

Factors associated with allergic rhinitis in children and adolescents from northern Mexico: International Study of Asthma and Allergies in Childhood Phase IIIB

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ABSTRACT

The epidemiology of allergic diseases has not been studied extensively in Mexico. The present study, based on the International Study of Asthma and Allergies in Childhood Phase IIIB survey, reports the prevalence of allergic rhinitis and the associated risk factors in the pediatric population in four cities in northern Mexico. Children (6–7 years old) and adolescents (13–14 years old) in public elementary and secondary schools were surveyed in 2002 and 2003. The subjects were chosen randomly from Ciudad Victoria, Mexicali, Monterrey, and Tijuana. The following categories were analyzed: occurrence of rhinitis symptoms (currently or in the last 12 months), rhinoconjunctivitis symptoms, a previous diagnosis of allergic rhinitis, and relevant environmental factors. Factors associated with rhinitis that were identified previously with the chi-squared test were analyzed using logistic regression. The number of valid questionnaires was 10,892 for schoolchildren and 12,299 for adolescents. In 6- to 7-year-old children, the following frequencies were determined: rhinitis (ever), 27.9%; current rhinitis, 24.2%; rhinoconjunctivitis, 9.2%; and diagnosis of allergic rhinitis, 5.5%. The corresponding frequencies in 13- to 14-year-old children were 33.3, 34.1, 18.4, and 3.8%. In both 6- to 7-year-old and 13- to 14-year-old children, all rhinitis items were associated with asthma symptoms, dermatitis symptoms, paracetamol consumption, and maternal smoking (odds ratio, >1; $p < 0.05$). The main risk factors associated with allergic rhinitis symptoms in children and adolescents from cities in northern Mexico were other allergic conditions, paracetamol consumption, and passive smoking.

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The prevalence of atopy continues to rise in some parts of the world.¹ The demand for resources to deal with these illnesses has also increased.² For this reason, the International Study of Asthma and Allergies in Childhood (ISAAC) was formed in the 1990s to study and compare the prevalence of asthma, allergic rhinitis, and eczema in populations in different countries using standardized methodology that allows international cooperation and data comparison.³

In the ISAAC Phase I, children 13–14 years of age at 155 centers in 56 countries ($n = 463,801$) and children 6–7 years ($n = 257,601$) at 91 centers in 38 countries were studied using a questionnaire that asked about asthma, rhinoconjunctivitis, and eczema symptoms. The questions were answered by the adolescents or, in the case of children, by the parents. During Phase I, questions about genetic, lifestyle, and environmental factors were included to establish a framework for further etiologic research.⁴ During Phase II, possible etiologic factors in children 9–11 years of age from 30 centers in 22 countries were studied by including skin-prick tests for atopy, total and specific serum IgE level determination, a hypertonic saline aerosol challenge, house-dust mite antigen measurement (for aeroallergen and endotoxin analysis), and DNA analysis for genetic polymorphisms associated with asthma and allergies. Phase II studied 9- to 11-year-old children because at this age the children could participate in the blood extraction and pulmonary function tests that were required in this phase.⁵ Phase III was performed

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with an instrument similar to Phase I and aimed to examine trends over time in the prevalence of asthma, rhinoconjunctivitis, and eczema symptoms in the centers that had participated in Phase I (Phase IIIA) and those that had not (Phase IIIB).⁶

The development of allergic rhinitis depends on complex interactions between genetic and environmental factors that still are not fully understood.⁷ In addition, recent studies have shown that environmental conditions *in utero* also influence the development of allergies.^{8,9} It is therefore very useful to study the epidemiology and prevalence of allergies in different regions not only to track the frequency of these diseases in particular areas, but also to identify risk factors that are specific to each region.

The epidemiology of allergic diseases has not been studied extensively in Mexico. The ISAAC study methodology, both Phase I and Phase III, was performed, in part, in the cities of Cuernavaca^{10,11} and Ciudad Juárez (Chihuahua).¹² Results from ISAAC Phase IIIB in children from the northern area of Mexico City have been reported previously.¹³ We still have very little information about the dimension and evolution of allergic diseases, as well as their variations, in different areas of Mexico. The present study was performed to determine the prevalence and risk factors associated with allergic rhinitis and rhinoconjunctivitis symptoms in the pediatric population in several cities in northern Mexico using data from ISAAC Phase IIIB.

