

Prevalence of symptoms of asthma, rhinitis, and atopic eczema among adolescents living in urban and rural areas in different regions of Brazil

D. Solé^a, V.E. Cassol^b, A.R. Silva^c, S.P. Teche^b, T.M. Rizzato^b, L.C. Bandim^c, E.S.C. Sarinho^c and I.C. Camelo-Nunes^a

^aDivision of Allergy, Clinical Immunology and Rheumatology, Dept of Pediatrics, Federal University of São Paulo-Escola Paulista de Medicina, São Paulo. ^bDivision of Pediatric Pneumology, Dept of Pediatrics, Federal University of Santa Maria, Rio Grande do Sul. ^cDivision of Pediatric Allergology, Dept of Pediatrics, Federal University of Pernambuco, Pernambuco, Brazil.

ABSTRACT

Background: In Brazil, studies evaluating the prevalence of asthma and allergic diseases among children living in rural area compared to urban area are rare. Some authors identified as risk factors for higher prevalence of current wheezing to have a family history of asthma, to have contact with pets, and being student in an urban school. The International Study of Asthma and Allergies in Childhood (ISAAC) phase 3 has shown higher prevalence of wheezing, nasal symptoms and cutaneous rash in the last 12 months in centers from Northern (N) and Northeastern (NE) regions of Brazil.

Objective: To evaluate if adolescents with similar genetic background, living in a rural area are protected against the development of symptoms of asthma, rhinitis, and atopic eczema when compared to those living in an urban area in the same region of the country.

Subjects and Method: Adolescents (13-14 year-old) living in Caruaru (Pernambuco) and in Santa

Maria (Rio Grande do Sul) were enrolled in this study (2002-2003). The adolescents filled in the ISAAC written questionnaire (WQ), previously translated and validated to the Brazilian culture (30-32). Data obtained were transcribed manually into a database (Epi-Info) supplied by ISAAC's coordinators and were statistically analyzed by the SSPS-12 software.

Results: The prevalence of asthma related symptoms were higher among those adolescents living in the urban centers in comparison to the rural ones. These differences were significant for wheezy ever, wheezy in the last 12 months, asthma ever, and wheezy with exercise in Caruaru and for wheezy ever and asthma ever, in Santa Maria. Comparing urban areas, the prevalence of asthma related symptoms in Caruaru was higher than in Santa Maria, except for wheezy ever and wheezy with exercise. The opposite was observed comparing rural areas: the prevalence of asthma (except for nocturnal cough) was higher in Santa Maria despite lesser severity of symptoms in this city.

Key words: Asthma in children. Wheezy. Prevalence. Urban center. Rural center. Exercise.

Correspondence:

Dirceu Solé
Rua Mirassol 236, apto 72
04044-010, Vila Mariana,
São Paulo, SP, Brazil
Phone/fax: + 55 11 5579 1590
E-mail: dirceusole.dped@epm.br

INTRODUCTION

Charles Blackley, more than 100 years ago, was the first to notice that hay fever was remarkably rare

in farming families¹. Since then an increasing prevalence of allergic diseases has been reported, and in a simple way, has been related to urbanization and western lifestyle²⁻¹¹.

Some of the factors being investigated as protective against the onset of asthma and allergic diseases include early exposure to infectious agents and/or endotoxins^{6,12}, to be born and growing up in a rural area^{1,13}, to live in an environment with great number of children^{6,12}, to have received low amounts of antibiotics, to have been long-term breast fed¹², and to have received a special diet (fresh fruits and vegetables, long-chain polyunsaturated fatty acids, and vitamin A) during the first year of life¹².

Growing up in farms, mainly in those engaged in cattle breeding, poultry or animal production has been linked to a lower prevalence of atopic sensitization and hay fever. However, epidemiological studies have shown conflicting evidences about the lower risk of atopic diseases in children living in rural areas compared to those living in urban areas¹⁴⁻¹⁸.

