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Ascaris, atopy, and exercise-induced bronchoconstriction in rural and urban South African children

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Abstract

Background—Populations with endemic parasitosis have high levels of IgE but low levels of allergic disease. We investigated the association between infection with the parasite *Ascaris* allergic sensitization, and exercise-induced bronchospasm (EIB).

Objective—We sought to investigate the effect of *Ascaris* infection on bronchial hyperreactivity, skin testing, and specific IgE levels.

Methods—A cross-sectional prevalence survey was conducted in urban and rural South African children to measure levels of EIB. A sample of children was enrolled in a nested case-control study for further investigation based on response to exercise. Analyses used weighted logistic regression.

Results—Geometric mean total IgE levels were higher in *Ascaris*-infected subjects (infected subjects: 451 IU (95% CI, 356-572) vs uninfected subjects: 344 IU (95% CI, 271-437), $P = 5.04$), and high levels of total IgE were positively associated with detection of specific IgE to the aeroallergens tested, but there was no significant association between *Ascaris* infection and titers of specific IgE. *Ascaris* infection was associated with a decreased risk of a positive skin test response (odds ratio, 0.63; 95% CI, 0.42–0.94; $P = .03$) but an increased risk of EIB (odds ratio, 1.62; 95% CI, 1.23-2.11; $P = .001$).

Conclusion—In areas of high parasite endemicity, *Ascaris* might induce an inflammatory response in the lungs independent of its effect on IgE production. This could explain some of the contradictory findings seen in studies examining the association between geohelminth infection, atopy, and asthma.

Intestinal parasitosis is pandemic in the developing world¹ but uncommon in the developed world. Helminths with a systemic phase in their lifecycle stimulate potent IgE responses in the human host.^{2,3} However, although subjects resident in rural areas of the developing world have a substantial prevalence of IgE to common inhalant allergens,^{4,5} they have low levels of atopic disease.

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Clinical implications: Variable airflow obstruction in highly parasitized populations might not be atopically mediated. Studies using change in spirometry as a surrogate for asthma might not be generalizable to less parasitized populations.

This has stimulated interest in the role of intestinal parasites in modulating the expression of allergic disease, but the relation between atopic disease and helminth infection remains unclear. Evidence from Venezuela⁶⁻⁸ suggests that parasitic infection and high total IgE levels might protect against the effects of allergens, possibly by blocking the mast cell response.^{9,10} More recently, it has been proposed that parasites might protect against atopy through a mechanism mediated by IL-10.¹¹ However, other studies have suggested that parasitic infection might cause wheeze by stimulating production of specific IgE against nonparasite allergens¹²⁻¹⁴ or that there is no causal link between parasitic infection and asthma.^{8,15} A better understanding of the association between parasitic infection and allergy might help to understand mechanisms of inflammation that lead to atopic disease. We report the results of a case-control study nested within a cross-sectional survey of children living in urban and rural areas of South Africa with the aim of determining the association between infection with *Ascaris lumbricoides* and the prevalence of exercise-induced bronchospasm (EIB), and allergic sensitization.

METHODS

Design

The prevalence of EIB was established in a cross-sectional survey of 18 rural schools in Kentani district of the rural Eastern Cape of South Africa and 6 urban schools in Khayelitsha, an informal urban settlement in the Western Cape. Schools in the urban area were contacted in order of construction, starting with the most recently built, and all schools approached agreed to participate in the study. In the rural area all 22 schools within an hour's drive from the study base were approached and invited to participate in the study, and 18 agreed. Rural and urban areas were visited alternately 4 times each for a month at a time to minimize the effect of seasonality on data collection.

All subjects underwent exercise testing to identify those with EIB. A positive exercise test result was defined as a decrease in FEV1 of 15% or greater or a decrease in F25-75 of 26% or greater¹⁶ after 6 minutes of free running. A negative test result was defined as a decrease in spirometric results after exercise of no greater than 10% of pre-exercise FEV1 or 20% of F25-75. Spirometric measurements were carried out according to European Respiratory Society guidelines¹⁷ with a portable spirometer (Vitalograph 2120; Vitalograph Ltd, Buckingham, United Kingdom).

All subjects identified with EIB and a random sample of subjects with a normal response to exercise were enrolled in a case-control study to examine factors that might explain rural-urban differences in the prevalence of asthma and allergy. Numbers of control subjects were selected in each school as a fixed proportion of the number of children available to act as control subjects.

Anthropometric measurements and skin testing were performed, blood was drawn for analysis, and stool samples were collected for examination for geohelminths. A parent or guardian then completed an interviewer-administered questionnaire, which collected information on potential confounding variables.

