

Environmental and socio-demographic factors associated to asthma in adolescents in Rio de Janeiro, Brazil

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Although asthma is of frequent occurrence, little is known about the factors associated with this disease in Brazil. We studied the association between asthma, environmental and socio-demographic factors in adolescents in Nova Iguaçu, Rio de Janeiro State. Cross-sectional study using the questionnaires about asthma and environmental factors from the International Study of Asthma and Allergies in Childhood (ISAAC). We performed bivariate analyses between asthma and the factors studied using prevalence ratio (PR), confidence intervals of 95% (95% CI) and Chi-squared test. Factors associated to asthma in a bivariate analysis were studied using logistic regression and odds ratio (OR). We included 3,033 students, aged 13–14 yrs, selected from 37 schools. The prevalence of asthma was 13.1%. Being female (OR = 1.40; 95%CI:1.11–1.77), the presence of a mother who smokes (OR = 1.32; 95%CI:1.04–1.66), a cat in the domicile (OR = 1.32; 95%CI:1.04–1.69), being the firstborn (OR = 1.34; 95%CI:1.07–1.68), frequent use of paracetamol (OR = 1.45; 95%CI: 1.15–1.84), the presence of rhinitis (OR = 5.15; 95%CI:3.89–6.82) and eczema (OR = 2.35; 95%CI:1.73–3.19) were independently associated to asthma. Environmental and socio-demographic factors were associated to asthma in adolescents in Rio de Janeiro, irrespective of the presence of others allergic diseases. Interventions acting on these factors may decrease the occurrence of asthma in this population.

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The hypothesis that improvement in the public health conditions occurring in the major urban centers as the second half of last century, leading to less natural exposure to bacterial infections, is related to the increase in the prevalence of asthma in developed countries with a western life style, such as the UK, Australia, New Zealand and the USA, gained popularity as a possible global unifying explanation for the increase in allergic diseases (1, 2). However, recent studies using the asthma questionnaire of the International Study of Asthma and Allergies in Childhood (ISAAC) have been demonstrating that the prevalence of asthma is high among adolescents in less developed countries such as

Brazil and others in Latin America, with some cities presenting higher indices of the disease among students aged 13–14 than the world average (3).

Epidemiological studies in different countries, in adolescents, have demonstrated associations between asthma and various factors, including being female (4), exposure to domiciliary allergens and exposure to bacterial endotoxins in early childhood (5), concomitance with other allergic diseases (6), environmental pollution (7), type of diet and obesity (8, 9), number of siblings and order of birth (10).

Although asthma exhibits a high prevalence in Brazil and constitutes an important problem for

public health, little is known about the factors that may influence this prevalence, pathogenesis and severity in our environment. The aim of this work was to study the association between environmental and socio-demographic factors and asthma in adolescents in Rio de Janeiro State.

Materials and methods

Study design and population

This cross-sectional study included in Phase III of the ISAAC and follows its methodological guidelines (11). It was conducted in Nova Iguacu, a municipality situated in the metropolitan region of Rio de Janeiro city, at an altitude of 25 m, and has a tropical climate. Its population is 754,485, constituted largely of low-income socio-economic classes, with a literacy rate of around 85% and whose principal economic activities are in industry and commerce (12). The study focused on students aged 13 and 14. At the time of study, there were about 32,000 adolescents in the age range of interest, distributed among 103 public schools and 75 private, the respective public-private proportions being approximately 2:1 (12). Schools were selected using a random number table. In accordance with the ISAAC protocol, to obtain a representative sample for each participating center, the sample size proposed is 3000 students, drawn from a minimum of 10 schools (11). The total number of schools drawn was determined by the number of students aged 13 and 14 in each school until completion of the suggested sample size. Those schools whose principals refused to participate, were excluded and substituted by others drawn in sequence.

Asthma, allergic rhinitis and atopic eczema

Asthma was defined by the overall global score proposed by Solé and collaborators. These authors validated the asthma module of the ISAAC questionnaire for adolescents in Brazil, and attributed to each question points ranging from 0 to 2 up to a maximum score of 14. Asthmatic patients who frequent the allergy outpatients clinic of a university institution for at least 1 yr were considered as the 'gold standard', and as the control group, patients in the same age range, attended by other specialty clinics, were used. At the cut-off point 6, the sensitivity and specificity for the diagnosis of asthma were 89% and 100% respectively (13). Adolescents who obtained an overall score ≥ 6 were considered asthmatic. Allergic rhinitis was

defined as a positive reply to the question, 'In the past 12 months, has this nose problem (sneezing or a running or a blocked nose) been accompanied by itch-watery eyes?', which present specificity of 96.5% compared with skin prick test for aeroallergens (14). Atopic eczema was defined by a positive reply to the question, 'Have you had itchy rash at any time in the past 12 months?'. The sensitivity and specificity of this question was evaluated in different studies and was found to vary from 74% to 93% (15).