Remes et al, evaluating adolescents, demonstrated a reduced risk of questionnaire-reported hay fever in children living in farms with livestock¹⁹. In another study, also in Finland, Kilpelainen et al observed a slightly reduced risk of asthma among farmer's children²⁰. When we interpret the results of these trials it is necessary to know that farms around the world certainly do not have the same scale and kind of operation. This would be responsible in part for the discrepancy observed among these studies. Downs et al, keeping this doubt in mind, have studied the prevalence of allergic diseases in two Australian rural towns with different farming activities: mixed and crop. They have observed a lower risk of atopy among those children that were born and lived at least 1 year in farms with mixed activity (livestock and crop)²¹.

In Brazil, studies evaluating the prevalence of asthma and allergic diseases among children living in rural area compared to urban area are rare. Maia et al evaluated the prevalence of asthma and related symptoms among adolescents living in Montes Claros, a small city in the countryside of the state of Minas Gerais, Southeastern of Brazil. They identified as risk factors for higher prevalence of current wheezing to have a family history of asthma, to have contact with pets, and being student in an urban school²².

The International Study of Asthma and Allergies in Childhood (ISAAC) phase 3 has shown higher prevalence of wheezing, nasal symptoms and cutaneous rash in the last 12 months in centers from Northern (N) and Northeastern (NE) regions of Brazil²³. As Brazil was colonized by Portuguese, invaded by several other nations and received in the last century mil-

lions of immigrants, Brazilian people hasn't a characteristic genetic pattern. This is one of the main difficulties for comparison between different centers from different regions of the country.

The aim of this study was to evaluate if adolescents with similar genetic background, living in a rural area are protected against the development of symptoms of asthma, rhinitis, and atopic eczema when compared to those living in an urban area in the same region of the country.

SUBJECTS AND METHODS:

Adolescents (13-14 year-old) living in Caruaru (state of Pernambuco) and in Santa Maria (state of Rio Grande do Sul) were enrolled in this study (2002-2003). They were selected as standardized by ISAAC protocol^{24,25} among those who had attended public and private schools localized in these cities. Information regarding the number of schools and students in each city was obtained from their respective City Education Secretaries official records. According to the place where they lived, adolescents were divided in two groups: urban (U) and rural (R).

Caruaru and Santa Maria are small countryside cities with different climate and socioeconomic status. Caruaru is in the NE region of Brazil, has 253,634 inhabitants (85.6 % urban) living in a total area of 928.08 Km². Its latitude is 8° 17' 00" S, its longitude is 35° 58' 34" W. Gr, and its altitude is 555m. Climate is hot semi-arid with a mean annual temperature of 24 °C²⁶. Santa Maria is in the S region, has 243,396 inhabitants (84.7 % urban) living in a total area of 1,823.1 Km². Its latitude is 29° 68' 17" S, its longitude is 53° 80' 69" W. Gr, and its altitude is 113 m. The climate in Santa Maria is subtropical, seasons are better defined, and the mean annual temperature is 19.2 °C²⁷.

According to the Brazilian Institute of Geography and Statistics (IBGE) an urban area was defined as those corresponding to towns (municipal headquarters), villages (county headquarters) or isolated urban areas, and a rural area was defined as all area out of the limits of an urban area²⁸.

Considerations about socioeconomic status were based on the state infant mortality index (number of dead children younger than 1 year old per 1,000 live births) and on the city Gross Domestic Product (GDP). During 2003, the infant mortality index in Pernambuco was 60.46 and the Caruaru's GDP was R\$1,042,163²⁶. The infant mortality in the state of Rio Grande do Sul was 18.99 and Santa Maria's GDP was R\$1,554,394²⁶ (US\$1.00 = 3.00 Brazilian Reais [R] in 2003).

The percentage of population in the age period of 13 to 14 years in the states of Rio Grande do Sul and Pernambuco was 4.0 % and 4.2 % of the total population living in Southern and Northern regions, respectively²⁹. Expecting to have at a difference of at least 6 % in the prevalence of current asthma (wheezy in the last 12 months) between adolescents living in rural and urban areas [mean prevalence of current asthma = 20 % (ISAAC fase 1)], with a test power of 80 %, and alpha risk of 5 %, the total number of evaluated adolescents would be 551.

In Caruaru the selection of adolescents was based on the distribution of the whole population: rural (14 %) and urban (86 %) inhabitants²⁶. Of the 3,026 adolescents enrolled, 2,674 (88.3 %) and 352 (11.7 %) were U and R, respectively. In Santa Maria participated 3,066 U adolescents and 3,057 R adolescents from 10 small cities in the neighborhood of Santa Maria.