METHODS

Study Design

This report is based on an observational, cross-sectional, descriptive study performed in children 6–7 years of age and adolescents 13–14 years of age in elementary and secondary schools in 2002 and 2003.

Questionnaire

The Spanish version of the ISAAC Phase IIIB questionnaire was used as the collection instrument (as part of ISAAC Latin America) in all elementary and secondary schools (public and private) in three cities in northern Mexico: Victoria, Mexicali, and Tijuana. In a fourth city, Monterrey, the researchers included only public schools in the city and nearby counties. Therefore, we did not use any method of randomization to obtain the sample size required for ISAAC Phase III design. Data collection was performed in participating cities by the following researchers: Alberto José Escalante-Domínguez, M.D. (Hospital General Tijuana, Baja California); Roberto Gerardo García-Almaraz, M.D. (Hospital Infantil de Tamaulipas, Ciudad Victoria, Tamaulipas); Sandra Nora González-Díaz, M.D. (Hospital Universitario “Dr. José E. González”, Monterrey, Nuevo León); and

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The ethics committee of each participating hospital previously approved the study design and methodology. Each participating school was in the metropolitan areas of the cities; however, in Monterrey, schools from seven other counties in the state of Nuevo León were also included. The objectives, as well as the procedure for collecting data, were explained to the participants and their parents, and informed consent was obtained for each included subject. For children 6–7 years of age, the questionnaires were completed by parents or tutors at the children’s homes. If there was no response after 1 week, another questionnaire was sent home, and then a third. If there was still no response, the student was included in the nonresponding group. Children 13 and 14 years of age answered the questions by themselves at school according to the suggestions in the Researcher’s Manual for ISAAC Phase IIIB³ after seeing a video about the questionnaire. The students that did not attend school the day the questionnaire was completed were included in the nonresponding group. The collection periods were between June 2001 and January 2003 in the participating cities. Each center was responsible for study-related expenses.

Primary Variables

The main variables in the study were the presence of rhinitis symptoms without a cold at least once in the last 12 months (current prevalence) or in the child’s lifetime (accumulated prevalence), a previous diagnosis of allergic rhinitis (by any physician, regardless of specialty), and symptoms of rhinoconjunctivitis (itchy and watery eyes plus nasal symptoms). In ISAAC Phase III, specific questions address each of these variables. Associated environmental factors (foods, passive smoking, use of acetaminophen paracetamol during the 1st year of life and in the last 12 months, number of siblings at home, exercise habits, etc.) were obtained using the environmental questions from the ISAAC Phase IIIB questionnaire.

Processing and Statistical Analysis

The data from the questionnaires were entered twice into the digital database at each center, and the data were sent later to the ISAAC International Data Center. Inconsistencies (*e.g.*, differences in the stated age) were identified and corrected by reviewing the original questionnaires. The databases were approved for inclusion in the global analysis of ISAAC Phase III, except for the center in Tijuana, because of a delay in sending final corrections. To detect variables that were likely to be related to an increased or decreased

Table 1 Prevalence of rhinitis (accumulated, current) and rhinoconjunctivitis (current) symptoms and rhinoconjunctivitis diagnosis (ever) in children 6–7 years old and adolescents 13–14 years old from four northern Mexican centers, according to the International Study of Asthma and Allergies in Childhood, Phase IIIB, 2001–2003