Subjects

Study subjects were children aged 8 to 12 years and were exclusively from the African population. At each school, class lists were collated by teachers. Children were then selected at random (by using random number tables) from these lists to participate in the study. When a child selected at random to take part in the study was not present in school on the day of testing, the next child on the class list was selected. Information on the distribution of EIB and risk factors was sparse before the study. In 1980, Vermeulen (personal correspondence) found 80% of a population of rural children in a rural area of the Eastern Cape to have serologic evidence of infection with parasites and a relative risk of EIB of 2 compared with those without parasites. It was calculated that 282 cases with an equal number of control subjects would provide 80% power to detect an odds ratio (OR) of 2 for risk of EIB when comparing infected with uninfected subjects. From the results of the pilot study, a conservative estimate of 8% for the mean prevalence of EIB in the combined study areas was made. Assuming an equal sample in the rural and urban areas, it was calculated that 3,500 children would need to be recruited into the cross-sectional survey to identify sufficient cases for the case-control study. In total, 1,671 children were recruited from the rural schools and 1,651 from the urban schools.

Assessment

Skin prick tests adapted the method described for the European Community Respiratory Health Study¹⁸ using plain lancets and the allergens *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis* (supplied by Dr E. Fernandez-Caldas), cockroach, Timothy grass, Bermuda grass, *Aspergillus* species, *Cladosporium* species, *Alternaria* species, cat, and dog; a negative saline control; and a positive histamine control (SmithKline Beecham, Bencard, Munch, Germany). A positive test response was defined as the presence of any skin wheal of greater than 0 mm after deduction of the size of the negative control.¹⁹ All skin testing was carried out by one investigator (J.C.) in both the rural and urban areas.

Specific IgE was assayed to *D pteronyssinus*, *B tropicalis*, cat, timothy grass, and *Aspergillus* species by using the CAP-IgE System (Pharmacia, Uppsala, Sweden). Samples were chilled immediately, and serum was separated from clotted blood within 4 hours and stored at 2208C. A positive test result for specific IgE was defined as RAST class 1 or greater.^{19,20}

Stool samples were analyzed for the presence of geohelminth eggs by the Department of Microbiology, Tygerberg Hospital, using an ether sedimentation technique.²¹ Data were collected on potential confounding variables by using a questionnaire administered in Xhosa by native Xhosa speakers. Number of years of education of the head of household and number of items from a standard list (motor vehicle, bicycles, radio, electric stove, gas stove, primus cooker, fridge, television, geyser, electric kettle, and telephone) owned by the household were recorded and used as a proxy for affluence.²² Information on children's exposure to environmental tobacco smoke was collected. The children's state of nutrition was measured and represented as body mass index (BMI), which was calculated as weight (in kilograms) divided by height (in meters) squared. Information on other measures, such as

skin fold thickness and upper arm circumference, were also collected but were not included in the final analysis because they did not improve the predictive ability of the final models when compared with BMI SD scores. All measurements were made and questionnaires were administered by trained fieldworkers using standardized techniques under direct supervision of J.C. Laboratory staff and interviewers were blind to the outcome of exercise testing.

Consent and ethical approval were obtained from the University of Cape Town Medical Research Ethics Committee. Parents or guardians of all study participants provided informed consent before testing.

Analysis

Recruitment into the nested case-control study was based on response to exercise testing. All subjects with a positive exercise test result were enrolled. Eleven percent of children were selected as control subjects before exercising by using random number tables. If one of these children responded positively to the exercise test, they were reclassified as a case, and the next child on the list compiled by using random allocation was designated as a control subject to ensure that the correct proportion of control subjects was recruited each day.

The primary outcome measures were EIB and allergic sensitization defined by using response to allergen skin testing and assay of allergen-specific RASTs. Analyses used standard methods for the analysis of surveys, in which participants' responses are weighted according to the inverse of the probability of selection as a control subject.²³ This method allows for reconstruction of the control group, allowing for the effects of oversampling of atopic subjects occurring as a result of use of EIB as a criterion for entry into the case-control study. This method permits analysis of atopy as a primary outcome.

Variance of BMI increased with age, and therefore it was necessary to calculate BMI SD (z) scores to permit analysis. Appropriate reference values for African children were not available, and therefore scores were calculated by using sex-specific reference curves for children in the United Kingdom.²⁴

Total IgE levels were measured in 754 subjects. The assay range is 5 to 5,000IU. One subject had a total IgE level of less than the reference range, and 30 subjects had a level of greater than 5,000 IU, the upper limit of the range of measurement. The manner in which this was handled in the analysis is discussed in the Methods section of this article's Online Repository at www.jacionline.org. Data were noted to have a log-normal distribution. Geometric means were calculated for log-normal data and compared by using the Student t test. CIs were calculated to allow for the clustered nature of the study design.

