

Prevalence of Atopic Eczema and Related Symptoms in Brazilian Schoolchildren: Results From the International Study of Asthma and Allergies in Childhood (ISAAC) Phase 3

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Abstract. *Background:* International comparisons of the prevalence of atopic eczema and related symptoms are scarce. The standardized protocol of the International Study of Asthma and Allergies in Childhood (ISAAC) facilitates investigation of prevalence all over the world.

Objective: To apply the ISAAC written questionnaire to evaluate the prevalence of atopic eczema and related symptoms among 6-7 year-old children and 13-14 year-old adolescents living in 20 Brazilian cities.

Methods: The ISAAC written questionnaire was filled in by 23 422 children aged 6-7 years and 58 144 adolescents aged 13-14 years living in 2 population centers in the north, 8 in the northeast, 1 in the midwest, 5 in the southeast, and 5 in the south.

Results: The prevalence of flexural eczema (itchy rash ever in characteristic places in the last 12 months) ranged from 5.3% to 13.0% for children and was lower among the adolescents (range, 3.4%–7.9%). Among children, the highest rates were observed in population centers in the northeast, mainly along the coast. Among adolescents the highest rates were observed in the north and northeast, mainly in Natal, Aracaju, and Vitória da Conquista. The northeastern countryside had higher prevalence rates of severe eczema (kept awake at night by this itchy rash in the last 12 months) in comparison to northeastern coastal centers. There was a significant correlation between the prevalence of flexural eczema and severe eczema for both age groups, separately (6-7 year-olds, $\rho=0.756$, $P<.004$; 13-14 year-olds, $\rho=0.874$, $P<.0001$) or grouped (6-7 plus 13-14 years-olds, $\rho=0.696$, $P<.0001$).

Conclusion: The prevalence of eczema and related symptoms is variable in Brazil, where the highest prevalence is found in the north and northeast; on the other hand, a higher prevalence of severe eczema was observed in Brazilian centers in the south.

Key words: Children. Atopic dermatitis. Atopic eczema. Prevalence. ISAAC. Epidemiology.

Resumen. *Antecedentes:* Las comparaciones internacionales sobre la prevalencia del eccema atópico y los síntomas relacionados son escasas. El protocolo estandarizado del Estudio Internacional del Asma y Alergias en la Infancia (ISAAC) facilita la investigación de su prevalencia en todo el mundo.

Objetivo: Aplicar el cuestionario escrito ISAAC para valorar la prevalencia del eccema atópico y los síntomas relacionados entre los niños de 6 y 7 años de edad y los adolescentes de 13 y 14 años que viven en 20 ciudades brasileñas.

Métodos: 23.422 niños de 6 y 7 años de edad y 58.144 adolescentes de 13 y 14, que vivían en dos poblaciones al Norte, ocho del Noreste, una del Medio Oeste, cinco del Sureste y cinco del Sur, respondieron al cuestionario escrito ISAAC.

Resultados: La incidencia de eccema en superficie flexora (erupción cutánea con picor en puntos característicos en los últimos 12 meses) fue de un 5,3% a un 13% entre los niños, con un porcentaje inferior entre los adolescentes

(rango, 3,4% =7,9%). Entre los niños, las tasas más elevadas se observaron en las poblaciones del Noreste, especialmente en las costeras. Entre los adolescentes, las tasas más elevadas se observaron en los del Norte y Noreste, especialmente en Natal, Aracaju y Vitória da Conquista. En las zonas rurales del interior del Noreste se detectó tasas más elevadas de eccema grave (imposibilidad de dormir por las noches debido al escozor del eccema en los últimos 12 meses) comparado con las poblaciones costeras del Noreste. Se observó una correlación importante entre la incidencia de eccema en superficie flexora y eccema grave para los dos grupos, separadamente (6-7 años de edad, $\rho = 0,756$, $P < 0,004$; 13-14 años de edad, $\rho = 0,874$, $P < 0,0001$) o agrupados (6-7 años de edad junto con los de 13-14 años de edad, $\rho = 0,696$, $P < 0,0001$).

