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ORIGINAL ARTICLE

Air Pollution and Recent Symptoms of Asthma, Allergic Rhinitis, and Atopic Eczema in Schoolchildren Aged Between 6 and 7 Years

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ABSTRACT

Objective: The objective of the study was to analyze the relationship between air pollutants and the prevalence of recent symptoms of asthma, allergic rhinitis, and atopic eczema in schoolchildren aged between 6 and 7 years.

Patients and Methods: The prevalence of recent (previous 12 months) symptoms of allergic diseases was obtained by means of the questionnaire of the International Study of Asthma and Allergies in Childhood (ISAAC), Spain, with the participation of 7 centers (Asturias, Barcelona, Bilbao, Cartagena, La Coruña, Madrid, and Valencia) and 20 455 schoolchildren aged between 6 and 7 years, from 2002 to 2003. The pollutant detection systems of the aforementioned centers provided the mean annual concentrations of sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and total suspended particulate matter.

Results: The annual average concentration of SO_2 showed a significant association with a higher prevalence of recent severe asthma (adjusted odds ratio [aOR] between level-1 and level-3 pollution, 1.32; 95% confidence interval [CI], 1.01–1.73), rhinitis (aOR, 1.56; 95% CI, 1.39–1.75), and rhinoconjunctivitis (aOR, 1.70; 95% CI, 1.45–2.00). The annual average concentration of CO was associated with a higher prevalence of rhinitis (aOR, 1.65; 95% CI, 1.34–2.04), rhinoconjunctivitis (aOR, 1.76; 95% CI, 1.31–2.37), and eczema (aOR, 1.55; 95% CI, 1.17–2.04). The annual average concentration for NO_2 and total suspended particulate matter showed inverse associations with the prevalence of nocturnal dry cough.

Conclusions: Findings suggest that air pollutants such as SO_2 and CO increase the risk of recent symptoms of asthma and allergic rhinitis in schoolchildren aged between 6 and 7 years in Spain.

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Contaminación del aire y síntomas recientes de asma, rinitis alérgica y eccema atópico en escolares de 6 y 7 años

RESUMEN

Introducción: El objetivo del estudio ha sido analizar la relación entre contaminantes del aire y la prevalencia de síntomas recientes de asma, rinitis alérgica y eccema atópico, en escolares de 6 y 7 años.
Pacientes y métodos: La prevalencia de síntomas de enfermedades alérgicas recientes (últimos 12 meses) se obtuvo mediante el cuestionario del estudio ISAAC (International Study of Asthma and Allergies in Childhood) España, con la participación de 7 centros (Asturias, Barcelona, Bilbao, Cartagena, La Coruña, Madrid y Valencia) y 20.455 escolares de 6 y 7 años, durante 2002–2003. De los sistemas de detección de contaminantes de los centros citados se obtuvieron datos de las concentraciones anuales medias de dióxido de azufre (SO_2), dióxido de nitrógeno (NO_2), monóxido de carbono (CO) y total de partículas en suspensión.
Resultados: La concentración media anual (CMA) de SO_2 se asoció significativamente con una mayor prevalencia de asma grave reciente (*odds ratio* ajustada [ORa], nivel 3 sobre nivel 1 de contaminación=1,32; intervalo de confianza [IC] del 95%, 1,01–1,73), rinitis (ORa = 1,56; IC del 95%, 1,39–1,75) y rinoconjuntivitis (ORa = 1,70; IC del 95%, 1,45–2,00). La CMA de CO se asoció con una prevalencia más alta de rinitis (ORa = 1,65; IC del 95%, 1,34–2,04), rinoconjuntivitis (ORa = 1,76; IC del 95%, 1,31–2,37) y eccema atópico (ORa = 1,55; IC del 95%, 1,17–2,04). Las CMA de NO_2 y de total de partículas en suspensión presentaron asociaciones inversas con la prevalencia de tos seca nocturna.
Conclusiones: Se indica qué contaminantes del aire, como SO_2 y CO, incrementan el riesgo de síntomas recientes de asma y rinitis alérgica en escolares de 6 y 7 años de nuestro medio.