After sample definition, the adolescents filled in the ISAAC written questionnaire (WQ), previously translated and validated to the Brazilian culture³⁰⁻³². The WQ was fulfilled in the classroom under the supervision of the researcher. Data obtained were transcribed manually into a database (Epi-Info) supplied by ISAAC's coordinators and were statistically analyzed by the SSPS-12 software. The frequency of affirmative answers to each question was considered according to the city evaluated. The comparison between U and R, in each city, were analyzed by the Chi-square test and the results were expressed as Odds ratio (OR) with 95 % confidence intervals (95 % CI)³³. The level of rejection of null hypothesis was 5 %. The study was approved by the Ethical Committee of Federal University of Pernambuco and Federal University of Santa Maria. A sign informed consent was obtained by all adolescents' parents.

RESULTS

In general the prevalence of asthma related symptoms were higher among those adolescents living in the urban centers in comparison to the rural ones (table I). These differences were significant for wheezy ever, wheezy in the last 12 months, asthma ever, and wheezy with exercise in Caruaru and for wheezy ever and asthma ever, in Santa Maria. Comparing urban areas, the prevalence of asthma related symptoms in Caruaru was higher than in Santa Maria, except for wheezy ever and wheezy with exercise. The opposite was observed comparing rural areas: the prevalence of asthma (except for nocturnal cough) was higher in Santa Maria despite lesser severity of symptoms in this city.

Except for the prevalence of nasal symptoms interfering with daily activities, all rhinitis related symptoms were significantly higher among adolescents living in urban area, in both cities (table II). As observed with asthma symptoms, the prevalence of rhinitis related symptoms was higher among U Caruaru adolescents in comparison to U Santa Maria adolescents. In the other hand, and contrary to that observed with asthma, the prevalence of rhinitis and its symptoms was higher among R Caruaru adolescents in comparison to R Santa Maria adolescents.

Table III shows data from ISAAC's eczema core WQ. In Caruaru there were not significant differences in the prevalence of eczema related symptoms between urban and rural adolescents. In Santa Maria, except for the prevalence of itchy rash in the last 12 months, all eczema symptoms were significantly more frequent in rural than in urban area. In Caruaru the prevalence of eczema related symptoms were higher than those in Santa Maria (except for the severity of symptoms = kept awake at night in the last 12 months), considering both urban and rural areas.

DISCUSSION

Brazil is a continental country, whose total area of 8,5 million square kilometers is cut in N by the Equator line and in SE by the Tropic of Capricorn. Secondary to its colonization, a period of slavery (mainly in NE and SE regions) and immigration in the last century (mainly to S and SE regions), Brazilian population has a high degree of miscegenation that explains the high Brazilian people heterogeneity characterizing us as a genetic cauldron. So, genetic studies or comparisons between Brazilian people living in different parts of the country are difficult. Trying to minimize bias we decided to study people living in rural and urban areas in the same neighborhood, in different regions of Brazil.

Sometimes, even studying people living in the same area, it is important to know that they have apparently the same genetic background. In a recent study, Soares et al have evaluated the prevalence of asthma and related symptoms applying ISAAC WQ among Indians living in a village near of the city of Maceió – the capital of Alagoas state (NE region of Brazil).

These individuals live in conditions very similar of those their ancestors used to live, in extreme poverty, low level of sanitation without potable water and sewer, high level of illiteracy, high frequency of helminthiasis and a mean income lower than US\$50³⁴.

In comparison to children living in Maceió, the prevalence of current asthma was lower, for both

Table I

Prevalence of asthma and related symptoms (%) among 13-14-year-old Brazilian schoolchildren according to city and region where they live (urban or rural): ISAAC Phase 3 – Odds ratio (OR) and 95 % Confidence interval (95%CI)