Rhinitis Symptoms by Category, Center, and Age	Children 6–7 yr Old					Adolescents 13–14 yr Old				
	<i>n</i>	<i>n</i>	Prevalence (%)	Lower Limits CI (%)	Upper Limits CI (%)	<i>n</i>	<i>n</i>	Prevalence (%)	Lower Limits CI (%)	Upper Limits CI (%)
Rhinitis symptoms ever										
Monterrey	799	2,973	26.9	25.3	28.5	1271	2,966	42.9	41.1	44.6
Ciudad Victoria	638	2,602	24.5	22.9	26.2	1417	3,121	45.4	43.7	47.1
Mexicali	762	2,468	30.9	29.1	32.7	1334	2,967	45.0	43.2	46.8
Tijuana	839	2,849	29.4	27.8	31.1	1283	3,245	39.5	37.9	41.2
Current rhinitis symptoms										
Monterrey	679	2,973	22.8	21.3	24.3	955	2,966	32.2	30.5	33.9
Ciudad Victoria	553	2,602	21.3	19.7	22.8	1093	3,121	35.0	33.3	36.7
Mexicali	695	2,468	28.2	26.4	29.9	1233	2,967	41.6	39.8	43.3
Tijuana	697	2,849	24.5	22.9	26.0	902	3,245	27.8	26.3	29.3
Current rhinoconjunctivitis symptoms										
Monterrey	252	2,973	8.5	7.5	9.5	402	2,966	13.6	12.3	14.8
Ciudad Victoria	190	2,602	7.3	6.3	8.3	616	3,121	19.7	18.3	21.1
Mexicali	313	2,468	12.7	11.4	14.0	862	2,967	29.1	27.4	30.7
Tijuana	233	2,849	8.2	7.2	9.2	359	3,245	11.1	10.0	12.1
Rhinoconjunctivitis diagnosis										
Monterrey	201	2,973	6.8	5.9	7.7	138	2,966	4.7	3.9	5.4
Ciudad Victoria	93	2,602	3.6	2.9	4.3	91	3,121	3.0	2.4	3.6
Mexicali	172	2,468	7.0	6.0	8.0	41	2,967	1.4	1.0	1.8
Tijuana	131	2,849	4.6	3.8	5.4	197	3,245	6.1	5.2	6.9

risk ($p \leq 0.10$) of symptoms of accumulated or current rhinitis, we performed a chi-squared test for categorical variables. The impact of possible associated factors and their relationships with environmental variables were analyzed by logistic regression using a conditional method to obtain models that explained each manifestation of rhinitis. Analysis was performed using SPSS 8.0 (SPSS, Inc., Chicago, IL).

RESULTS

A total of 25,162 students were eligible to complete the questionnaire; of these, 1971 (8%) did not participate. The final sample consisted of 23,191 questionnaires that were completed: 10,892 (47%) from children 6–7 years of age and 12,299 (53%) from adolescents 13–14 years of age. Tables 1 and 2 show the prevalence for both sexes by age group. For children 6–7 years of age, the global frequency for rhinitis symptoms (ever) was 27.9% (range, 24.5–30.9%) and the global frequency for current rhinitis symptoms was 24.2% (range, 21.3–28.2%). With re-

gard to rhinoconjunctivitis symptoms, the global frequency was 9.2% (range, 7.3–12.7%), but the global frequency for allergic rhinitis diagnosis was 5.5% (range, 3.6–7.0%). Compared with the children, the adolescent group had a higher prevalence for each category except for the diagnosis of allergic rhinitis (3.8%). These figures are in line with data reported by others for allergic rhinitis in this region of Latin America, which has the highest prevalence of allergic diseases in pediatric patients in the world.¹⁴

Table 3 shows the risk factors that were identified by logistic regression analysis to be associated with allergic rhinitis symptoms. The main factors for increased risk (odds ratio [OR] > 1; $p < 0.05$) of symptoms of both rhinitis or rhinoconjunctivitis (either current or previous) in 6- to 7-year-old children were asthma symptoms (current wheezing or wheezing in the last 12 months), symptoms suggestive of eczema or diagnosed eczema, use of acetaminophen in the 1st year of life or in the last 12 months, and current maternal tobacco smoking. Similarly, the main factors for increased risk of symptoms of rhinitis or rhinoconjunctivitis (either current or previous)

Table 2 Prevalence of rhinitis symptoms (accumulated, current), rhinoconjunctivitis symptoms (current), and allergic rhinitis diagnosis (ever) in children 6–7 yr old and adolescents 13–14 yr old, by gender, from four northern Mexican centers according to International Study of Asthma and Allergies in Childhood, Phase IIIB, 2001–2003