Conclusión: La prevalencia de eccema y síntomas relacionados es variable en Brasil, donde es mayor en el Norte y Noreste. Por otro lado, se observó una prevalencia mayor de eccema grave en poblaciones del Sur del país.

Palabras clave: Niños. Dermatitis atópica. Eccema atópico. Prevalencia. ISAAC. Epidemiología.

Introduction:

Recent epidemiological studies evaluating the frequency of atopic eczema in several countries have shown differences in prevalence [1-11]. The prevalence of atopic eczema, as well as of asthma and other allergic diseases, has been increasing [2-6, 12-14]. However, differences in definitions, patient identification criteria, and methods applied in each study make the comparisons of the results unreliable.

The development of the International Study of Asthma and Allergies in Childhood (ISAAC) has allowed a better understanding and comparability of methods about epidemiology of atopic eczema [1].

Phase I of the ISAAC study sought to describe the magnitude and geographic distribution of atopic eczema, asthma, and allergic rhinoconjunctivitis in as many countries of the world as possible by using single-page written core questionnaires to assess the prevalence and severity of these diseases [15]. This cross-sectional questionnaire survey was conducted on random samples of schoolchildren aged 6 to 7 years (optional) and 13 to 14 years (compulsory) from centers in 56 countries throughout the world. At the end of ISAAC phase 1, in 1995, data about prevalence of atopic eczema was available for 256 410 children aged 6 to 7 years in 90 centers and 458 623 children aged 13 to 14 years in 153 centers [1].

Results were quite variable, with the difference between the highest (20.5%) and the lowest values (0.3%) reaching 60 fold [1, 16]. High prevalence rates of atopic eczema (over 15%) were observed in urban centers from Africa, Australia, and Northern and Western Europe and low rates (under 5%) in China, Eastern Europe, and central Asia [1, 16]. In Latin America and Eastern Asia values were intermediary [1]. In all centers the prevalences of atopic eczema were higher among young children (6-7 years old), mainly among females [1, 16, 17].

In Brazil, Recife, Salvador, São Paulo, Curitiba, and Porto Alegre were the centers that participated in ISAAC phase 1. Considering the 6-7-year-old schoolchildren (SC) the prevalence of flexural eczema (itchy rash ever in characteristic places in the last 12 months) varied from 6.6% (Porto Alegre) to 9.8% (Recife), with a mean value

of 7.3% [1, 16, 17]. In this age group the prevalence of severe eczema (kept awake at night by this itchy rash in the last 12 months) ranged from 0.2% (Recife) to 0.6% (Porto Alegre), with a mean value of 0.5% [1, 16, 17]. A higher prevalence of severe atopic eczema was observed in places with lower prevalence of flexural eczema. Among the adolescents (13-14 years old) the prevalence of atopic eczema ranged from 3.7% (São Paulo) to 9.2% (Salvador), with a mean value of 5.3% [1, 16, 17]. The prevalence of severe eczema ranged from 0.2% (Salvador) to 0.9% (Porto Alegre), with a mean value of 0.5% [1, 16, 17].

In 2002, ISAAC Phase 3 began, with the main objective of examining time trends in the prevalence of asthma and allergic diseases in centers and countries that have participated in ISAAC Phase 1. Phase 3 was a repetition of phase 1, after at least 5 years. Centers involved in phase 1 were invited to participate in ISAAC phase 3; new centers were also invited to enter the study [15, 18].

The aim of this study was to evaluate the prevalence of self reported atopic eczema and related-symptoms among schoolchildren from 21 Brazilian centers located in different areas of the country. The research questions were: 1) Would the increased number of participating centers (a 3-fold increase), from all regions of Brazil, give us more details about the prevalence of atopic eczema and related symptoms in the country? and 2) Could these data tell us more about the real distribution of the disease in Brazil?