Introduction

The effect of air pollution on allergic diseases is the subject of debate. Some researchers consider it to be responsible for the observed increase in these diseases in the pediatric population of developed countries, whereas others believe its effect to be slight.[1,2] Epidemiologic research on air pollution as a potential risk factor for allergic diseases has increased in recent years despite the considerable methodological difficulties involved. These difficulties include the following: type of study design; pollutants to be evaluated, their measurement, and the interactions between them; diagnosis of symptoms or diseases in the short or long term and whether they are allergic or not; populations studied; potential confounding factors, climate, geographic, and socioeconomic variables; and the statistical models.

Several epidemiologic studies have found that exposure to air pollutants and traffic exhaust fumes is associated with the risk of developing allergic rhinitis[3] and asthma[4,5] in pediatric populations; other studies, however, were not able to show these effects and the debate remains open.[6]

The International Study of Asthma and Allergies in Childhood (ISAAC) has made it possible to obtain standardized measurements of symptoms of these diseases in school-going populations, with large sample sizes.[7] Spain currently has standardized measurements of air pollutants in several cities, obtained via the monitoring networks managed by the regional environmental agencies and city councils.[8] However, studies on the impact of air pollution on pediatric populations are rare in Spain.

Phase III of the ISAAC study was carried out in Spain during 2002 with the participation of 8 centers.[9] Considerable differences were observed in the study of the geographic distribution of the prevalence of asthma and allergic rhinitis.[10,11] One of the working hypotheses was that the estimated differences might be linked to the air pollutants in the respective centers. The objective of this study was to analyze the association between air pollutants and the prevalence of recent symptoms of asthma, allergic rhinitis, and atopic eczema.

Patients and Methods

We performed a semi-individual population-based study[12] based on the ISAAC cross-sectional study. This study presents 3 standardized questionnaires to estimate the prevalence of asthma, allergic rhinitis, and atopic eczema; the questionnaires were to be completed by the parents of schoolchildren between the ages of 6 and 7 years. Permission for the children to take part in the study was obtained from their parents and the Asturias regional ethics committee approved the study for all the centers.

Complete information on risk factors was obtained in the following 6 of the 8 centers taking part in phase III of the ISAAC study: Asturias, Barcelona, Bilbao, Cartagena, Madrid, and Valencia, together with La Coruña, which performed the study in 2003. The median participation of the school-going population was 77.4% (range, 89.2%-53.4%).

The exposure variables correspond to the mean concentrations over 24 hours of the air pollutants sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and total suspended particulate matter (TSP) in 2002, except in the case of Madrid and La Coruña, where the figures correspond to 2003. This information and the mean annual figures for temperature and relative humidity were obtained from the environmental agencies of the autonomous communities of Asturias, Catalonia, Galicia, Madrid, Murcia, Basque Country, and Valencia. We considered 3 levels of exposure, according to mean annual levels of pollutants (percentiles 0-25 [level 1], percentiles 26-74 [level 2], and percentile 75 or higher [level 3]). For Barcelona and Madrid, the data were obtained from the stations near the ISAAC centers in these cities and for Asturias, data were obtained from the towns of Avilés, Gijón, and Oviedo.

The variables (recent symptoms of asthma, allergic rhinitis, and atopic eczema) were collected from the ISAAC questionnaire[10,11] and cases were considered using the definitions shown in Table 1. As well as the ISAAC questionnaire, the parents completed an environmental questionnaire on risk factors that was developed by the ISAAC center in New Zealand (http://isaac.auckland.ac.nz) and included questions relating to the type of energy used in the home, the presence of animals in the home, exposure to tobacco smoke, use of antibiotics and paracetamol, number of older siblings, mother's educational level, use of oral contraceptives by the mother, and breastfeeding. These factors and the mean annual figures for temperature and humidity were studied as potential confounding factors. The question on the frequency of trucks passing through the street where the child's home is located was not included in order to prevent overadjustment with the studied pollutants.