Question	Caruaru			Santa Maria		
	Urban N = 2,674	Rural N = 352	OR (95 % CI)	Urban N = 3,066	Rural N = 3,057	OR (95 % CI)
Wheezy ever	32.6*	23.0	1.62 (1.25-2.10)*	42.1*	37.4	1.10 (1.06-1.31)*
Wheezy last 12 months	18.6*	12.5	1.60 (1.15-2.22)*	16.7	15.3	1.12 (0.97-1.28)
More than 4 attacks last 12 months	3.1	2.5	1.22 (0.61-2.45)	1.9	1.3	1.45 (0.97-2.18)
Sleep disturbance last 12 months	11.9	12.2	0.97 (0.69-1.36)	3.8	4.1	0.93 (0.72-1.20)
Speech problem last 12 months	5.0	4.8	1.04 (0.62-1.74)	3.8	3.8	1.01 (0.77-1.31)
Asthma ever	21.1*	8.5	2.87 (1.95-4.20)*	14.9*	11.1	1.40 (1.21-1.62)*
Wheeze with exercise last 12 months	18.2*	12.8	1.52 (1.10-2.10)*	19.0	18.8	1.01 (0.89-1.15)
Cough at night last 12 months	39.2	35.8	1.16 (0.92-1.46)	32.4	32.6	0.99 (0.89-1.10)

p* < 0.05Table II**

Prevalence of rhinitis and related symptoms (%) among 13-14-year-old Brazilian schoolchildren according to city and region where they live (urban or rural): ISAAC Phase 3 – Odds ratio (OR) and 95 % Confidence interval (95%CI)

Question	Caruaru			Santa Maria		
	Urban N = 2,674	Rural N = 352	OR (95 % CI)	Urban N = 3,066	Rural N = 3,057	OR (95 % CI)
Sneezing, runny or blocked nose ever	39.2*	19.6	2.60 (1.98-3.42)*	17.9*	14.9	1.25 (1.09-1.43)*
Sneezing, runny or blocked nose ever in the last 12 months	27.2*	12.5	2.61 (1.88-3.63)*	12.2*	10.2	1.21 (1.04-1.42)*
Nose problem with itchy, watery eyes in the last 12 months	16.3*	8.2	2.17 (1.46-3.22)*	6.6*	4.7	1.41 (1.13-1.76)*
Interference with daily activities	9.2	10.8	0.84 (0.58-1.20)	7.9	8.2	0.97 (0.80-1.16)
Rhinitis ever	22.7*	13.1	1.95 (1.41-2.70)*	17.7*	10.8	1.78 (1.53-2.06)*

p* < 0.05Table III**

Prevalence of atopic eczema and related symptoms (%) among 13-14-year-old Brazilian schoolchildren according to city and region where they live (urban or rural): ISAAC Phase 3 – Odds ratio (OR) and 95 % Confidence interval (95%CI)

Question	Caruaru			Santa Maria		
	Urban N = 2,674	Rural N = 352	OR (95 % CI)	Urban N = 3,066	Rural N = 3,057	OR (95 % CI)
Ever had an itchy rash that was coming and going for at least 6 months	16.3	17.3	0.93 (0.70-1.25)	10.5	12.6*	0.81 (0.70-0.95)*
Itchy rash in the last 12 months	10.4	9.4	1.12 (0.77-1.64)	6.8	7.9	0.85 (0.70-1.03)
Itchy rash ever in characteristic places	6.4	7.4	0.86 (0.56-1.32)	3.6	4.8*	0.74 (0.57-0.95)*
Itchy rash that cleared in the last 12 months	10.2	10.5	0.97 (0.67-1.39)	5.5	7.8*	0.68 (0.56-0.84)*
Kept awake at night by this itchy rash in the last 12 months	5.9	7.1	0.82 (0.53-1.27)	8.7	11.6*	0.73 (0.61-0.86)*
Ever had eczema	14.1	14.2	0.99 (0.72-1.36)	9.8	11.8*	0.81 (0.69-0.96)*

**p* < 0.05

age periods evaluated: six times among children aged 6-7 years (4 % × 24 %) and less among adolescents aged 13-14 years (10.0 % × 14.7 %)^{23,35}.

The first impression we have when analyzing these data is that the Hygiene Hypothesis could be played a role in the results of prevalence of asthma among these Indian children population.

However, it is important to point out that children living in the city of Maceió and these Indians are genetically different once the level of miscegenation among Indians almost does not exist³⁴. So we could not make any speculation about the role of Hygiene Hypothesis in the data observed. Because of this we decided to study population been apparently of the same genetic background, living in different places in the same region of the country.