Subjects and Methods

Twenty-one centers from 20 Brazilian cities participated. Schoolchildren were selected as standardized by the ISAAC protocol [15, 18]. The cities, states, regions/areas, in which ISAAC phase 3 were carried out were as follows: Manaus (Amazonas, north); Belém (Pará, north); Natal (Rio Grande do Norte, northeast); Recife (Pernambuco, northeast); Caruaru (Pernambuco, northeast); Maceió (Alagoas, northeast); Aracaju (Sergipe, northeast); Feira de Santana (Bahia, northeast); Salvador (Bahia, northeast); Vitória da Conquista (Bahia, northeast); Brasília (Distrito Federal, midwest); Belo Horizonte (Minas Gerais, southeast); Nova Iguaçu (Rio de Janeiro, southeast); São Paulo (west and south, São Paulo, southeast); Santo André (São Paulo, SE); Curitiba (Paraná, South [S]); Itajaí (Santa Catarina, South [S]); Passo Fundo (Rio Grande do Sul, S), Porto Alegre (Rio



Location of Brazilian centers participating in the International Study of Asthma and Allergies in Childhood.

Grande do Sul, S) and Santa Maria (Rio Grande do Sul, S) (figure). Some of these centers had their data approved by the ISAAC International Data Center and were considered as ISAAC's official centers (Tables 1 and 3).

The ISAAC written questionnaire, previously translated and validated for use within the Brazilian culture [17, 19, 20], was applied to 23 422 children (6-7 year olds) and to 58 144 adolescents (13-14 year olds). Subjects were selected among those who had attended public and private schools located in the aforementioned cities. Information regarding the number of schools and students in each area was obtained from the records of the respective city education officials. After definition of the sample, the adolescents (13-14 year olds) and the parents or guardians of the 6-7 year old children filled in the questionnaire. The data obtained were transcribed for a database (Epi-Info) supplied by the ISAAC coordinators. In this study we only evaluated the responses to the eczema core of the questionnaire.

The frequency of affirmative answers to each question was analyzed by age group and compared with the χ^2 test [21].

Those children with a positive response to the question about the presence of an itchy rash in the last 12 months (question 2) were considered to have current eczema. The results were expressed as odds ratios (OR) with 95% confidence intervals (CI) for flexural eczema (had this itchy rash in the last 12 months in characteristic places) and severe eczema (kept awake at night by this itchy rash in the last 12 months) for each center relative to a reference center (Santo André). Brazilian regions with at least 2 centers

were grouped and compared. In the northeast we compared the prevalence of atopic eczema and related symptoms according to the place where the subjects lived: coastal (Natal, Recife, Maceió, Aracaju, Salvador) or countryside (Caruaru, Feira de Santana, Vitória da Conquista).

In the states of Pernambuco (PE) and Rio Grande do Sul (RS), where the population apparently shares the same genetic background, we compared the prevalence of atopic eczema and related symptoms according to the area where the adolescents lived: urban or rural (PE: rural Caruaru vs urban Recife; RS: rural Santa Maria and Passo Fundo vs urban Porto Alegre)

The relationship between the prevalence of flexural eczema and severe eczema, for each group separately and both together, and the relationship between the prevalence of eczema, flexural eczema and severe eczema and the latitude of the centers were calculated with the Spearman correlation coefficient (ρ). In all tests the level for rejection of the null hypothesis was 5%.

Results

In children aged 6-7 years, the prevalence of itchy rash in the last 12 months varied from 7.3% to 13.3%; flexural eczema varied from 5.3% to 13.0%; severe eczema from 2.1% to 9.1%; and ever had eczema (physician-diagnosed eczema) from 7.9% to 15.4% (Table 1). The highest rates of flexural and severe eczema were observed in Natal and Aracaju and the lowest in Santo André (Table 1).

