



Prevalence of symptoms of asthma, rhinitis, and atopic eczema among Brazilian children and adolescents identified by the International Study of Asthma and Allergies in Childhood (ISAAC) – Phase 3

Dirceu Solé,¹ Gustavo F. Wandalsen,² Inês Cristina Camelo-Nunes,³
Charles K. Naspitz¹; ISAAC - Grupo Brasileiro⁴

Abstract

Objective: To determine the prevalence of symptoms of asthma, rhinitis, and atopic eczema among schoolchildren aged 6 to 7 years and adolescents aged 13 to 14 years in 20 Brazilian cities by using the standardized ISAAC written questionnaire, and to assess the association of this prevalence with latitude, altitude and average annual temperature of collaborating centers.

Methods: Schoolchildren and adolescents from five Brazilian regions participated in the study, totaling 23,422 ISAAC questionnaires answered by schoolchildren's parents and 58,144 questionnaires answered by adolescents. The values for latitude, altitude and average annual temperature were obtained from the Brazilian Institute of Geography and Statistics.

Results: The mean prevalence rates among schoolchildren and adolescents were respectively 24.3 and 19.0% for active asthma; 12.6 and 14.6% for rhinoconjunctivitis; and 8.2 and 5.0% for atopic eczema. A significant negative association was observed between latitude and physician-diagnosed asthma among schoolchildren, severe asthma, physician-diagnosed asthma, eczema and atopic eczema among adolescents. No association with altitude was found.

Conclusions: The prevalence of asthma, rhinitis and atopic eczema in Brazil varies considerably. Higher prevalence rates, especially of asthma and eczema, were found at centers located closer to the equator.

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1. Professor titular, Universidade Federal de São Paulo – Escola Paulista de Medicina (UNIFESP-EPM), São Paulo, SP, Brasil.
2. Mestre, UNIFESP-EPM, São Paulo, SP, Brasil.
3. Doutora, Pesquisadora Associada, UNIFESP-EPM, São Paulo, SP, Brasil.
4. ISAAC - Brazilian Group: Maria Socorro Cardoso (Manaus, Amazonas); Bruno A. Paes Barreto (Belém, Pará); Vera Dantas (Natal, Rio Grande do Norte); Murilo Britto (Recife, Pernambuco); Almerinda R. Silva, Emanuel Sarinho (Caruaru, Pernambuco); Francisco J. Passos Soares, Mércia Lamenha Medeiros Santos (Maceió, Alagoas); Jackeline Motta, Ricardo Gurgel (Aracaju, Sergipe); Leda Solano de Freitas (Feira de Santana, Salvador e Vitória da Conquista, Bahia); Wellington Borges (Brasília, Distrito Federal); Paulo Augusto Camargos (Belo Horizonte, Minas Gerais); Fábio Kuschnir, Antônio José Ledo Alves da Cunha (Nova Iguaçu, Rio de Janeiro); Antônio Carlos Pastorino (São Paulo – Oeste, São Paulo); Karyn Chacon de Mello (São Paulo – Sul, São Paulo); Cassia Gonzalez, Neusa F. Wandalsen (Santo André, São Paulo); Carlos Riedi, Nelson A. Rosário Filho (Curitiba, Paraná); Cláudia Benhardt (Itajaí, Santa Catarina); Arnaldo Porto (Passo Fundo, Rio Grande do Sul); Gilberto B. Fischer (Porto Alegre, Rio Grande do Sul); Vítor E. Cassol (Santa Maria, Rio Grande do Sul).