Although in this study, the prevalence of helminthiasis was not appraised, Nascimento Silva did not observe any difference in the prevalence of asthma between low socio-economic children with or without ascariasis, living in Campina Grande, a city located near to Caruaru³⁶.

An inverse relationship between mean annual outdoor temperature and humidity and the prevalence of asthma, allergic rhinoconjunctivitis, and atopic eczema among children from 146 ISAAC's phase I participant centers was documented: high temperature and humidity were associated to lower prevalence³⁷. In this study we observed the opposite.

Despite climate and cultural differences between people living in the NE and S of Brazil, the rural way of life in both are quite similar. In general, farm's houses in Brazil are different from those in Europe^{5,13,14}. While small animals (dog, duck, hen) circulate freely among human beings, the big ones (e.g cows, horses) are maintained in stables, frequently far away from the house. In these areas consuming unpasteurized milk is frequent.

It has been reported that reduction of allergic diseases among children who were born and raised in a farm environment, in comparison to those living in urban area, is due to their exposure to poultry and livestock³⁸⁻⁴⁰. Until recently, exposure to high levels of endotoxin was associated with exposure to farm animals, presence of pets in home, number of people living in the house and cleaning habits⁴¹. However, results of a study carried out on children from rural areas in Europe, evaluating farm-related exposures and health outcomes, revealed that levels of endotoxin and extracellular polysaccharides were associated to health outcomes independently of the farm exposures⁴². In a birth cohort study the increased endotoxin exposure was associated with a reduced risk of allergic sensitization and eczema, and with an increased risk of non-atopic wheeze,

only in children with the CC genotype at -159 of the CD14 gene⁴³.

In India, Vedanthan et al have evaluated possible factors related to development of asthma and allergic diseases among children from two different communities: urban and rural. They observed that those children who live with close animal contact and mud flooring and who were exclusively breastfed (at least 6 months) in infancy are less likely to develop asthma, rhinitis, and atopic sensitization³⁸.

In general, we observed a tendency for higher values of prevalence of asthma and rhinitis but not eczema related symptoms among those adolescents living in urban area, as in Caruaru as in Santa Maria. Our data confirms that living in a rural area is associated to a decrease in the prevalence of symptoms related to asthma and allergic rhinitis among Brazilian children from two different regions of the country.

REFERENCES

1. Brabäck L. Does farming provide protection from asthma and allergies? *Acta Paediatr* 2002; 91:1147-49.
2. Strachan DP. Hay fever, hygiene and household size. *BMJ* 1989; 299: 1259-60.
3. Brabäck L, Breborowicz A, Dreborg S, Knutsson A, Pieklik H, Björkstén B. Atopic sensitization and respiratory symptoms among Polish and Swedish school children. *Clin Exp Allergy* 1994; 24: 826-35.
4. Braun-Fahrlander C, Wutrich B, Gassner M, Grize L, Sennhauser FH, Varonier HS et al. Validation of a rhinitis symptom questionnaire (ISAAC core questions) in a population of Swiss school children visiting the school health services. *International Study of Asthma and Allergies in Childhood. Pediatr Allergy Immunol* 1997; 8: 75-82.
5. Björkstén B, Dumitrascu D, Foucard T, Khetsuriani N, Khaitov R, Leja M, Lis G, Pekkanen J, Priftanji A, Riiikjarv MA. Prevalence of childhood asthma, rhinitis and eczema in Scandinavia and Eastern Europe. *Eur Respir J* 1998; 12:432-7.
6. Strachan DP. The role of environmental factors in asthma. *Br Med Bull* 2000; 56: 865-82.
7. Chakravarthy S, Singh RB, Swaminathan S, Venkatesan P. Prevalence of asthma in urban and rural children in Tamil Nadu. *Natl Med J India*. 2002; 15: 260-3.
8. Rojas Molina N, Legorreta Soberanis J, Olvera Guerra F. Prevalence and asthma risk factors in municipalities of the State of Guerrero, Mexico *Rev Alerg Mex* 2001; 48: 115-8.
9. Hijazi N, Abalkhail B, Seaton A. Diet and childhood asthma in a society in transition: a study in urban and rural Saudi Arabia. *Thorax* 2000; 55: 775-9.
10. Hasan MM, Gofin R, Bar-Yishay E. Urbanization and the risk of asthma among schoolchildren in the Palestinian Authority. *J Asthma* 2000; 37: 353-60.
11. Nilsson L, Castor O, Lofman O, Magnusson A, Kjellman NI. Allergic disease in teenagers in relation to urban or rural residence at various stages of childhood. *Allergy* 1999; 54: 716-21.
12. Warner JO. The hygiene hypothesis. *Pediatr Allergy Immunol* 2003; 14: 145-6.
13. Von Ehrenstein OS, Von Mutius E, Illi S, Baumann L, Bohm O, von Kries R. Reduced risk of hay fever and asthma among children of farmers. *Clin Exp Allergy* 2000; 30: 187-93.