Demographics and environmental factors

Gender, the level of the mother's education (categorized as illiterate or primary and secondary or advanced); the presence of older siblings (0 vs. 1 or more) and the area where the schools were located, were defined according to the replies to the questionnaires. Nova Iguacu is divided administratively into five areas denominated Integrated Planning Sectors (IPS): North – excluded from the research, as it is an environmental preservation area, occupied by only 1% of the population; the Southeast, Northeast and Northwest IPSs, where the majority of the schools are located in semi-rural areas, with paved streets and little road vehicle traffic, were categorized for the purposes of the study as rural locations; and the Central IPS, where the schools are situated in the densely populated areas, close to major highways, was categorized as an urban location (12). Exposure to tobacco smoke was defined by replies to the questions: 'Does either parent (or your guardian) smoke cigarettes?' and categorized into male and female. The presence of pets was evaluated by the question: 'In the last 12 months, have you had a cat/dog at home?'; exposure to environmental pollutants, such as particulates from diesel combustion, was evaluated from replies to the question: 'How often do trucks pass through the street where you live, on weekdays?', replies, such as, 'Frequently through the day' and 'Almost the whole day', being considered as significant exposure (16). Prior use of paracetamol was evaluated by replies to the question: 'In the past 12 months, how often, on average, have you taken paracetamol (Tylenol®, Dórico®)?' The taking of this medicine at least once a month in the last 12 months was regarded as important for this study (17).

Data collection

The interviewers were trained and received the manual of the study detailing the procedure for

applying the questionnaires. The data collection was performed between April and September 2002. All the 13–14 yr olds, irrespective of academic level, present at school on the day of the questionnaire, participated. For detection of asthma, a structured, self-applicable and validated questionnaire was used (11), consisting of eight questions about the disease symptoms, present and past, and also their degree of severity. The investigation was limited to the last 12 months in order to reduce errors of memory and possible seasonal interference. For the environmental factors, a self-applicable questionnaire was used, the 'Environmental Questionnaire – 13–14 age group', developed by the ISAAC Steering Committee (ISC) (18), filled after the questionnaire about asthma. Heeding ISC orientation, some of the original questions were excluded in order to adapt them to local conditions. The translation and customization of the questionnaire to our scenario were evaluated by a pre-test, conducted at a public school selected at random and not included in investigation. The data on allergic rhinitis and atopic eczema were obtained by means of translated, validated ISAAC questionnaires appropriate for these diseases (19, 20).

Statistical analysis

The variables were described using frequency distribution. Bivariate analyses were initially conducted between asthma and the environmental and socio-demographic factors. Comparisons between proportions were performed using the chi-squared test, the strength of the associations was quantified by prevalence ratio (PR) and tested for statistical significance using 95% confidence intervals (CI). Then, logistic regression and an odds ratio (OR) were used by means of multivariate models to study the association of each factor with asthma independently. The software, STATA version 7.0 (Stata Corp., College Station, TX, USA) was used for the analysis.

Ethical aspects

The school principals and those responsible for the students gave their informed consent. The study was approved by the Ethics Committee from the University Hospital Clementino Fraga Filho, Universidade Federal do Rio de Janeiro.

Results

A total of 3262 questionnaires were filled, although 77 were excluded because of filling