Symptoms Prevalence by Category	n	n	Prevalence (%)	Lower Limit CI 95%	Upper Limit CI 95%
Children 6–7 yr old					
Rhinitis symptoms ever					
Male	1569	5470	28.7	27.5	29.9
Female	1469	5422	27.1	25.9	28.3
Global	3038	10,892	27.9	26.2	29.6
Rhinitis symptoms in last 12 mo					
Male	1372	5470	25.1	23.9	26.2
Female	1252	5422	23.1	22.0	24.2
Global	2624	10,892	24.2	22.6	25.8
Rhinoconjunctivitis symptoms in last 12 mo					
Male	511	5470	9.34	8.57	10.11
Female	477	5422	8.80	8.04	9.55
Global	988	10,892	9.2	8.1	10.2
Allergic rhinitis diagnosis					
Male	340	5470	6.2	5.6	6.9
Female	257	5422	4.7	4.2	5.3
Global	597	10,892	5.5	4.6	6.3
Adolescents 13–14 yr old					
Rhinitis symptoms ever					
Male	2513	6017	41.8	40.5	43.0
Female	2792	6282	44.4	43.2	45.7
Global	5305	12,299	33.3	32.0	34.6
Rhinitis symptoms in last 12 mo					
Male	1980	6017	32.9	31.7	34.1
Female	2203	6282	35.1	33.9	36.2
Global	4183	12,299	34.1	32.5	35.8
Rhinoconjunctivitis symptoms in last 12 mo					
Male	1976	21,784	16.9	15.9	17.8
Female	3441	38,098	19.5	18.5	20.4
Global	6405	70,774	18.2	17.5	18.9
Allergic rhinitis diagnosis					
Male	228	6017	3.8	3.3	4.3
Female	239	6282	3.8	3.3	4.3
Global	467	12,299	3.8	3.1	4.4

for 13- to 14-year-old children were current or previous symptoms of asthma, symptoms suggestive of eczema or diagnosed eczema (current or previous), use of acetaminophen in the last 12 months, and the presence of at least one tobacco smoker at home.

We found no relationship between rhinitis and the use of antibiotics in the 1st year of life. Interaction with older siblings resulted in a decreased risk of diagnosis of allergic rhinitis in children but not in adolescents. In adolescents, no protective factors were associated with a lower risk of rhinitis symptoms.

DISCUSSION

Environmental factors and lifestyle appear to be important in the expression of allergic diseases.⁷ This study is the first to explore risk factors for allergic rhinitis in a pediatric population in northern Mexico using standardized methodology (the ISAAC study). Others have reported that the gross national product per capita (GNPpc) can be a confounding factor that should be considered when analyzing epidemiological studies of allergic diseases,¹⁵ especially in studies that analyze populations from countries with

different GNPpc's. In 2003, the GNPpc of Mexico was US\$6230.00, which places it in the group of countries with an upper-middle income.¹⁶ Although the GNPpc varies greatly from state to state in Mexico, the individuals included in this study were from states in which the GNPpc's are similar and higher than the national average,¹⁷ ruling out this potential bias. In our study population, a greater percentage of adolescents had current or previous symptoms of rhinitis and diagnoses of allergic rhinitis compared with the younger age group. The tendency for the prevalence of allergic rhinitis to increase with age has been shown in other longitudinal studies of the natural history of the disease.¹⁸ Although, the underlying cause is unknown, this could be caused by increased exposure to allergens over the years¹⁹ with the subsequent development of allergic rhinitis.