14. Brabäck L, Kälvesten L. Urban living as a risk for atopic sensitization in Swedish schoolchildren. *Pediatr Allergy Immunol* 1991; 2:14-9.
15. Yemaneberhan H, Bekele Z, Venn A, Lweis S, Parry E, Britton J. Prevalence of wheeze and asthma and relation to atopy in urban and rural Ethiopia. *Lancet* 1997; 350: 85-90.
16. Nathan RA, Meltzer EO, Selner JC, Storms W. Prevalence of allergic rhinitis in the United States. *J Allergy Clin Immunol* 1997; 99: S808-S814.
17. Filipiak B, Heinrich J, Schafer T, Ring J, Wichmann HE. Farming, rural lifestyle and atopy in adults from southern Germany – results from the MONICA/KORA study Augsburg. *Clin Exp Allergy* 2001; 31:1829-38
18. Barnes M, Cullinan P, Athanasaki P, MacNeill S, Hole AM, Harris J, Kalogeraki S, Chatzinikolaou M, Drakonakis N, Bibaki-Liakou V, Newman Taylor AJ, Bibakis I. Crete: does farming explain urban and rural differences in atopy? *Clin Exp Allergy* 2001; 31:1822-8
19. Remes ST, Pekkanen J, Soininen L, Kajosaari M, Husman T, Koivikko A. Does heredity modify the association between farming and allergy in children? *Acta Paediatr* 2002; 91: 1163-9.
20. Kilpelainen M, Terho EO, Helenius H, Koskenvuo M. Farm environment in childhood prevents the development of allergies. *Clin Exp Allergy* 2000; 30: 201-8.
21. Downs SH, Marks GB, Mitakakis TZ, Lööppi JD, Car NG, Peat JK. Having lived on a farm and protection against allergic diseases in Australia. *Clin Exp Allergy* 2001; 31:570-5
22. Maia JG, Marcopito LF, Amaral AN, Tavares BF, Santos FA. Prevalence of asthma and asthma symptoms among 13 and 14-year-old schoolchildren, Brazil *Rev Saude Publica*. 2004; 38: 292-9.
23. Solé D, Wandalsen GF, Camelo-Nunes IC, Naspitz CK; ISAAC-Brazilian Group. 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. *J Pediatr (Rio J)* 2006; 82:341-6.
24. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, Mitchell EA, Pearce N, Sibbald B, Stewart AW, ISAAC Steering Committee. International study of asthma and allergies in childhood (ISAAC): rationale and methods. *Eur Respir J* 1995; 8: 483-491.
25. Elwood P, Asher MI, Beasley R, Clayton TO, Stewart AW; ISAAC Steering Committee. The International Study of Asthma and Allergies in Childhood (ISAAC): phase III rationale and methods. *Int J Tuberc Lung Dis* 2005; 9: 10-6.
26. Caruaru, portal da cidade. www.caruaru.pe.gov.br/dados-gerais.asp - accessed in 07/09/2007
27. Instituto Brasileiro de Geografia e Estatística (IBGE) – População - Indicadores sociais – Indicadores sociais mínimos in http://www.ibge.gov.br/home/estatistica/populacao/condicaoodevida/indicadoresminimos/default_minimos.shtm – accessed in 07/09/2007
28. Instituto Brasileiro de Geografia e Estatística (IBGE) – Definição de área urbana e rural in <http://www.ibge.gov.br/home/estatistica/populacao/trabalhoerendimento/pnad98/sau de/metodologia.shtm> - accessed in 07/09/2007
29. Instituto Brasileiro de Geografia e Estatística (IBGE)–Populações–Crianças e adolescentes– in http://www.ibge.gov.br/home/estatistica/populacao/criancas_adolescentes/default.shtm - accessed in 07/09/2007