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Introduction

The International Study of Asthma and Allergies in Childhood (ISAAC) was an important accomplishment for epidemiological studies on the prevalence of asthma and allergic diseases among children and adolescents. ISAAC was designed to evaluate the prevalence of asthma and allergic diseases among children and adolescents in different regions of the world, using a standardized self-administered written questionnaire and/or a video questionnaire.^{1,2} ISAAC self-administered written questionnaire (WQ) has been the most widely used method, since it can be easily applied, has a low cost, and does not require the presence of a trained interviewer.^{1,2}

The target population should include schoolchildren within a specific geographic area (ISAAC center) aged 13 to 14 years and 6 to 7 years. The participation of schoolchildren aged 6 to 7 years, albeit recommendable, was not mandatory.

The study sample should include all children within the selected age range from a random sample of schools.

After determining the geographic area and the schools that should be included, each center should choose adolescents aged 13 to 14 years from the school database, and apply the WQ. The selection of 6 to 7-year-olds should follow the same criteria, and the parents of these children would have to answer the WQ.

In ISAAC phase 1, a total of 463,801 adolescents (13 to 14 years old) from 155 centers in 56 countries (Europe, Asia, Africa, North America, South America, and Oceania) were interviewed, as well as 257,800 schoolchildren (6 to 7 years old) from 91 centers in 38 countries, from the same continents, except África.²⁻⁵

The analysis of results at the end of phase 1 revealed variable rates among schoolchildren and adolescents in terms of the prevalence of wheezing in the last 12 months (active asthma), between 4.1 and 32.1% for schoolchildren and between 2.1 and 32.2% for adolescents.^{2,3} The lowest rates were observed in the Republic of Georgia and Estonia, whereas the highest rates were described in Australia.^{2,3} In both age groups, Brazil ranked among the countries with the highest prevalence rates.^{3,6}

As to rhinitis, there was also a large variation in the prevalence of related symptoms.⁴ The prevalence of nasal symptoms in the absence of colds in the last year ranged from 1.5 to 41.8% among schoolchildren and from 3.2 to 66.6% among adolescents.⁴ On the other hand, nasal symptoms associated with eye symptoms (allergic rhinoconjunctivitis) ranged from 0.8 to 14.9% among schoolchildren and from 1.4 to 39.7% among adolescents.⁴ In general, the prevalence rates for asthma and rhinitis were concordant: centers with a low asthma prevalence (less than 5%: Indonesia, Albania, Romania, Georgia and Greece) showed a low rhinitis prevalence, and those with a high asthma prevalence (greater than 30%: Australia, New Zealand, and the United Kingdom) also showed a high rhinitis prevalence.^{3,4}

The results for atopic eczema (AE) varied more widely (up to 60 times), ranging between 0.3 and 20.5%.^{2,5} The highest rates (greater than 15%) were observed in urban centers in Africa, Australia, Northern and Western Europe, whereas the lowest ones (less than 5%) were found in China, Eastern Europe and Central Asia.^{2,5}

Based on these data, several other studies were carried out to assess the relationship between the prevalence of asthma and of allergic diseases and possible risk factors. Routine immunization,⁷ tuberculosis notifications^{8,9} and nutritional status¹⁰ were some of the analyzed factors. In a recent study, Weiland et al. assessed the possible relationship between latitude, relative humidity and annual variation of temperature of ISAAC centers included in phase 1 and the prevalence of asthma and of allergic diseases.¹¹ They found a negative relationship between these parameters and the prevalence of asthma symptoms. On the other hand, the prevalence of eczema

symptoms was positively related to latitude and negatively related to average temperature, i.e., places with smaller temperature variations were associated with higher prevalence rates.¹¹ In conclusion, these authors assert that climate plays an important role and can interfere in the prevalence of asthma and AE.¹¹

In Latin America, at the end of ISAAC phase 1, Mallol et al. described a significant relationship between asthma prevalence and severity and the latitude of participating centers,¹² some of which were Brazilian.

The small number of Brazilian centers in phase 1, combined with the absence of centers in some Brazilian regions, did not allow for such a study.^{6,13,14} The present study aimed to assess the relationship between the prevalence of symptoms of asthma, rhinitis, and eczema and the latitude of different official ISAAC phase 3 Brazilian centers and others that have only applied the ISAAC protocol.