When we performed a comparative analysis of the four centers, Ciudad Victoria had the lowest percentage of children 6–7 years of age with symptoms of rhinoconjunctivitis (7.3%), and Tijuana had the lowest percentage of adolescents with symptoms of rhinoconjunctivitis (11.1%). The highest rates were reported in Mexicali for both age groups (12.7% for children and 29.1% for adolescents). These data showed considerable variation, particularly for adolescents. In a previous study, the relationship of some climatic factors and the prevalence of allergic diseases around the world were analyzed using data obtained from ISAAC Phase I. A positive relationship was found between asthma and the estimated average annual relative humidity, and a negative relationship was found between asthma and altitude and annual variation of outdoors temperature and humidity. A positive correlation with latitude and a negative correlation with annual outside average temperature were found for the prevalence of eczema. However, there was no significant association with any climatic factor for rhinitis symptoms.²⁰

Some of the climatic characteristics of the study centers and the corresponding rhinoconjunctivitis symptom frequencies are shown in Table 4.^{21,22} Mexicali is notable in that it reported higher rates of rhinoconjunctivitis in both groups of subjects and has the lowest altitude of the included centers. In children, the next highest rate was in Monterrey, and the third highest was in Tijuana. Because Monterrey and Ciudad Victoria are at very different altitudes than Mexicali, there was no relationship between altitude and the prevalence of rhinoconjunctivitis in this study. However, other climatic factors, such as average annual inside temperature, outside temperature, inside relative humidity, etc., were not studied, and their impact on allergic rhinitis should not be ruled out. The results of the ISAAC Phase III in 21 Brazilian centers showed a significant negative association between latitude and

physician-diagnosed asthma and atopic eczema, particularly among adolescents. However, that study did not find any relationship between climatic factors and allergic rhinitis symptoms,²³ which is in agreement with the international analysis report of ISAAC Phase III. The close relationship of allergic diseases appears to be related to common genetic and environmental factors; however, current evidence shows that climatic factors affect allergic symptoms in different ways. Further research is needed, especially for allergic rhinitis.

A study of children in the northern area of Mexico City by Del Rio Navarro *et al.* reported a twofold greater prevalence of rhinoconjunctivitis symptoms in children 6–7 years of age than what we found (20.3% versus 9.2%).¹³ In addition, the report of the global prevalence of rhinoconjunctivitis symptoms in infancy, based on data from ISAAC Phase III,¹⁴ showed substantial differences in frequencies at centers within the same country, just as we observed in Mexico. In terms of global variation in the prevalence and severity of asthma symptoms, the ISAAC Phase III report also noted some differences at centers in the countries,²⁴ although these differences were not so marked. The reason for this variability is currently unknown. Because the findings are similar in different parts of the world, there does not seem to be methodological bias; however, a different investigator collected the data at every center, which is a potential source of bias. It is possible that interactions between genetic and environmental factors result in a wide range of clinical symptoms, even in a population with the same ethnic background. Additional studies are needed to determine the underlying causes of prevalence variation found in centers within a country, especially in studies with methodology similar to that used in ISAAC Phase II.

The prevalence of nasal and ocular symptoms merits special attention, because this is the best predictor of allergic rhinitis.¹⁸ In our series, the prevalence of rhinoconjunctivitis symptoms was in line with results of previous studies^{10,11} in children, but the prevalence was twofold greater for adolescents. This discrepancy may be caused by differences in study design because the ISAAC methodology was followed incompletely in the previous studies (the age of the included population was different). For comparison and to clarify these differences, future studies must have the same design. The diagnosis of allergic rhinitis was low (4.6% in our series) considering the data for rhinoconjunctivitis symptoms, suggesting a high level of underdiagnosis. The original question in the ISAAC Phase IIIB survey that related to this topic did not discriminate between primary care doctors and specialists. The low number of allergic rhinitis diagnoses agrees with the observation that according to a global map from ISAAC Phase III, Latin America has one of the highest incidences of severe rhinoconjunctivitis. This may be related to poor

Table 3 Rhinitis symptoms, rhinoconjunctivitis symptoms, and diagnosis of allergic rhinitis risk factors by categories and gender, obtained with logistic regression model in children 6–7 yr old and adolescents 13–14 yr old from four northern Mexican centers according to International Study of Asthma and Allergies in Childhood, Phase IIIB, 2001–2003