Table 1. Prevalence of Eczema and Related Symptoms Among 6-7- and 13-14-year-old Brazilian Schoolchildren Determined by Using the International Study of Asthma and Allergies in Childhood (ISAAC) Written Questionnaire in the Different Brazilian Centers. ISAAC Phase 3*

Center	Latitude °South	6-7 Year Olds						13-14 Year Olds					
		No.	RASH (12)	SITES (EV)	RAWAKE (12)	ECZEMA (EV)	No.	RASH (12)	SITES (EV)	RAWAKE (12)	ECZEMA (EV)		
Belém	1.27	-	-	-	-	-	1773	11.8	6.2	3.9	12.6		
Manaus	3.06	3011	12.0	8.0	4.7	15.2	3009	10.7	5.8	5.0	14.2		
Total North		3011	12.0	8.0	4.7	15.2	4782	11.1	6.0	4.6	13.6		
Natal	5.47	855	13.1	13.0	8.5	13.6	1020	9.6	7.2	5.8	11.2		
Recife ‡	8.03	-	-	-	-	-	2865	10.1	5.0	4.1	12.2		
Caruaru ‡	8.17	-	-	-	-	-	3026	10.3	6.5	6.1	14.1		
Maceió †	9.39	1990	10.6	7.6	4.7	10.0	2745	7.5	4.0	3.3	6.4		
Aracaju †	10.54	2443	13.0	11.4	9.1	9.9	3041	11.2	7.9	8.3	13.1		
Feira de Santana ‡	12.16	440	7.3	8.2	7.3	9.3	1732	8.5	5.8	6.6	2.5		
Salvador †	12.58	998	8.6	7.3	5.7	14.4	3020	10.7	6.5	6.1	2.2		
Vitória da Conquista ‡	14.51	399	10.5	8.3	7.8	13.3	1679	10.4	7.7	8.8	2.5		
Total Northeast		7125	11.2	8.2	6.4	9.8	19128	9.9	6.2	6.0	8.5		
Brasília ‡	15.46	-	-	-	-	-	3009	10.2	5.6	5.8	13.6		
Total Midwest		-	-	-	-	-	3009	10.2	5.6	5.8	13.6		
Belo Horizonte ‡	19.55	-	-	-	-	-	3088	9.1	5.2	5.1	12.0		
Nova Iguaçu †	22.45	3249	13.3	9.8	6.0	15.4	3185	9.0	4.1	3.3	9.4		
São Paulo west †	23.30	3312	12.4	9.5	5.2	112.0	3181	9.7	6.9	5.4	8.6		
São Paulo, south †	223.32	3047	11.0	7.3	3.2	13.1	3161	7.1	3.6	2.2	12.7		
Santo André ‡	23.39	2167	8.1	5.3	2.1	7.9	3232	7.1	3.4	2.0	12.2		
Total Southeast		11775	11.6	8.3	4.4	12.5	15847	8.4	4.6	3.6	11.0		
Curitiba ‡	25.25	-	-	-	-	-	3628	6.3	3.7	1.5	4.1		
Itajaí †	26.54	1511	10.7	8.7	3.4	13.5	2737	7.0	4.0	3.9	9.0		
Passo Fundo ‡	28.15	-	-	-	-	-	2949	8.6	5.5	4.6	13.4		
Porto Alegre ‡	28.15	-	-	-	-	-	3007	7.0	5.0	5.0	11.7		
Santa Maria ‡	29.41	-	-	-	-	-	3057	7.7	4.8	5.7	10.6		
Total South		1511	10.7	8.7	3.4	13.5	15378	7.3	4.5	4.0	9.7		
Total		23422	11.5	8.2	5.0	12.1	58144	8.9	5.0	4.4	10.2		

* ISAAC indicates International Study of Asthma and Allergies in Childhood; RASH (EV), ever had itchy rash that was coming and going for at least 6 months; RASH (12), this itchy rash appeared in the last 12 months; SITES (EV), itchy rash ever in characteristic places; RAWAKE (12), kept awake at night by this itchy rash in the last 12 months; ECZEMA (EV), ever had eczema.

† ISAAC phase 3 official center (both age groups).