Patients and methods

Twenty-one centers in 20 Brazilian cities participated in this study. The students were selected as recommended by the ISAAC protocol.^{1,15} Each center, after determination of the geographic area where the study should be carried out, requested the Municipal Department of Education a list of schools located in that area. After that, the schools were randomly selected (random number table). The following cities, states, and regions were included in the study: Manaus, Amazonas, North (N); Belém, Pará, N; Natal, Rio Grande do Norte, Northeast (NE); Recife, Pernambuco, NE; Caruaru, Pernambuco, NE; Maceió, Alagoas, NE; Aracaju, Sergipe, NE; Feira de Santana, Bahia, NE; Salvador, Bahia, NE; Vitória da Conquista, Bahia, NE; Brasília, Distrito Federal, Midwest (MW); Belo Horizonte, Minas Gerais, Southeast (SE); Nova Iguaçu, Rio de Janeiro, SE; São Paulo (West and South), São Paulo, SE; Santo André, São Paulo, SE; Curitiba, Paraná, South (S); Itajaí, Santa Catarina, S; Passo Fundo, Rio Grande do Sul, S; Porto Alegre, Rio Grande do Sul, S; Santa Maria, Rio Grande do Sul, S. Some of these centers had their data approved by the ISAAC International Data Center and were considered as ISAAC phase 3 official centers (Tables 1 and 2). The study was approved by the respective local Research Ethics Committees, and all participants signed an informed consent form prior to the interviews.

The following cities did not assess 6 to 7-year-olds (not mandatory): Belém, Recife, Caruaru, Brasília, Belo Horizonte, Curitiba, Passo Fundo, Porto Alegre and Santa Maria.

The study began in 2002 and finished in 2003, as recommended by ISAAC, using the same dates for data collection, whenever possible, in all centers. In the southern

region, where the seasons of the year are more clearly defined, the study was carried out before springtime in order to avoid possible seasonal influences.

After definition of the sample, the ISAAC WQ, which had been previously translated into Brazilian Portuguese and validated,^{14,16,17} was answered by the parents of schoolchildren aged 6 to 7 years (n = 23,422) and by adolescents (n = 58,144, aged 13 to 14 years). The data were manually transferred to the database provided by ISAAC coordinators.

In the asthma module, there were questions about symptoms, severity and diagnosis of asthma, such as: wheezing in the last 12 months (active asthma); wheezing severe enough to limit speech in the last 12 months (severe asthma); asthma ever (physician-diagnosed asthma).^{1,3}

In the rhinitis module, there were questions about rhinitis symptoms, allergic rhinoconjunctivitis and severe forms of rhinitis: sneezing, runny nose, and blocked nose at any time in the last 12 months (rhinitis); nose problems accompanied by itchy-watery eyes in the last 12 months (allergic rhinoconjunctivitis); nose problem interfering with daily activities (severe rhinitis).^{1,4}

The questions about eczema referred to its symptoms and severity: skin rash which was coming and going in the

last 12 months (eczema); skin rash at characteristic sites (atopic eczema); itchy rash causing sleep disturbance in the past 12 months (severe eczema).^{1,5}

The data about latitude, altitude and average annual temperature for each of the participating centers were obtained from the Brazilian Institute of Geography and Statistics.¹⁸

The following non-parametric tests were used for data analysis: Spearman's rank correlation coefficient (RS) and the 95% confidence interval (95%CI). The significant level was set at 5% for all tests.

Results

Among schoolchildren, the mean prevalence rates were: 24.3% for active asthma, with higher rates in São Paulo – West and in Vitória da Conquista; 6.1% for severe asthma, with higher rates in São Paulo – West and in Natal; 10.3% for physician-diagnosed asthma (Manaus and Natal); 25.7% for rhinitis (Bahia, Feira de Santana, Salvador and Vitória da Conquista); 12.6% for rhinoconjunctivitis (Bahia); 17.1% for severe rhinitis (Bahia); 11.5% for eczema, (Nova Iguaçu, Natal and Aracaju); 8.2% for atopic eczema (Natal, Aracaju and Nova Iguaçu); and 5.0% for severe eczema (Natal and Aracaju) (Table 1).