	<i>p</i>	OR	CI 95% –	CI 95% +	<i>p</i>	OR	CI 95% –	CI 95% +
Rhinitis ever in boys 6–7 yr old								
Wheezing ever	0.000	2.5	2.9	2.1				
Current wheezing	0.000	2.6	3.4	2.0				
Rash ever	0.000	1.9	2.3	1.5				
Eczema diagnosis ever	0.000	3.0	4.3	2.0				
Current paracetamol	0.000	1.4	1.6	1.2				
Rhinitis ever in girls 6–7 yr old								
Current wheezing	0.000	3.9	4.9	3.1				
Eczema ever	0.000	2.5	3.6	1.8				
Pasta in diet last year	0.022	0.9	1.0	0.8				
Paracetamol first year	0.000	1.6	1.8	1.4				
Paracetamol last year	0.000	1.3	1.4	1.1				
Antibiotics first year	0.030	1.2	1.3	1.0				
Current maternal smoke	0.004	1.4	1.7	1.1				
Current rhinitis in boys 6–7 yr old								
Wheezing ever	0.000	1.9	2.3	1.6				
Current wheezing	0.000	2.6	3.4	2.0				
Asthma diagnosis ever	0.000	1.7	2.2	1.3				
Rash ever	0.000	2.1	2.6	1.7				
Paracetamol first year	0.000	1.4	1.6	1.2				
Current maternal smoke	0.036	1.3	1.6	1.0				
Current rhinitis in girls 6–7 yr old								
Current wheezing	0.000	4.8	6.1	3.9				
Rash ever	0.000	2.3	2.9	1.9				
Paracetamol first year	0.000	1.8	2.1	1.5				
Antibiotics first year	0.012	1.2	1.4	1.0				
Current maternal smoke	0.021	1.3	1.6	1.0				
Current rhinoconjunctivitis in boys 6–7 yr old								
Wheezing ever	0.000	2.0	2.7	1.5				
Current wheezing	0.000	3.4	4.6	2.4				
Rash ever	0.000	3.1	4.0	2.4				
Paracetamol last year	0.000	1.4	1.7	1.2				
Current maternal smoke	0.010	1.5	2.0	1.1				
Rhinitis ever in boys 13–14 yr old								
Wheezing ever	0.000	3.3	4.2	2.6				
Rash ever	0.000	2.2	2.8	1.7				
Potato	0.001	0.8	0.9	0.7				
Fruit	0.003	1.2	1.4	1.1				
Pasta	0.008	1.2	1.3	1.0				
Rhinitis ever in girls 13–14 yr old								
Wheezing ever	0.000	3.1	3.9	2.5				
Rash ever	0.000	3.3	4.2	2.6				
Seafood	0.000	1.3	1.5	1.2				
Butter	0.000	1.3	1.5	1.1				
Fast-food	0.000	0.8	0.9	0.7				
Smokers	0.001	1.1	1.2	1.0				
Margarine	0.003	0.8	0.9	0.7				
Current rhinitis in boys 13–14 yr old								
Wheezing ever	0.000	3.3	4.1	2.6				
Rash ever	0.000	2.3	2.9	1.8				
Seafood	0.000	1.2	1.4	1.1				
Potato	0.000	0.8	0.9	0.7				
Smokers	0.000	1.2	1.2	1.1				
Paracetamol last year	0.001	1.2	1.4	1.1				
Current rhinitis in girls 13–14 yr old								
Wheezing ever	0.000	2.5	3.1	2.0				
Current wheezing	0.001	1.6	2.1	1.2				
Rash ever	0.000	2.5	3.1	2.1				
Seafood	0.000	1.4	1.5	1.3				
Butter	0.000	1.4	1.5	1.3				
Current rhinoconjunctivitis in boys 13–14 yr old								
Wheezing ever	0.000	3.4	4.1	2.8				
Meat	0.000	0.8	0.9	0.7				
Seafood	0.000	1.7	1.9	1.5				
Rice	0.000	1.5	1.7	1.3				
Nuts	0.000	1.4	1.6	1.2				