‡ ISAAC phase 3 official center for 13-14 year olds

Table 2. Comparison of the Prevalence of Eczema and Related Symptoms in 6-7-year-old Brazilian Schoolchildren According to the Region Where They Live; and in the Northeast Region, by Coastal or Countryside. ISAAC Phase 3*

Question	Region			Northeast		
	Northeast (n=7125)	Southeast (n=11775)	OR (95% CI)	Coastal (n=6286)	Countryside (n=839)	OR (95% CI)
Itchy rash in the last 12 months	11.2	11.6	1.04 (0.9–1.14)	11.6	8.8	1.23 (0.96–1.58)
Itchy rash ever in characteristic places	8.2	8.3	0.98 (0.88–1.09)	7.5	8.2	0.91 (0.70–1.18)
Kept awake at night by this itchy rash in the last 12 months	6.4	4.4	1.50 (1.32–1.71) †	7.1	7.5	0.89 (0.65–1.13)
Ever had eczema	9.8	12.5	1.32 (1.20–1.45) †	29.4	11.2	2.95 (2.36–3.68) †

* ISAAC indicates International Study of Asthma and Allergies in Childhood; OR, odds ratio; CI, confidence interval.

† $P < .05$.

Table 3. Odds Ratio for Atopic Eczema Symptoms in Brazilian ISAAC Centers: Written Questionnaire. 6-7-Year-Old and 13-14-Year-Old Age Groups; Relative to a Reference Center: Santo André

Center	6-7 Years Old			13-14 Years Old		
	No.	Flexural Eczema Ever	Night Waking in 12 Months	No.	Flexural Eczema Ever	Night Waking in 12 Months
Belém	–	–	–	1773	1.86 (1.42–2.44) †	2.00 (1.42–2.83) †
Manaus ‡	3011	1.57 (1.25–1.97) †	2.27 (1.62–3.18) †	3009	1.74 (1.36–2.21) †	2.60 (1.93–3.50) †
Natal	855	2.66 (2.02–3.50) †	4.31 (2.95–6.28) †	1020	2.17 (1.60–2.94) †	3.04 (2.12–4.36) †
Recife §	–	–	–	2865	1.49 (1.16–1.92) †	2.13 (1.56–2.90) †
Caruaru §	–	–	–	3026	1.96 (1.54–2.49) †	3.19 (2.39–4.26) †
Maceió ‡	1990	1.46 (1.14–1.88) †	2.26 (1.58–3.24) †	2745	1.19 (0.91–1.55)	1.70 (1.23–2.35) †
Aracaju ‡	2443	2.29 (1.83–2.87) †	4.63 (3.53–6.40) †	3041	2.42 (1.92–3.05) †	4.49 (3.40–5.94) †
Feira de Santana §	440	1.59 (1.08–2.35) †	3.62 (2.28–5.75) †	1732	1.72 (1.31–2.27) †	3.52 (2.58–4.81) †
Salvador ‡	998	1.41 (1.04–1.91) †	2.79 (1.88–4.15) †	3020	1.96 (1.55–2.49) †	3.19 (2.39–4.26) †
Vitória da Conquista §	399	1.61 (1.08–2.41) †	3.88 (2.43–6.21) †	1679	2.36 (1.82–3.06) †	4.75 (3.52–6.41) †
Brasília §	–	–	–	3009	1.67 (1.31–2.14) †	3.08 (2.30–4.11) †
Belo Horizonte §	–	–	–	3088	1.54 (1.20–1.97) †	2.64 (1.96–3.54) †
Nova Iguaçu ‡	3249	1.95 (1.56–2.43) †	2.96 (2.14–4.10) †	3185	1.20 (0.92–1.55)	1.69 (1.23–2.31) †
São Paulo, west ‡	3312	1.88 (1.51–2.35) †	2.54 (1.83–3.53) †	3181	2.10 (1.66–2.65) †	2.81 (2.10–3.76) †
São Paulo, south ‡	3047	1.41 (1.12–1.78) †	1.55 (1.09–2.21) †	3161	1.05 (0.81–1.37)	1.09 (0.77–1.54)
Santo André ‡	2167	1.00	1.00	3232	1.00	1.00
Curitiba §	–	–	–	3628	1.07 (0.83–1.38)	0.78 (0.54–1.12)
Itajaí ‡	1511	1.69 (1.31–2.20) † †	1.64 (1.10–2.46) †	2737	1.16 (0.88–1.51)	1.99 (1.46–2.73) †
Passo Fundo §	–	–	–	2949	1.62 (1.27–2.08) †	2.38 (1.76–3.21) †
Porto Alegre §	–	–	–	3007	1.48 (1.15–1.90) †	2.26 (1.95–3.52) †
Santa Maria §	–	–	–	3057	1.41 (1.10–1.81) †	2.99 (2.23–4.00) †