Table 1. Sample characteristics – Nova Iguacu, RJ – 2002

Variables	Total (n = 3033)	Frequency (%)	95% CI
Asthma	398	13.1	11.9–14.3
Age (yr)			
13	1710	56.4	54.5–58.1
14	1323	43.6	41.8–45.4
Gender			
Male	1521	50.1	48.3–51.9
Female	1512	49.9	48.0–51.6
School type			
Public	2114	69.6	68.0–71.3
Private	919	30.4	28.6–31.9
School location			
Southwest	474	15.6	14.3–16.9
Northeast	403	13.3	12.0–14.5
Center	1800	59.4	57.5–61.0
Northwest	356	11.7	10.6–12.9
Cigarette smoking*			
Mother	741	24.7	23.1–26.3
Father	700	23.4	21.8–24.9
Non-smokers	1561	51.9	50.1–53.7
Cat in domicile**			
Yes	803	26.8	25.2–28.4
No	2193	73.2	71.5–74.7
Dog in domicile†			
Yes	2328	77.4	75.8–78.8
No	680	22.6	21.1–24.1
Intense truck traffic‡			
Yes	1641	54.6	52.8–56.4
No	1362	45.4	43.5–47.1
Mother's education§			
First Grade – Primary	1562	52.0	50.2–53.2
Second Grade – Secondary	786	26.3	24.6–27.8
Advanced	359	11.9	10.8–13.1
No schooling	293	9.8	8.72–10.8
Older siblings			
None	1147	37.8	36.0–39.5
1	938	30.9	29.2–32.6
2 or more	948	31.3	29.5–32.9
Use of paracetamol¶			
Yes	878	29.8	28.2–31.5
No	2061	70.2	68.4–71.7
Rhinitis			
Yes	275	9.1	8.0–10.1
No	2758	90.9	89.8–91.9
Eczema			
Yes	281	9.3	8.25–10.3
No	2752	90.7	89.6–91.7

Missing information: *31; **37; †25; ‡30; §33; ¶94.

errors, and 152 students were not the right age for the purposes of this study. Table 1 presents the main characteristics of the 3033 students, from 19 public schools and 18 private, whose questionnaires were subjected to analysis. 398 students (13.1%) were diagnosed as asthmatic. The mean and median score among the asthmatic were 8.43 and 8.0, respectively, whereas, among the non-asthmatic, the values were 1.12 and zero. The relative proportion between public and private school students was 2.3:1.

Table 2 presents the result of the bivariate analyses. The strongest associations found

Table 2. Result of the bivariate analysis between asthma and environmental/socio-demographic factors in adolescents in Nova Iguaçu – RJ, 2002

Factors	Asthma		PR	95% CI	p-value
	Yes [n = 398 (%)]	No [n = 2635 (%)]			
Gender					
Male	150 (9.9)	1371 (90.1)	1.0	1.38–2.01	0.000*
Female	248 (16.4)	1264 (83.6)	1.66		
School location					
Rural	152 (12.3)	1081 (87.7)	1.0	0.92–1.34	0.29
Urban	246 (13.7)	1554 (86.3)	1.11		
Mother smokes					
No	283 (12.3)	2001 (87.7)	1.0	1.031–1.53	0.028
Yes	115 (15.5)	626 (84.5)	1.25		
Father smokes					
No	303 (13.1)	1999 (86.9)	1.0	0.81–1.24	1.00
Yes	92 (13.1)	608 (86.9)	1.000		
Cat in domicile					
No	270 (12.3)	1923 (87.7)	1.0	1.02–1.52	0.033
Yes	123 (15.3)	680 (84.7)	1.24		
Dog in domicile					
No	87 (12.7)	593 (87.3)	1.0	0.83–1.30	0.70
Yes	309 (13.8)	2019 (86.2)	1.04		
Intense truck traffic					
No	166 (12.1)	1210 (87.9)	1.0	0.96–1.40	0.118
Yes	228 (14.0)	1398 (86.0)	1.16		
Mother's education					
Illiterate/primary	234 (12.6)	1621 (87.4)	1.00	0.92–1.34	0.157
High/advanced	161 (14.1)	984 (85.9)	1.11		
Older siblings					
Yes	222 (11.8)	1664 (88.2)	1.00	1.08–1.57	0.006
No	176 (15.3)	971 (84.7)	1.30		
Use of paracetamol					
No	225 (11.0)	1836 (89.0)	1.00	1.40–2.04	0.000*
Yes	162 (18.5)	716 (81.5)	1.69		
Rhinitis					
No	281 (10.2)	2477 (91.0)	1.0	3.50–4.98	0.000*
Yes	117 (42.5)	158 (57.5)	4.18		
Atopic eczema					
No	316 (11.5)	2436 (88.5)	1.0	2.06–3.13	0.000*
Yes	82 (29.2)	199 (70.8)	2.54		

PR, prevalence ratio; CI, confidence interval; *p < 0.001.

were asthma with rhinitis (PR 4.18; 95% CI, 3.50–4.98) and eczema (PR, 2.54; 95% CI, 2.06–3.13), as well as the use of paracetamol (PR, 1.69; 95% CI, 1.40–2.04). No association was found between asthma and tobacco smoking on the part of the father or that of both parents; the presence of a dog at home in the last 12 months, or dogs and cats together in the same domicile; intense truck traffic, and the mother's educational level. Table 3 presents the results of the multivariate analysis. The factors associated with asthma in the bivariate analysis remained as independent factors for asthma.