Table 1
Definitions of Cases of Recent Symptoms of Asthma, Allergic Rhinitis, and Atopic Eczema, Based on the ISAAC Questionnaire

1. Recent wheezing
Affirmative answer to the question, Has your child had chest wheezing in the past 12 months?
2. Recent severe asthma
Affirmative answer to the question on recent wheezing and any of the following answers to the following questions:
How many attacks of wheezing has your child had in the past 12 months? 4 or more attacks
How many times has your child woken up in the night due to wheezing in the past 12 months? One or more nights per week
In the past 12 months, was the chest wheezing severe enough for your child to have to stop to breathe every 2 words? Yes
3. Nocturnal dry cough
Affirmative answer to the question, Has your child had a dry cough at night apart from a cough associated with a cold or chest infection, in the past 12 months?
4. Rhinitis
Affirmative answer to the question, Has your child suffered from sneezing, or a runny or blocked nose not associated with a cold or 'flu' in the past 12 months?
5. Rhinoconjunctivitis
Affirmative answer to the question, Has your child had these nose problems accompanied by itchy, watery eyes in the past 12 months?
6. Atopic eczema
Affirmative answer to the question on the location of red marks in the past 12 months: Did these itchy red marks appear in one of the following places: elbow-joint fold, behind the knees, on the instep, under the buttocks, around the neck, eyes or ears?

Statistical Analysis

The prevalence of symptoms was calculated by dividing the total number of participants in each ISAAC center by the number of cases. The Pearson product moment correlation was used to study the correlations between the pollutants. Multivariate logistic regression models were used to quantify the associations between exposures and the result variables. Each result variable and the potential confounding factors were studied, and factors with a statistical significance of P=.25 were included in the model to obtain a final model with associated factors with a significance of P<.05. When this model was obtained, we incorporated the concentrations of pollutants in the 3 levels described, and the odds ratios (OR), their tendency, and the 95% confidence intervals (CI) were calculated. We used the STATA statistical software package, version 6.0 (Stata Corporation, College Station, Texas, USA). The goodness of fit of the models was studied using the Hosmer-Lemeshow goodness-of-fit test.

Results

The study included 20 455 schoolchildren between the ages of 6 and 7 years (49.8% boys) from the 7 centers (Table 2). Three of the centers were located in the Mediterranean area, 1 in central Spain, and 3 in the Atlantic area. The median temperature was 14.6°C and the median relative humidity was 73%.

Table 3 shows a summary of the mean annual concentrations of pollutants in the ISAAC centers. There were considerable differences between the centers, particularly for NO_2 and SO_2. The minimum for NO_2 was 9.6 µg/m^3 (24 h) and the maximum was 59.9 µg/m^3 (24 h), where as the minimum and maximum for SO_2 were 4.0 and 19.9 µg/m^3 (24 h), respectively. The correlations of the pollutants (Table 4) were positive between SO_2 and CO and between NO_2 and TSP; the correlations were negative between the other pollutants. Prevalences of recent symptoms (Table 5) showed large differences between the centers, particularly for nocturnal dry cough and rhinitis.

Table 6 shows the results of the logistic regression analysis. The mean annual concentrations of SO_2 were associated with prevalences of rhinitis, rhinoconjunctivitis, recent severe asthma, and nocturnal dry cough, with significant adjusted tendencies. In all the prevalences of symptoms, except nocturnal dry cough, higher adjusted OR were observed at higher levels of SO_2 concentration; this is particularly clear in the case of rhinoconjunctivitis (adjusted OR between level-3 and level-1 pollution [aOR_{3-1}], 1.70; 95% CI, 1.45–2.00), rhinitis (aOR_{3-1}, 1.56; 95% CI, 1.39–1.75), and recent severe asthma (aOR_{3-1}, 1.32; 95% CI, 1.01–1.73). Higher mean annual concentrations of CO were associated with higher prevalences of rhinitis (aOR_{3-1}, 1.65; 95% CI,

Table 2
Characteristics of the Study Population and Climate Variables in the Spanish ISAAC Centers (n=20 455)[a]

Variables, No. (%)	
Age	
6 years	9 817 (48.0%)
7 years	10 631 (52.0%)
Sex	
Girls	10 249 (50.2%)
Boys	10 165 (49.8%)
Geographic area	
Mediterranean	
Cartagena	2 726 (13.3%)
Valencia	3 393 (16.6%)
Barcelona	2 902 (14.2%)
Central Spain	
Madrid	2 344 (11.5%)
Atlantic	
Bilbao	3 046 (14.9%)
Asturias	3 027 (14.8%)
La Coruña	3 017 (14.8%)
Born in Spain	
Yes	19 228 (94.7%)
No	1 077 (5.3%)
Educational level of mother	
Higher and university education	6 232 (30.5%)
Medium-low and no schooling	14 223 (69.5%)
Climate variables	
Mean annual temperature	
Range	13.9°C–20.2°C
Median	14.6°C
Mean (SD)	16°C (2.3°C)
Mean annual relative humidity	
Range	59%–81%
Median	73%
Mean (SD)	71.8% (6.8%)

Abbreviation: SD, standard deviation.
[a]Data are unavailable for some values.

