergency department visits, even though there were efficient medications available for asthma control.<sup>41,42</sup> In the present study, patients who had emergency visits to a physician's office, hospital, or clinic had a 59% chance of having uncontrolled asthma. In a study conducted to verify if uncontrolled asthma is associated with the use of health resources in 5 Latin American countries (Argentina, Brazil, Mexico, Puerto Rico and Venezuela), it was concluded that 93% of the studied population had partially and uncontrolled asthma, and that these patients used more medication and health services when compared to those with controlled asthma.<sup>43</sup> In another study, conducted in Saudi Arabia, they found that asthma was not controlled or partially controlled in 97.7% of the patients preceding emergency department visits.<sup>44</sup>

Uncontrolled asthma not only increases visits to emergency departments and hospitalizations, but it also affects daily living activities. In the present study, more than 50% of patients had limitations in daily activities in all age groups and in 5 countries. Similarly, the AIRLA study, which assessed the quality of asthma treatment and control in Latin America and assessed asthma-related perception, knowledge, and attitudes, found that 79% of adults and 68% of children reported that asthma symptoms limit activities of daily living.<sup>7</sup>

As asthma control was very low in young asthmatics, it would be important to develop specific programs for the parents and/or caregivers assisting this young population. For example, periodical meetings with multiprofessional staff for specific age groups, with topics for discussions about the disease, its pathophysiology, consequences of low

adherence to treatment, and the importance of a good control of the disease. Also, cell phone lines are widespread and readily available and could be used to improve on follow-up care.

Our study had some limitations. Although 5 Latin American countries were included, they may not represent the asthmatic population of the region. However, it is very difficult for studies with this type of design to cover the entire population of a continent. In addition, it was not reported in which areas of the cities these participants lived; whether or not they were living in economically disadvantaged regions could have influenced their levels of asthma control. Another limitation was that the questionnaires of participants aged 12-17 were completed by their parents, which may have resulted in some information bias. Besides that, pulmonary function tests were not performed in this study to identify the associated deficits that would also merit close follow-up. Medical diagnosis of asthma based on symptoms has usually been used in large studies as a valued epidemiological diagnosis of asthma.<sup>5</sup> Self-reported questionnaires as a tool for asthma diagnosis may lead the patients to misinterpret dyspnea by the fact of having low exercise capacity, cough due to gastroesophageal reflux, or sputum from upper airways as like in rhinitis. We did not confirm the asthma diagnosis by medical records, but patients assured they had a medical diagnosis besides being treated with asthma medications.

Other respiratory conditions such as chronic obstructive pulmonary disease (COPD) have not been excluded. COPD would be an important differential diagnosis, as, by definition, it has similar symptoms and airflow limitation. However, the low asthma control observed in the 3 studied age groups were similar. The fact that the asthma control in the group >40 years was very similar to the other 2 age groups, 12-17 years and >17-40 years, when the diagnosis of COPD is very uncommon, make us to believe that a possible diagnosis of COPD has not influenced the results. A spirometry test with high responsiveness could partially help to diagnose asthma, however, it has been shown that COPD patients may also present bronchial hyperresponsiveness.<sup>45</sup> Patients with associated pulmonary function deficits would

benefit if they were closely followed, however, this was not an objective of the study.

## CONCLUSIONS

We conclude that in the 3 age groups studied, there was low asthma control, with no difference among the countries evaluated. Venezuela was the country in which patients were most likely to have uncontrolled asthma, which may have some association with the socioeconomic problems the country has been facing. Also, we clearly observed that patients who used asthma controller medication had the greatest chance of having controlled asthma, and those who had emergency visits to doctors' offices, hospitals, or clinics were most likely to have uncontrolled asthma.

### Declaration of Competing Interest

The authors report no competing interests.

### Financial support

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### Agreement to publish the work

All authors agree with study publication.

### Ethics committee approval

Research Ethics Committee of the Federal University of São Paulo Hospital, São Paulo (No. 250.155).

### Appendix A. Supplementary data

Supplementary data to this article can be found online at doi: <https://doi.org/10.1016/j.waojou.2020.100113>.

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