Table 1 – Prevalence of symptoms of asthma, rhinitis and atopic eczema among children (aged 6 to 7 years) in different Brazilian centers – International Study of Asthma and Allergies in Childhood (ISAAC) - Phase 3

Center	South latitude	Altitude m	Avg temp	n	Active asthma*	Severe asthma [†]	PD asthma [‡]	Rhinitis [§]	Rhinoconj [¶]	Severe rhinitis ^{¶¶}	Ecz ^{**}	Atopic ecz ^{††}	Severe ecz ^{‡‡}
Manaus ^{§§}	3.06	92	32	3,011	24.4	6.6	20.8	19.5	10.6	13.2	12.0	8.0	4.7
North – total				3,011	24.4	6.6	20.8	19.5	10.6	13.2	12.0	8.0	4.7
Natal	5.47	30	28	855	29.0	7.8	16.1	23.3	13.3	20.8	13.1	13.0	8.5
Maceió ^{§§}	9.39	16	25	1,990	24.3	7.4	9.6	24.7	11.3	14.3	10.6	7.6	4.7
Aracaju ^{§§}	10.54	4	25	2,443	16.5	4.5	11.3	19.9	10.3	16.3	13.0	11.4	9.1
Feira de Santana	12.16	235	24.1	440	20.7	5.2	6.4	35.9	15.5	24.3	7.3	8.2	7.3
Salvador ^{§§}	12.58	8	24	998	17.2	3.0	7.7	39.8	17.4	26.0	8.6	7.3	5.7
Vitória da Conquista	14.51	923	20	399	24.3	8.5	11.5	31.3	17.3	21.8	10.5	8.3	7.8
Northeast – total				7,125	21.0	5.8	10.6	26.1	12.7	18.5	11.2	8.2	6.4
Nova Iguaçu ^{§§}	22.45	25	21.8	3,249	26.3	7.0	10.4	24.8	12.2	16.6	13.3	9.8	6.0
São Paulo – West ^{§§}	23.30	760	20	3,312	31.2	8.4	7.1	28.9	15.1	19.7	12.4	9.5	5.2
São Paulo – South ^{§§}	23.32	760	20	3,047	24.4	4.8	6.3	28.2	12.7	17.6	11.0	7.3	3.2
Santo André ^{§§}	23.39	755	23	2,167	23.9	2.9	4.9	30.9	13.2	16.5	8.1	5.3	2.1
Southeast – total				11,775	26.7	6.0	7.3	27.9	13.3	17.7	11.6	8.3	4.4
Itajaí ^{§§}	26.54	1	21	1,511	20.6	6.8	10.3	19.3	13.3	14.5	10.7	8.7	3.4
South – total				1,511	20.6	6.8	10.3	19.3	13.3	14.5	10.7	8.7	3.4
Overall total				23,422	24.3	6.1	10.3	25.7	12.6	17.1	11.5	8.2	5.0

Avg temp = average temperature; n = number of participants PD asthma = physician-diagnosed asthma; rhinoconj = rhinoconjunctivitis; ecz = eczema

* Wheezing in the last 12 months.

† Physician-diagnosed asthma: wheezing severe enough to limit speech to only two words at a time in the last 12 months.

‡ Asthma ever.

§ Sneezing, runny, or blocked nose at any time in the last 12 months.

¶ Rhinoconjunctivitis: nose problem accompanied by itchy-watery eyes in the last 12 months.

¶¶ Rhinitis interfering with daily activities.

** Eczema: itchy rash which was coming and going in the last 12 months.

†† Atopic eczema: skin rash at characteristic sites (skin folds, etc.).