Table 3
Mean Annual Concentrations of Air Pollutants in the 7 Spanish ISAAC Centers in 2002[a]

	SO_2, 24 h (µg/m^3)	CO, 24 h (µg/m^3)	NO_2, 24 h (µg/m^3)	TSP, 24 h (µg/m^3)
Minimum	4.0	0.5	0 9.6	38.0
25th percentile	10.2	0.50	19.0	42.4
Median	12.0	0.7	45.0	49.4
75th percentile	16.7	0.9	55.9	58.2
Maximum	19.9	1.2	59.9	59.7
Mean (SD)	12.4 (4.6)	0.8 (0.2)	40.4 (18.8)	50.5 (7.5)

Abbreviations: CO, carbon monoxide; SD, standard deviation; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; TSP, total suspended particles.
[a]Centers in La Coruña and Madrid, 2003.

Table 4
Correlation Coefficients for the Mean Annual Concentrations of Air Pollutants in the Spanish ISAAC Centers in 2002[a]

	SO_2	CO	NO_2	TSP
SO_2	1.00			
CO	0.6203	1.00		
NO_2	−0.5505	−0.5458	1.00	
TSP	−0.1615	−0.3641	0.4410	1.00

Abbreviations: CO, carbon monoxide; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; TSP, total suspended particulates.
[a]Centers in La Coruña and Madrid, 2003.

Table 5
Prevalence (%) of Recent Symptoms of Asthma, Allergic Rhinitis, and Atopic Eczema in the Past 12 Months in the Spanish ISAAC Centers in 2002[a]

	Wheezing	Recent Severe Asthma	Nocturnal Dry Cough	Rhinitis	Rhinoconjunctivitis	Eczema
Minimum	8.4	2.0	14.7	10.1	4.0	4.3
25th percentile	9.2	3.2	17.0	16.3	7.9	5.4
Median	11.0	3.6	20.7	20.1	9.1	7.0
75th percentile	12.2	4.0	21.6	23.3	11.0	7.9
Maximum	12.9	4.7	23.6	24.7	11.8	8.7

[a]Centers in La Coruña and Madrid, 2003.

1.34-2.04), rhinoconjunctivitis (aOR_{3-1}, 1.76; 95% CI, 1.31–2.37), and atopic eczema (aOR_{3-1}, 1.55; 95% CI, 1.17–2.04), although the tendency of this model did not show a good fit (*P*=.0074). Associations were not found between mean annual concentrations of NO_2 and the symptoms studied, except for nocturnal dry cough, for which the association was negative. Although no associations were found in the adjusted tendencies, the levels with higher concentrations of NO_2 had higher ORs than the lower levels for prevalences of rhinitis, wheezing, and recent severe asthma. Mean annual concentrations of TSP showed negative associations with rhinitis and nocturnal dry cough, though the model for rhinitis did not show a good fit in the Hosmer-Lemeshow goodness-of-fit test (χ^2=19.55; *P*=.0122). The logistic regression models showed a good fit in general for all symptoms, except the models for atopic eczema and concentrations of CO, NO_2, and TSP.

Discussion

The results of this study indicate that, in schoolchildren between the ages of 6 and 7 years, the higher the concentration of SO_2, the greater the risk of presenting rhinitis, rhinoconjunctivitis, and recent severe asthma. In the centers with higher concentrations of CO, the risk of symptoms of rhinitis and rhinoconjunctivitis was greater. Furthermore, higher concentrations of NO_2 and TSP were associated with a lower risk of nocturnal dry cough.