Table 3 Continued

	<i>p</i>	OR	CI 95% -	CI 95% +		<i>p</i>	OR	CI 95% -	CI 95% +
Current rhinoconjunctivitis in girls 6-7 yr old	0.000	2.6			Current rhinoconjunctivitis in girls 13-14 yr old	0.000	2.4		
Wheezing ever	0.000	2.4	3.7	1.9	Wheezing ever	0.000	3.3	3.3	1.7
Current wheezing	0.000	2.4	3.6	1.6	Rash ever	0.000	3.4	4.4	2.6
Current rash	0.000	3.0	4.5	2.0	Seafood	0.000	1.6	1.9	1.4
Pulses (beans, peas)	0.002	0.8	0.9	0.6	Butter	0.000	1.4	1.6	1.2
Paracetamol first year	0.001	1.7	2.3	1.2	Nuts	0.000	1.4	1.7	1.2
Paracetamol last year	0.000	2.0	2.5	1.5	Potato	0.000	0.7	0.8	0.6
Older siblings	0.006	1.2	1.3	1.0	Fast-food	0.000	0.7	0.8	0.6
Rhinoconjunctivitis ever in boys 6-7 yr old	0.000	2.7	4.0	1.8	Rhinoconjunctivitis ever in boys 13-14 yr old	0.000	2.9	4.1	2.0
Wheezing ever	0.001	2.2	3.5	1.4	Current wheezing	0.000	3.0	4.5	2.0
Current wheezing	0.000	4.5	7.7	2.6	Asthma ever	0.000	2.1	2.9	1.5
Eczema diagnosis ever	0.002	1.7	2.4	1.2	Rash ever	0.000	4.0	7.0	2.3
Antibiotics first year	0.001	0.5	0.7	0.3	Eczema ever				
Tertiary mother education									
Rhinoconjunctivitis ever in girls 6-7 yr old	0.000	3.3	4.9	2.3	Rhinoconjunctivitis ever in girls 13- yr old	0.000	2.1	3.1	1.5
Wheezing ever	0.000	3.6	6.7	1.9	Wheezing last year	0.000	3.5	5.2	2.4
Eczema ever	0.032	1.9	3.5	1.1	Asthma ever	0.000	2.2	3.1	1.6
Mother smoking last year	0.044	0.6	1.0	0.4	Rash ever	0.000	6.6	10.8	4.0
Tertiary mother education	0.051	0.8	1.0	0.6	Eczema ever	0.048	0.7	1.0	0.6
Pulses (beans, peas)					Dog in home last year				

Table 4 Climatic conditions of four cities from northern Mexico and current rhinoconjunctivitis symptoms prevalence rates in children 6–7 yr old and adolescents 13–14 yr old, according to International Study of Asthma and Allergies in Childhood, Phase IIIB: 2001–2003

City	Location (latitude and longitude)	Altitude (MASL)	Outdoor Temperature	Outdoor Relative Humidity	Current Rhinoconjunctivitis Prevalence	
					6–7 yr	13–14 yr
Mexicali	LN 30°53' LO 115°66'	3	Maximum, 50°C Minimum, –5°C	56%	12.7%	29.1%
Tijuana	LN 32°31' LO 117°	20	Maximum, 29°C Minimum, 12°C	65%	8.2%	11.1%
Ciudad Victoria	LN 23°44' LO 99°07'	320	Maximum, 47°C Minimum, 0–4°C	50%	7.3%	19.7%
Monterrey	LN 23°11' LO 101°14'	537	Maximum, 41°C Minimum, 1.1°C	56%	8.5%	13.6%

MASL = meters above sea level.

medical diagnosis and treatment. To improve our approach to allergic diseases in childhood, we need to improve medical knowledge at the primary care level. However, it is possible that the prevalence was overestimated,²⁵ because the ISAAC data were derived from a questionnaire.

International variation in the prevalence of rhinitis and other allergic diseases and the relationship of this variation with seasonal and perennial allergens (using the ISAAC Phase II methodology),^{26–28} was analyzed recently. Atopy could not explain all of the symptoms, particularly in centers in countries with lower GNPpc's. This emphasizes the need to increase our knowledge of nonatopic factors in the expression of allergic diseases, especially in subjects with symptoms that are not usually related to atopy (e.g., rhinitis without ocular symptoms).