Discussion

Despite being high, the prevalence of asthma among Nova Iguaçu adolescents was comparat-

Table 3. Results of the multivariate analysis between asthma and environmental/socio-demographic factors in adolescents in Nova Iguaçu – RJ, 2002

Variables	OR	95% CI	p-value
Female	1.40	1.11–1.77	0.004
Mother smokes	1.29	1.01–1.66	0.039
Cat in domicile	1.32	1.04–1.69	0.025
Firstborn	1.34	1.07–1.68	0.011
Use of paracetamol	1.45	1.15–1.84	0.002
Allergic rhinitis	5.15	3.89–6.82	0.000*
Atopic eczema	2.35	1.73–3.19	0.000*

OR, odds ratio; *p < 0.001.

ively low in relation to that in other cities in Brazil participating in the ISAAC study Phase III. Environmental, socio-economic and genetic factors have been indicated as probably responsible for the different indices of the disease observed between national and international centers (21).

In our study, we observed a predominance of asthma in female adolescents, which conforms to the cross-sectional and longitudinal studies carried out in this age range (4, 22). In general, young men present significantly more chance of developing wheezing and asthma in the first years of life, this risk growing up to age 6–8 yr, declining gradually until adolescence, the period in which the disease becomes more prevalent in women (22). Although recognized, the association of being female and asthma in adolescence has not been well established until today, as a cause. The possible factors pointed out being a history of atopy in parents, especially in the mother, the calibre of the airways associated with hormonal influences, being overweight in the pre-school years, psycho-social aspects and environmental exposures peculiar to each gender. Moreover, epidemiological studies of adolescents have demonstrated possible differences in the level of interest in the actual filling of the questionnaires, with young men tending to underestimate, and young women to overestimate, their symptoms (23).

Several studies have associated the mother smoking with the development of asthma in childhood and adolescence. A longitudinal study conducted in Germany showed that exposure to cigarette smoke during pregnancy significantly increased the risk of sensitivity to aeroallergens [relative risk (RR), 2.27; 95% CI: 1.14–4.52] and asthma in school age (RR: 2.46; 95% CI: 1.28–4.73), suggesting possible synergic mechanisms among genetic and environmental factors in the expression of atopy and asthma *in utero* (24).

In Tucson, Arizona, children under 2-yr-old, whose mothers, but not fathers, smoked at least

10 cigarettes/day presented greater risk of developing asthma between 3 and 6 yr old than those whose mothers were non-smokers (25). A systematic revision showed that children aged 0–2 yr old, whose parents smoked were at higher risk of presenting wheezing, coughing and asthma at 5 and 16 yr old, this risk being greater among pre-school children and for mothers who smoke than for school students and fathers who smoke (26). Withers and collaborators, studying the natural history of respiratory symptoms in a cohort of children aged 6–8 and 14–16 yr, found a significant association with current, persistent symptoms and a late onset of asthma among smokers, whether passive or active (27). Considering these results, the institution of interventions aimed at decreasing smoking could bring benefits in reducing the asthma symptoms in Nova Iguacu students.

Exposure to cats, but not to dogs or both pets, was significantly associated with asthma in our sample. In Stockholm, Sweden, analyzing the interaction between environmental factors and atopy in children 1–4 yr old, whose parents smoke, Lindfors et al. (28) demonstrated an additional effect between exposure to tobacco smoke and allergens from animals, promoting a greater degree of sensitivity to cats, but not to dogs. Overall, it appears that the sensitivity to cats is a risk factor for asthma in childhood and adolescence. However, epidemiological studies about this association have provided findings of difficult interpretation (29). Some show a protective effect from exposure to dogs and cats regarding the development asthma in childhood, but not in adolescents and adults while others report that the effects of association with asthma may vary according to the age of exposure, type of animal and allergic predisposition (30, 31). Their protective effect from exposure to domesticated animals in relation to asthma in childhood has been explained by allergenic stimulation inducing tolerance and/or microbial immuno-stimulation by endotoxins (31). Future studies should be carried out about the degree of sensitivity to pets and its association with asthma in our environment.