The link between concentrations of SO_2 and its secondary compounds (acid aerosols) and the prevalence of bronchitis and other respiratory symptoms in pediatric populations and exacerbation of symptoms in asthmatic patients is well known.[13] Recent studies in pediatric populations have found associations between the prevalence of allergic diseases and concentrations of this pollutant in Poland and the Czech Republic,[14] Brazil,[15] Taiwan,[16] and France,[17] although this association has not been found in other studies.[18] In schoolchildren in Cartagena,[19] a higher prevalence of atopic dermatitis was observed in the area of the city with higher concentrations of SO_2 and TSP. Furthermore, an increase has been reported in consultations due to allergic rhinitis in association with increased concentrations of SO_2.[20] The increases in recent symptoms associated with higher concentrations of SO_2 might be due to the effect of these concentrations on the respiratory system, where they produce irritation and inflammation, thereby facilitating the onset of the symptoms of allergic diseases; this could lead to the increase in the prevalence of these diseases in the susceptible population. This agent may also be an indicator of other air pollutants not included in this study.

CO is not considered to have any effect at the concentrations recorded in our study.[16] Nevertheless, higher prevalences of allergic rhinitis and asthma have been observed on areas with higher concentrations of CO.[21] NO_2 is the indicator of so-called modern pollution, caused by traffic and industrial processes,[22] and increases in asthma and wheezing have been reported at higher concentrations of this pollutant.[23,24] In our study, however, this agent revealed no association with the prevalence of symptoms of allergic diseases; this finding agreed with those of other authors[17] and the pollutant was only associated with a reduction in the prevalence of nocturnal dry cough. Concentrations of TSP have been associated with the prevalence of respiratory symptoms in the pediatric population[25] and, in Valencia, concentrations of black smoke were predictive of hospital emergency visits due to asthma in adults.[26] The negative associations of concentrations of TSP and NO_2 with the risk of nocturnal dry cough may have been due to the negative correlations with concentrations of SO_2 and CO.

This study, carried out in schools[27], has a large sample size and included the largest urban and industrial areas in Spain. The questions referred to recent symptoms in order to avoid possible information bias.[28] The semi-individual design made it possible to control for different confounding factors and adjust for other variables; standardized methods were followed in the measurement of the pollutants. Two pollutants (NO_2 and TSP) presented higher mean annual values than those considered to be the maximum for the protection of human health, according to European guidelines (40 $\mu g/m^3$).[29]

The limitations of the study include the following: *a)* the transversal design of the study made it impossible to establish a conclusive cause-effect relationship between the pollutants and the symptoms studied; *b)* exposure was considered to be the same for all the schoolchildren in each center, as an aggregate datum, and this would involve some classification bias as there may be considerable differences in pollutant concentrations within the same city. In Madrid and Barcelona, we studied the stations corresponding to the ISAAC centers, and in Asturias, we studied 3 large towns (Avilés, Oviedo, and Gijón), which included 75% of the population of the ISAAC study in Asturias: *c)* measurement of exposure is only a general reflection of the state of the pollutants in each center, and it has been stated that measurements from fixed stations would indicate personal exposure with few errors for TSP but with less certainty for NO_2[30]; *d)* it was not possible to study other pollutants such as ozone and particulate matter up to 10 or 2.5 micrometers (PM_{10} or $PM_{2.5}$), as measurements for these pollutants were not available for all the participating centers; *e)* bias may be present in the comprehension of the questions by the parents, as no objective medical diagnosis was made[31]; *f)* children with respiratory diseases or a family history of allergy may have moved from the urban centers to more peripheral areas, and this would underestimate the risk in these centers; and *g)* the study did not take into account other factors such as genetic predisposition,[32] interaction between pollutants, or unknown factors that may have had an effect.

In summary, the results of the study indicate that air pollutants such as SO_2 and CO increase the risk of recent symptoms of asthma and allergic rhinitis in schoolchildren between the ages of 6 and 7 years in Spain. Further study of these exposures and their effects may be of use in order to prevent them in future.