* ISAAC indicates International Study of Asthma and Allergies in Childhood;

† $P < .05$;

‡ ISAAC phase 3 official center (both age groups)

§ ISAAC phase 3 official center for 13-14 year olds.

Table 4. Comparison of the Prevalence of Eczema and Related Symptoms in 13-14-Year-Old Brazilian Schoolchildren According to the Region Where They Lived and in the Northeast Region as Coastal or Countryside. ISAAC Phase 3

Question	Region				χ^2	Northeast		OR (95% CI)
	North, 4782	Northeast, 19 128	Southeast, 15 847	South, 15 378		North Coastal 12 691	North Countryside, 6437	
Itchy rash in the last 12 months	11.1	9.9	8.4	7.3	N > NE > SE > S	9.9	9.8	1.01 (0.91-1.11)
Itchy rash ever in characteristic places	6.0	6.2	4.6	4.5	N, NE > SE, S	6.0	6.6	0.90 (0.80-1.02)
Kept awake at night by this itchy rash in the last 12 months	4.6	6.0	36	4.0	NE > N, SE, S N > S, ES S > SE	5.5	6.9	0.79 (0.70-0.89)†
Ever had eczema	13.6	8.5	11.0	9.7	N > SE > S > NE	8.7	8.0	1.10 (0.99-1.23)

* ISAAC indicates International Study of Asthma and Allergies in Childhood; OR, odds ratio; CI, confidence interval; N, north; S, south; E, east

The comparison between centers in the northeast and southeast showed the prevalence of severe eczema to be significantly higher in the northeast (Table 2). The prevalence of physician-diagnosed eczema was higher in the southeast. There were no differences in the prevalence of itchy rash in the last 12 months and flexural eczema (Table 2).

In the northeast the comparison between coastal and countryside centers showed significantly higher values for physician-diagnosed eczema in the coastal region (Table 2).

Considering Santo André as the reference, we observed a significantly higher risk of developing flexural eczema and severe eczema, among children aged 6-7 years old, in Natal, Aracaju, Vitoria da Conquista, and Nova Iguaçu (Table 3).

In the adolescent group the prevalence of itchy rash in the last 12 months varied from 6.3% to 11.8%; flexural eczema varied from 3.4% to 7.9%; severe eczema from 1.5% to 8.8%; and physician-diagnosed eczema from 2.2% to 14.2% (Table 1). Prevalence rates were quite variable and the analysis of data grouped by region showed values significantly higher in the north and northeast, except for physician-diagnosed eczema, which achieved the lowest mean rate in the northeast region (Table 4).

Considering the northeast region, the prevalence of severe eczema was significantly lower among adolescents living in coastal centers (Table 4). People with apparently the same genetic background but inhabiting different centers in Pernambuco (northeast) and Rio Grande do Sul (south) were compared (Table 5). In both states the prevalence of flexural eczema and severe disease were higher in countryside centers (Table 5).

Considering Santo André as the reference, we observed the highest risk of flexural eczema in Natal, Aracaju, Vitória da Conquista, and São Paulo-West; centers with the highest frequency of severe disease were Natal, Caruaru, Aracaju, Feira de Santana and Vitória da Conquista (Table 3).

The relationship between the prevalence of flexural eczema and severe eczema was significant considering each group separately (6-7 year olds: $\rho=0.756$, $P<.004$; 13-14 year olds: $\rho=0.874$, $P<.0001$), as well as considering both age groups together.