‡‡ Severe eczema: itchy rash causing sleep disturbance in the last 12 months.

§§ ISAAC phase 3 official center.

Among adolescents, the mean prevalence rates were as follows: 19.0% for active asthma, with higher rates in Salvador and Vitória da Conquista; 4.7% for severe asthma, with higher rates in Vitória da Conquista and Aracaju; 13.6% for physician-diagnosed asthma (Belém, Porto Alegre and Caruaru); 29.6% for rhinitis (Belém, Salvador and Vitória da Conquista); 14.6% for allergic rhinoconjunctivitis (Belém, Salvador and Vitória da Conquista); 17.4% for severe rhinitis (Bahia); 8.9% for eczema (Belém, Aracaju and Salvador); 5.0% for atopic eczema (Aracaju, Vitória da Conquista and Natal); and 4.4% for severe eczema (Bahia and Aracaju) (Table 2).

The association between latitude and the prevalence of symptoms and severity of asthma, rhinitis and AE showed a negative statistical significance for physician-diagnosed asthma (RS = -0.622; 95%CI -0.885 to -0.056; p = 0.031)

among schoolchildren, severe asthma (RS = -0.565; 95%CI -0.806 to -0.163; p = 0.008), physician-diagnosed asthma (RS = -0.479; 95%CI -0.761 to -0.046; p = 0.028), eczema (RS = -0.718; 95%CI -0.881 to -0.405; p = 0.0002) and atopic eczema (RS = -0.530; 95%CI -0.788 to -0.115; p = 0.013) among adolescents. In other words, the smaller the latitude (close proximity to the equator), the higher the prevalence of affirmative answers to the questions.

With regard to the average annual temperature, there was a positive association with physician-diagnosed asthma (RS = 0.459; 95%CI 0.02 to 0.749; p = 0.037), and also with eczema (RS = 0.541; 95%CI 0.129 to 0.794; p = 0.011) among adolescents. Thus, the higher the average annual temperature, the higher the prevalence of physician-diagnosed asthma and eczema.

Table 2 - Prevalence of symptoms of asthma, rhinitis and atopic eczema among adolescents (aged 13 to 14 years) in different Brazilian centers – International Study of Asthma and Allergies in Childhood (ISAAC) - Phase 3