Table 6
Air Pollutants and Symptoms of Asthma, Allergic Rhinitis, and Atopic Eczema in the Past 12 Months, by Levels of Pollutant Concentration With Tendency and Odds Ratios Adjusted Using Logistic Regression[a]

	SO_2, 24 h (μg/m³)	CO, 24 h (μg/m³)	NO_2, 24 h (μg/m³)	TSP, 24 h (μg/m³)
Rhinitis				
Level 1	1.00	1.00	1.00	1.00
Level 2, OR [95% CI]	1.40 [1.26–1.56]	0.94 [0.84–1.05]	0.96 [0.79–1.18]	0.26 [0.19–0.34]*
Level 3, OR [95% CI]	1.56 [1.39–1.75]	1.65 [1.34–2.04]	1.84 [1.15–2.96]	0.84 [0.76–0.94]*
Tendency, *P*	<.001	.011	.270	.047
Rhinoconjunctivitis				
Level 1	1.00	1.00	1.00	1.00
Level 2, OR [95% CI]	1.49 [1.29–1.73]	0.99 [0.87–1.15]	0.75 [0.65–0.86]	0.25 [0.17–0.37]
Level 3, OR [95% CI]	1.70 [1.45–2.00]	1.76 [1.31–2.37]	0.98 [0.85–1.14]	0.82 [0.71–0.95]
Tendency, *P*	<.001	.047	.856	.145
Wheezing				
Level 1	1.00	1.00	1.00	1.00
Level 2, OR [95% CI]	0.98 [0.87–1.12]	0.89 [0.77–1.03]	1.14 [0.87–1.49]	0.73 [0.50–1.07]
Level 3, OR [95% CI]	1.08 [0.94–1.25]	1.01 [0.78–1.31]	1.37 [0.74–2.52]	1.06 [0.93–1.22]
Tendency, *P*	.341	.524	.360	.233
Recent severe asthma				
Level 1	1.00	1.00	1.00	1.00
Level 2, OR [95% CI]	1.29 [1.02–1.63]	0.87 [0.67–1.12]	1.07 [0.67–1.71]	0.37 [0.19–0.72]
Level 3, OR [95% CI]	1.32 [1.01–1.73]	1.54 [0.97–2.46]	2.10 [0.71–6.24]	0.89 [0.70–1.13]
Tendency, *P*	.027	.424	.998	.567
Nocturnal dry cough				
Level 1	1.00	1.00	1.00	1.00
Level 2, OR [95% CI]	1.50 [1.12–2.00]	0.88 [0.78–1.01][b]	0.59 [0.46–0.76]	0.43 [0.31–0.59]
Level 3, OR [95% CI]	1.17 [1.02–1.33]	1.05 [0.83–1.33][b]	0.72 [0.44–1.17]	0.92 [0.70–1.22]
Tendency, *P*	<.001	.604	.012	<.001
Atopic eczema				
Level 1	1.00	1.00	1.00	1.00
Level 2, OR [95% CI]	1.12 [0.98–1.29]	1.06 [0.92–1.23]	0.86 [0.75–0.99]	0.68 [0.46–1.01]
Level 3, OR [95% CI]	1.15 [0.99–1.35]	1.55 [1.17–2.04]	0.90 [0.77–1.05]	1.00 [0.86–1.16]
Tendency, *P*	.063	.025[b]	.180[b]	.755[b]

Abbreviations: CO, carbon monoxide; CI, confidence interval; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; TSP, total suspended particulates.

[a]The odds ratios of the different symptoms were adjusted as follows: *a)* rhinitis: sex, use of antibiotics or paracetamol in the first year of life, use of paracetamol in the past 12 months, maternal smoking, elder siblings, electric heating, temperature, and humidity; *b)* rhinoconjunctivitis: sex, use of antibiotics or paracetamol in the first year of life, use of paracetamol in the past 12 months, maternal smoking, electric heating, and temperature; *c)* wheezing: sex, use of antibiotics or paracetamol in the first year of life, use of paracetamol in the past 12 months, maternal smoking, cooking with gas, presence of a cat in the home in the first year of life, temperature, and humidity; *d)* recent severe asthma: sex, use of antibiotics or paracetamol in the first year of life, use of paracetamol in the past 12 months, maternal smoking, cooking with electricity, temperature, and humidity; *e)* nocturnal dry cough: age, sex, use or oral contraceptives by the mother, use of antibiotics or paracetamol in the first year of life, use of paracetamol in the past 12 months, maternal smoking, gas heating, presence of a cat or dog in the home in the first year of life, temperature and humidity; and *f)* eczema: educational level of mother, use of antibiotics or paracetamol in the first year of life, maternal smoking, cooking with gas or electricity, and temperature.

[b]Goodness of fit of model, $P<.05$.

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