Among children aged 6-7 years old there was no significant relationship between the latitude of the centers and the prevalence of current eczema ($\rho=-0.21$; 95% CI, -0.71 to 0.43 ; $P=.512$); flexural eczema ($\rho=-0.245$; 95% CI, -0.73 to 0.40 ; $P=0.442$) and severe eczema ($\rho=-0.54$; 95% CI, -0.84 to 0.07 ; $P=.07$).

Among the adolescents, the latitude of the centers was significantly related to the prevalence of current eczema ($\rho=-0.72$, 95% CI, -0.88 to -0.41 ;

Table 5. Comparison of the Prevalence of Eczema and Related Symptoms in 13-14-Year-Old Brazilian Schoolchildren With the Same Genetic Background and Living in Urban or Rural Areas in the Northeast or South. ISAAC Phase Three*

Question	Northeast		South		OR		
	Recife	Caruaru	Passo Fundo (a) N = 2949	Porto Alegre (b) N = 3007	Santa Maria (c) N = 3057	95% CI a × b	95% CI b × c
Itchy rash in the last 12 months	10.1	10.3	8.6	7.0	7.7	1.27 (1.05–1.53)†	1.12 (0.92–1.36)
Itchy rash ever in characteristic places	5.0	6.5	5.5	5.0	4.8	1.10 (0.88–1.38)	0.96 (0.76–1.21)
Kept awake at night by this itchy rash in the last 12 months	4.1	6.1	4.6	5.0	5.7	0.67 (0.53–0.85)†	1.14 (0.91–1.43)
Ever had eczema	12.2	14.1	13.4	11.7	10.6	1.17 (1.00–1.36)†	0.97 (0.83–1.13)

* ISAAC indicates International Study of Asthma and Allergies in Childhood; OR, odds ratio; CI, confidence interval. † $P < .05$

$P = .0002$) and flexural eczema ($\rho = -0.53$; 95% CI, -0.79 to -0.12 ; $P = .013$), but not with the prevalence of severe eczema ($\rho = -0.29$; 95% CI, -0.65 to -0.18 ; $P = .206$).

Discussion

Reliable diagnostic criteria for atopic eczema are essential in order to permit international comparisons and to identify possible risk factors for disease. In recent years, the ISAAC written questionnaire has been applied as a tool for diagnosing asthma, rhinitis, and atopic eczema among schoolchildren worldwide. However, the effectiveness of the eczema core of the written questionnaire has been disputed.

Haileamlak et al [22] evaluated the ISAAC eczema core as a predictive tool for the diagnosis of atopic eczema in Ethiopian children. They compared the ISAAC criterion with the refinement of Hanifin and Rajka's diagnostic criteria in the United Kingdom, and checked both by physical examination. Neither the ISAAC criterion nor UK criterion performed especially well in predicting cases of atopic eczema in this survey. Chan et al [23] validated the Chinese version of the ISAAC written questionnaire (eczema core), comparing it to a dermatologist's clinical examination. They concluded that the translated questionnaire was less effective than the English version in assessing the prevalence of atopic eczema. Miyake et al [24] pointed out that a translation error in the eczema core of the questionnaire applied in Japan was probably the explanation for the higher prevalences of the disease and related symptoms observed among Japanese schoolchildren [24]. Cultural conceptions of terminology, differences between parents' and children's perception of symptoms, the transient nature of the signs of atopic eczema, differences in what doctors perceive to constitute a typical case, and problems with questionnaire translation are given as possible reasons for these findings [22].

In contrast to those studies, the validated Portuguese translation of the eczema core for use in the Brazilian culture has been shown to be reproducible, appropriate, and able to distinguish children with atopic dermatitis from control children [17]. Significant agreement was observed between the ISAAC global cutoff score and the ISAAC criterion for atopic eczema utilized in this study [17].

In Brazil, ISAAC phase 3 saw a 3-fold increase in the number of participating centers in comparison with ISAAC phase 1: 12 centers studied children as well as adolescents and 21 studied adolescents only. The data gathered certainly give us a more representative sample of

Brazilian schoolchildren. The comparison between the mean prevalence of flexural eczema observed in phase 1 (8.2% for children aged 6-7 years old and 5.0% for adolescents aged 13-14 years old) [17] with that in phase 3 (7.3% for children and 5.3% for adolescents) allowed us to conclude that flexural eczema is decreasing among children and increasing among adolescents.