The phenotypes of allergic diseases such as asthma and allergic rhinitis are closely related in terms of their epidemiology and are usually present in family groups, suggesting shared etiology. This relationship is termed “chronic allergic respiratory syndrome”²⁹ and was evident in the pediatric population in this study: we found that the main risk factor for the development of rhinitis was asthma symptoms (current or past wheezing or an asthma diagnosis). Conversely, the main risk factor for the development of asthma is allergic rhinitis.^{13,30,31} Thus, primary care physicians must be aware of the close relationship of these diseases to ensure timely diagnosis and treatment. Eczema (both symptoms and a medical diagnosis) was also identified as a risk factor for the development of allergic rhinitis in both age groups studied, supporting the concept of “atopic march.” Thus, eczema is related to a greater risk of developing allergic rhinitis and asthma in Mexican

children, as has been shown in other populations.³² Diverse environmental and lifestyle factors can contribute to the expression of allergic diseases, especially during the 1st years of life; these factors include diet, maternal smoking, obesity, exposure to microbes, allergens, pets in the home, and use of antibiotics and acetaminophen.^{33–38}

In our study population, the use of acetaminophen (during the first 12 months of life and within the last 12 months) for treatment of infection-related fever was associated with a greater risk of rhinitis in both age groups. Because of the cross-sectional nature of the ISAAC Phase III design, we can not know if this drug has a causal effect or whether patients were treated with acetaminophen for their allergy symptoms, which may resemble symptoms of infection. A proposed etiologic mechanism for asthma is a depletion of glutathione in the lungs. At least in toxic doses, acetaminophen metabolites bind irreversibly to glutathione, decreasing the ability to mitigate oxidative stress produced by reactive oxygen species. This triggers a cascade of epithelial desquamation, edema, release of leukotrienes, bronchoconstriction, and inflammatory cell stimulation.³⁶ Although it has not been shown whether a similar phenomenon occurs with rhinitis, the epidemiological evidence in this study supports a similar mechanism. This is in accordance with data from a previous study in Mexico³⁷ and with the global report of ISAAC Phase III in children 6–7 years of age regarding the association of acetaminophen with the risk of asthma, rhinoconjunctivitis, and eczema.³⁸ Prospective studies are needed to evaluate the causal relationship between acetaminophen and allergic diseases.

It is noteworthy that current maternal smoking or the presence of at least one smoker in the home was positively associated with symptoms of rhinitis and aller-

gic rhinitis, especially in children. Other reports have indicated a causal relationship between exposure to tobacco smoke during pregnancy and early infancy and allergic diseases, especially asthma.⁷ The proposed mechanism is that tobacco smoke reduces $\alpha 1$ -antitrypsin, a lung protease that blocks normal inactivation of allergenic house-dust mite proteases in the airways. This results in an increased risk of sensitization to these allergens.⁷

The ISAAC questionnaire includes data related to foods in the diet. In our series, margarine intake was associated with rhinitis symptoms in children as well as adolescents (OR = 1.18 in both groups). Potato intake had a negative relationship (OR = 0.88) with rhinitis only in adolescents. These observations contrast with those of Ellwood *et al.*,³⁹ who found that the prevalence of asthma, rhinitis, and eczema was inversely related to starch, cereal, and vegetable intake. However, because the ISAAC Phase I and III studies are both based on a cross-sectional survey, this observation is subject to several types of bias. Thus, the current information has many limitations and must be verified in studies that use a different methodology.

This study has several limitations. Data were collected using a questionnaire, so the responses depended in part on the subject's or parent's memory. This could introduce bias, and the prevalence must be considered an estimate. Longitudinal studies and studies using other diagnostic parameters are needed to confirm the results of this cross-sectional study. In addition, the ISAAC Phase III study can not discriminate between atopic disease and related nonatopic diseases, such as rhinitis, especially in countries such as Mexico where the income varies widely in the population and where nonatopic factors may be important.

Despite its limitations, this study helps establish the prevalence of rhinitis and other childhood allergic diseases in children and adolescents in Mexico and identifies environmental elements that may affect the expression of allergic diseases. This information is valuable in that it encourages timely diagnosis and treatment of allergic diseases by primary care physicians. It also suggests preventive measures that can be taken to protect children from developing allergic rhinitis, such as changes in the child's environment.

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