Center	South latitude	Altitude m	Avg temp	n	Active asthma*	Severe asthma [†]	PD asthma [‡]	Rhinitis [§]	Rhinoconj	Severe rhinitis [¶]	Ecz ^{**}	Atopic ecz ^{††}	Severe ecz ^{‡‡}
Belém ^{§§}	1.27	10	26	1,773	23.1	5.0	32.8	47.4	28.5	14.6	11.8	6.2	3.9
Manaus	3.06	92	32	3,009	18.1	5.8	19.7	23.0	12.8	14.6	10.7	5.8	5.0
North – total				4,782	19.9	5.5	24.6	32.0	18.6	14.6	11.1	6.0	4.6
Natal	5.47	30	28	1,020	18.9	5.2	16.2	32.0	20.0	23.8	9.6	7.2	5.8
Recife ^{§§}	8.03	4	30	2,865	19.1	4.1	18.0	35.8	14.5	19.0	10.1	5.0	4.1
Caruaru ^{§§}	8.17	555	26	3,026	17.9	5.0	19.7	25.5	15.4	17.5	10.3	6.5	6.1
Maceió ^{§§}	9.39	16	25	2,745	14.8	5.0	13.8	26.4	13.8	15.3	7.5	4.0	3.3
Aracaju ^{§§}	10.54	4	25	3,041	18.7	6.8	15.4	25.6	17.4	22.5	11.2	7.9	8.3
Feira de Santana ^{§§}	12.16	235	24.1	1,732	21.5	6.2	5.8	33.0	17.2	25.3	8.5	5.8	6.6
Salvador ^{§§}	12.58	8	24	3,020	24.6	5.9	13.7	44.2	24.4	28.2	10.7	6.5	6.1
Vitória da Conquista ^{§§}	14.51	923	20	1,679	30.5	9.1	13.2	39.8	24.4	31.1	10.4	7.7	8.8
Northeast – total				19,128	20.3	5.8	14.5	32.4	13.3	17.9	9.9	6.2	6.0
Brasília ^{§§}	15.46	1171	20.5	3,009	19.7	5.1	14.8	29.3	15.4	21.1	10.2	5.6	5.8
Mid-west – total				3,009	19.7	5.1	14.8	29.3	15.4	21.1	10.2	5.6	5.8
Belo Horizonte ^{§§}	19.55	858	21	3,088	17.8	4.8	9.8	26.1	14.5	18.1	9.1	5.2	5.1
Nova Iguaçu ^{§§}	22.45	25	21.8	3,185	11.8	3.3	7.3	17.4	8.9	10.1	9.0	4.1	3.3
São Paulo - Oeste ^{§§}	23.30	760	20	3,181	21.9	5.6	8.9	30.1	19.8	20.2	9.7	6.9	5.4
São Paulo – Sul ^{§§}	23.32	760	20	3,161	18.7	2.9	10.4	27.4	12.2	14.5	7.1	3.6	2.2
Santo André ^{§§}	23.39	755	23	3,232	23.2	3.0	8.9	28.4	13.8	15.4	7.1	3.4	2.0
Southeast – total				15,847	18.7	3.9	9.1	25.9	13.8	15.7	8.4	4.6	3.6
Curitiba ^{§§}	25.25	934	17	3,628	18.9	3.1	9.2	39.2	17.2	20.4	6.3	3.7	1.5
Itajaí ^{§§}	26.54	1	21	2,737	12.3	2.6	11.1	22.1	12.9	14.7	7.0	4.0	3.9
Passo Fundo ^{§§}	28.15	687	17.5	2,949	20.5	4.8	14.6	29.5	16.6	21.0	8.6	5.5	4.6
Porto Alegre ^{§§}	28.15	10	20	3,007	18.2	4.8	21.2	32.1	15.9	20.0	7.0	5.0	5.0
Santa Maria	29.41	151	19.2	3,057	15.3	3.8	11.1	20.6	9.6	15.9	7.7	4.8	5.7
South – total				15,378	19.3	3.8	13.3	29.2	15.6	18.5	7.3	4.5	4.0
Overall total				58,144	19.0	4.7	13.6	29.6	14.6	17.4	8.9	5.0	4.4

Avg temp = average temperature; n = number of participants PD asthma = physician-diagnosed asthma; rhinoconj = rhinoconjunctivitis; ecz = eczema

* Wheezing in the last 12 months.

† Physician-diagnosed asthma: wheezing severe enough to limit speech to only two words at a time in the last 12 months.

‡ Asthma ever.

§ Sneezing, runny, or blocked nose at any time in the last 12 months.

|| Rhinoconjunctivitis: nose problem accompanied by itchy-watery eyes in the last 12 months.

¶ Rhinitis interfering with daily activities.

** Eczema: itchy rash which was coming and going in the last 12 months.

†† Atopic eczema: skin rash at characteristic sites (skinfolds, etc.).

‡‡ Severe eczema: itchy rash causing sleep disturbance in the last 12 months.

§§ ISAAC phase 3 official center.

Discussion

Higher prevalence rates for asthma and for allergic diseases were observed in centers in the Northern and Northeastern regions, except for the asthma prevalence, which was also high in the Southern region. The threefold increase in the number of assessed centers in comparison to ISAAC phase 1,^{6,13,14} the inclusion of centers from all Brazilian regions, and the high response rate^{2,3} allow us to consider the sample to be representative of Brazil.