The mean prevalence of severe eczema showed a significant increase in both age groups (5.0% for children and 4.4% for adolescents), independently to those centers that had the higher values in phase 1 [25].

The highest prevalence of atopic eczema and related symptoms such as flexural eczema and severe eczema were observed in centers in the northeast and north (Tables 2, 3, 4, and 5). Brazil is a country with continental dimensions, whose total area of 8.5 million square kilometers is cut in the north by the equator and in the southeast by the Tropic of Capricorn [26]. Its climate varies from area to area. In the northern, northeastern, and midwestern areas, the climate is tropical with a dry and lingering summer and a rainy winter. In the south and southeast the climate is temperate; seasons are better defined in the south [26].

Heat and humidity have been named as risk factors for atopic eczema. Weiland et al [27] investigated the relationship between climate and atopic diseases using worldwide data from 146 centers of the ISAAC phase 1 study. Considering the data from ISAAC written questionnaire atopic eczema core, they found that a prevalence of eczema symptoms in both age groups increased with latitude and decreased with mean annual outdoor temperature. Worldwide indoor relative humidity was negatively associated with eczema symptoms in 6-7 year-old children. These findings suggest that climate may affect the prevalence of atopic eczema in children according to those authors.

In contrast, in our study we observed an inverse relationship between latitude and the prevalence of eczema and flexural eczema. We observed a positive relationship between the prevalence of flexural eczema and severe eczema and mean outdoor temperature (data not shown). Nnokura et al [28] identified heat intolerance, excessive sweating and humidity as aggravating factors for atopic eczema in Nigerian patients with atopic eczema. McNally et al [29] demonstrated a positive relationship between symptoms of atopic eczema and dampness in the home. Evaluating people apparently with the same genetic background but living in places with similar mean outdoor temperature and different levels of outdoor humidity (coastal vs countryside) we observed higher values in places with low humidity (Tables 2 and 5).

Exposure to hard water and higher risk of atopic eczema in children of primary school-age was documented by ecological studies in the UK [30] and Japan [31]. In Brazil, water composition does not differ substantially and the available water can not be characterized as hard.

Fernandez-Mayoralas et al [32] evaluated the influence of air pollution on the prevalence of atopic eczema in 13-14-year-old schoolchildren living in the city of Cartagena, Spain. High levels of atopic eczema and severe eczema

were observed among those exposed to high levels of air pollutants. In our study we have not observed any influence of air pollution on atopic eczema prevalence, studied mainly in the southeast where there were centers with high levels of air pollution (São Paulo and Santo André) (data not shown).

Another point of concern is the relationship between socioeconomic status and the prevalence of atopic eczema and related-symptoms. Depending on the criteria applied to characterize status the results observed would be different. In this study we did not find a significant relationship between low socioeconomic status (infant mortality, poverty index, and average nominal income for subjects older than 10 years of age) [33] and the prevalence of flexural eczema and severe eczema (data not shown). In another study, Mercer et al [34] evaluated the relationship between status (place of residence, duration of urbanization) and prevalence of atopic eczema (recurrent itchy rash in the last year) and observed a weak association between longer period of urbanization and atopic eczema.

Limitations of our study resulted mainly from the cross-sectional design, as the time sequence of events can not be established with certainty and the areas compared may differ markedly with regard to various risk factors discussed. Thus there may be substantial confounding if there were an attempt to infer a cause-effect relationship.

Although ISAAC phase 3 data collection has been concluded around the world, the final results are as yet unknown. As we had observed at the end of ISAAC phase 1, in this study our data reinforce the heterogeneity of the prevalence of atopic eczema and related symptoms around Brazil. The largest prevalence index of atopic eczema was found in the north and northeast, although a higher prevalence of severe eczema was observed in centers in the south. Further studies evaluating etiology, genetics, and environmental risk factors are necessary in order to allow us to conclude more about atopic eczema and related-symptoms among Brazilian children.

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