30. Yamada E, Vanna AT, Naspitz CK, Solé D. International study of asthma and allergies in childhood (ISAAC): validation of the written questionnaire (eczema component) and prevalence of atopic eczema among Brazilian children. *J Investig Allergol Clin Immunol* 2002;12:34-41.
31. Solé D, Vanna AT, Yamada E, Rizzo MC, Naspitz CK. International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire: validation of the asthma component among Brazilian children. *J Investig Allergol Clin Immunol* 1998;8:376-82.
32. Vanna AT, Yamada E, Arruda LK, Naspitz CK, Solé D. International Study of Asthma and Allergies in Childhood: validation of the rhinitis symptom questionnaire and prevalence of rhinitis in schoolchildren in São Paulo, Brazil. *Pediatr Allergy Immunol* 2001;12:95-101.
33. Fletcher RH, Fletcher SW, Wagner EH - *Epidemiologia clínica: elementos essenciais*, 3ª ed, Artes Médicas, Porto Alegre, 1996, p. 281.
34. Almeida LS, Vilela RB, Soares FJP. Saúde indígena: o caso Xucuru-Kariri in Almeida LS, Vilela RB, Soares FJP (ed) *Xucuru-Kariri: Saúde na Fazenda Canto – Maceió*, EDUFAL, 2005, pp 9-32.
35. Soares FJP, Moreira Jr FJ, Andrade Filho JL, Gameleira KPD, Costa BSM. Prevalência de asma brônquica em crianças e adolescentes indígenas da tribo Xucuru-Kariri em Palmeira dos Índios – AL. In Almeida LS, Vilela RB, Soares FJP (ed) *Xucuru-Kariri: Saúde na Fazenda Canto – Maceió*, EDUFAL, 2005, pp 119-142.
36. Nascimento Silva MT, Andrade J, Tavares-Neto J. Asthma and ascariasis in children aged two to ten living in a low income suburb. *J Pediatr (Rio J)* 2003;79:227-32
37. Weiland SK, Hüsing A, Strachan DP, Rzehak P, Pearce N. Climate and the prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema in children. *Occup Environ Med* 2004; 61: 609-15.
38. Vedanthan PK, Mahesh PA, Vedanthan R, Holla AD, Liu AH. Effect of animal contact and microbial exposures on the prevalence of atopy and asthma in urban vs rural children in India. *Ann Allergy Asthma Immunol* 2006; 96:571-8.
39. Braun-Fahrlander C, Riedler J, Herz U, Eder W, Waser M, Grise L, Maisch S, Carr D, Gerlach F, Bufe A, Lauener RP, Schierl R, Renz P, Nowak D, von Mutius E (2002) Environmental exposure to endotoxin and its relation to asthma in school-age children. *N Engl J Med* 347: 869-77
40. Waser M, Schierl R, von Mutius E, Maisch S, Carr D, Riedler J, Eder W, Schreuer M, Nowak D, Braun-Fahrlander C and the ALEX Study Team. Determinants of endotoxin levels in living environments of farmers' children and their peers from rural areas. *Clin Exp Allergy* 2004;34:389-97
41. Thorne PS, Metwali N, Avol E, McConnel RS. Surface sampling for endotoxin assessment using electrostatic wiping cloths. *Ann Occup Hyg* 2005; 49:401-6
42. Ege MJ, Frei R, Bieli C, Schram-Bijkerk D, Waser M, Benz MR, Weiss G, Nyberg F, van Hage M, Pershagen G, Brunekreef B, Riedler J, Lauener R, Braun-Fahrlander C, von Mutius E; PAR-SIFAL Study team. Not all farming environments protect against the development of asthma and wheeze in children. *J Allergy Clin Immunol* 2007;119:1140-7
43. Simpson A, John SL, Jury F, Niven R, Woodcock A, Ollier WE, Custovic A. Endotoxin exposure, CD14, and allergic disease: an interaction between genes and the environment. *Am J Respir Crit Care Med* 2006;174:386-392