Some of our findings can be discussed in relation to the hypothesis of hygiene, although this is currently the object of criticism and controversies (32). There is evidence that family size has been decreasing throughout the last few decades in more developed countries, and this change seems to be an important determinant of the increase in the atopic diseases in children, adolescents and adults (2). Besides this, there seems to exist a strong association between the

birth order and asthma, with a higher prevalence of the disease in firstborn (33). This association was also observed in the adolescents of our study, irrespective of the number of younger siblings or the fact of being an only child. According to the hygiene theory, these findings suggest that the repeated infections transmitted in early childhood by older siblings, crèche and school mates could prevent atopic replies in the younger through a deviation in the immunological balance from lymphocytes $T_H 2$ to $T_H 1$ (32).

The frequent use of paracetamol was strongly associated with asthma in our sample. This association has been described as much in adults as in children, whether through ecological studies relating the increase in sales of the medicine to the prevalence of asthma measured by ISAAC in different countries, or by case-control studies (17, 34). Frequent use of paracetamol could influence asthma and rhinitis in reducing the levels of glutation reduced in the nasal mucus and lower airways, thereby deviating the oxidative/non-oxidative balance in favor of the first segment, favoring inflammation in these places (34). However, as the concomitant use of other analgesics and non-hormonal anti-inflammatories was not evaluated in our study, this finding must be analyzed with caution. Nevertheless, in 2002, Nova Iguacu presented a large number of dengue fever cases. On that occasion, use of paracetamol was recommended by the public health organs to treat the fever characteristic of the disease. This fact suggests that there may indeed have been excessive use of the medication during the research period (35).

Epidemiological studies have consistently shown that asthma and rhinitis are strongly associated, and that rhinitis is a risk factor for the development of asthma (7, 36). The general correlation between the two diseases in children and adolescents analyzed by ISAAC Phase I was significant, the tendency of the prevalence of rhinitis to accompany asthma in the different countries analyzed being of particular interest (1). In our sample, rhinitis was the factor that was associated more strongly with asthma, the presence of ocular symptoms being indicative of an atopic etiology for the disease (14).

Likewise, atopic eczema was significantly associated with asthma in Nova Iguacu adolescents. Studies that evaluate probable factors that lead to the clinical expression of this cutaneous disease and its forms of evolution, show that, in the majority of cases, those who remained affected into adolescence and adulthood presented disseminated infant disease, a family history of atopic eczema and co-morbidity with asthma

and/or allergic rhinitis (37). The case-control study, conducted in Cartagena, Spain, based on the ISAAC questionnaire, showed that school pupils, aged 13–14, with atopic eczema had a greater chance of developing allergic rhinitis (OR: 3.33; 95% CI: 2.45–4.54), asthma (OR: 3.85; 95% CI: 2.74–5.42) and allergic asthma (OR: 4.91; 95% CI: 3.12–7.59) than the control group, the severity of the eczema being directly related to the association with the other allergic diseases in this sample (38). Besides this, it was observed that the younger the age at the onset of atopic eczema, the higher the risk of sensitivity to aeroallergens and of the development of asthma at school age. Longitudinal studies started at birth have demonstrated that the natural history of the atopic manifestations is characterized by the typical progression sequence. In general, the clinical signs of eczema precede those of asthma and rhinitis, this progression being frequently referred to as the atopic march suggesting a relation among the three allergic diseases, which is in accordance with the current vision that contemplates atopy as a systemic disease (22, 39). Furthermore, in relation to allergic rhinitis and atopic eczema, our results showed that the environmental and socio-demographics factors analyzed were associated with asthma regardless of the occurrence of these two diseases.

Our study has limitations. As it is a cross-sectional study, with the exposure and outcome being measured simultaneously, it was not possible in some cases to determine the temporality of the association. For example, if the exposure to a cat or mother's tobacco smoke preceded the appearance of asthma in the adolescents. On the contrary, the finding of associations already detected in other places, by this or another method, make our results probable, indicating a need for subsequent analytical studies to provide confirmation.

In summary, being female, the presence of a smoking mother, having at least one cat in the domicile, being the firstborn and frequent use of paracetamol are shown to be associated with asthma, irrespective of the presence of allergic rhinitis and atopic eczema. Further longitudinal studies that consider the importance of the genetic-environmental relation would allow better knowledge about the influence of these factors on the establishment of asthma in Rio de Janeiro. These findings also indicate that preventive interventions, reducing exposure to and occurrence of these factors, may have an impact on the prevalence of asthma in Nova Iguaçu adolescents.

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