ISAAC phase 1 in Latin America collected data from 17 centers in nine countries and included 36,264 schoolchildren and 52,549 adolescents. The prevalence of asthma and associated symptoms was high and variable, as that which has been described in industrialized countries or developed regions.¹² The prevalence of active asthma ranged from 8.6 to 32.1% among schoolchildren and from 6.6 to 27.0% among adolescents, and the highest prevalence rates were observed in regions closest to the equator. Moreover, no relationship was found between exposure to environmental pollution, early exposure to respiratory and gastrointestinal infections and asthma prevalence.¹² These data cast some doubt on the validity of the Hygiene Hypothesis for Latin America as a whole.¹²

Weiland et al. investigated the relationship between climate (latitude, annual variation of temperature (difference between maximum and minimum annual temperatures) and indoor relative humidity) and the prevalence of atopic diseases by using the data from ISAAC phase 1 (146 centers). Asthma symptoms were inversely related to altitude, variation of annual temperatures and indoor relative humidity.¹¹ The analysis of some of these data showed that the prevalence of asthma symptoms increased in western European countries in association with the increase in the estimated annual mean of indoor relative humidity.¹¹ In the present study, we observed a significant negative relationship to physician-diagnosed asthma among schoolchildren and to physician-diagnosed asthma and severe asthma among adolescents. This may be explained by different approaches to and different nomenclature of the disease across Brazil. However, when we considered the prevalence of severe forms, we found the same behavior among adolescents. This certainly explains the higher asthma prevalence in the Northern region. This is corroborated by the significant positive association between the average annual temperature and the prevalence of physician-diagnosed asthma.

With regard to rhinitis and its associated symptoms, we did not find a statistically significant association between rhinitis prevalence and the analyzed parameters for both age groups, as also observed in other studies.¹¹ Nevertheless, there was a significant negative relationship between the prevalence of eczema and of atopic eczema and latitude. Higher rates were observed in Northern

Brazil, and the prevalence of eczema was higher in regions with higher average temperatures. Exposure to higher and constant temperatures, high level of environmental humidity, greater exposure of the skin due to insufficient clothing, combined with the higher frequency of skin disorders in this region are some of the reasons for the increase in the prevalence of eczema, a disorder that may be characterized by different skin symptoms. However, the exposure of patients with atopic eczema to the same factors above does not increase the prevalence of this disease. In this case, heat and humidity are considered risk factors for AE. Differently from the findings of the present study, Weiland et al. observed an increase in the prevalence of eczema and related symptoms in both age groups, with an increase in latitude and a decrease in the variation of the average annual temperature, as well as with an increase in indoor relative humidity.¹¹

Nnoruka et al. assessed Nigerian children with AE and found heat intolerance, excessive sweating, and indoor humidity as aggravating factors for AE,¹⁹ similarly to what has been described by other authors.²⁰ Fernández-Mayoralas et al. found out that air pollution had some influence over the prevalence of AE among adolescents who lived in Cartagena (Spain).²¹ The authors observed high prevalence rates for AE and for severe forms of the disease among those who were exposed to higher levels of pollution.²¹ In the present study, we did not find any influence of air pollution over the prevalence of AE, especially when we consider São Paulo and Santo André, where the highest levels of air pollution in Brazil are usually detected.

In conclusion, after the increase in the number of centers participating in this study regarding ISAAC phase 1, and similarly to the results obtained for Latin America at the end of phase 1, we found a higher frequency of physician-diagnosed asthma among schoolchildren and adolescents, and more severe forms of asthma, eczema and atopic eczema among adolescents living close to the equator. The identification of risk factors to which individuals living in these centers may be exposed is a crucial step to unravel the etiopathology of asthma and of allergic diseases in these regions.

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Correspondence:

Dirceu Solé

Rua Mirassol 236 / 72, Vila Clementino
CEP 04044-010 – São Paulo, SP – Brazil
E-mail: dirceus@ajato.com.br