A summary model of the data is presented in Table I. Unadjusted ORs are presented together with results from 2 regression analyses. Models were constructed after univariate analysis of potential explanatory variables. Any variable with a P value of less than 0.25 for strength of association with EIB was considered for inclusion in the final model. All multivariate models included urban residence because this was the variable by which data were stratified. Other variables were then tested in the model: coefficients for each variable were compared with coefficients in a model that did not contain that variable. Variables that

did not appear to be important, either because they were not significant in themselves or because they had no substantial effect on other associations in the model, were dropped, and a new model was tested. Where effects were not themselves significant but altered other parts of the model, as with the socioeconomic variables in Table I, they were left in the model for the reader to assess. The final models were derived to include the minimum number of variables to explain the difference in risk of EIB between urban and rural areas. Age and sex were included in the final model because of evidence that parasite burden decreases with increasing age and varies between male and female subjects.²⁵

Dual data entry was performed in Epi-info, and analyses were undertaken with Stata 7 software (StataCorp, College Station, Tex)²³ by using techniques for survey data (svy: command set).

RESULTS

Description of data

The prevalence survey included 1,671 children in rural schools and 1,651 children in urban schools. EIB was identified in 8.7% (n=5146) of rural and 14.9% (n=5246) of urban children. Twelve of the children with positive exercise test results were lost to follow-up. Further examinations were undertaken in 773 children (380 cases and 393 control subjects), 754 consenting to skin prick testing and providing blood samples and 743 providing stool samples. Parents of 696 children (370/436 urban and 326/337 rural children) completed questionnaires. Children not providing samples did not differ from children providing samples in respect to age, sex, or airways responsiveness after exercise.

Characteristics of the children are shown in Table II. Children with a normal response to exercise were shorter and lighter and from less affluent homes (assessed by using tertiles of parental education and items owned) than cases and were less likely to live in an urban area. Levels of total IgE and the prevalence of subjects with specific IgE did not differ between cases and control subjects.

A positive skin test response was the variable most strongly associated with risk of EIB, and in children with EIB, the mean skin wheal diameter was larger. After control for urban residence, age, and sex, there was a modest association between EIB and exposure to environmental tobacco smoke (OR, 1.26; 95% CI, 0.98-1.57) with a magnitude similar to that observed in previous studies of childhood asthma,²⁶ but given the modest sample size, the association did not achieve statistical significance at a P value of .05 (P = 0.06). Number of siblings was also considered as an explanatory variable for EIB, but no significant association was found (OR, 1.46; 95% CI, 0.56-3.77; P = 0.82 comparing >1 sibling with no siblings).

Helminth infection

Isolated *Ascaris* infection was found in 200 subjects, and co-infection with *Ascaris* and *Trichuris* was observed in 257 subjects. Infection with *Ascaris* was associated with an increased risk of EIB (OR, 1.62; 95% CI, 1.23-2.11; P = 0.001) on univariate analysis, but infection with *Trichuris* showed no significant association (OR, 0.99; 95% CI, 0.74-1.35; P

= .99; data presented in Table E1 in this article's Online Repository at www.jacionline.org). This association was the same in rural and urban children. There was no evidence for confounding by age or sex.

Parasitic infection was not associated with risk of detection of specific IgE to nonparasite allergens either together (OR, 1.18; 95% CI, 0.81-1.73; $P = 0.38$) or individually, with the exception of specific IgE to timothy grass, which was more common in those with *Ascaris* infection (5.9% of those without an *Ascaris* infection and 11.8% of those who were infected; $P = 0.02$, χ^2 test). No difference in RAST class was detected for any allergen in subjects infected with *Ascaris* compared with uninfected subjects.

Infection with *Ascaris* was associated with a marginally reduced risk of a positive skin test response on univariate analysis. After addition of specific IgE and urban residence to the model, *Ascaris* infection was associated with a reduced risk of a positive skin test response (OR, 0.63; 95% CI, 0.42-0.94; $P = 0.03$). As would be expected, the presence of IgE specific for individual allergens was strongly associated with an increased risk of a positive skin test response after testing with the allergen to which specific IgE was detected (data are presented in Tables E3 and E4 in this article's Online Repository at www.jacionline.org).

Total IgE

Serum total IgE levels varied from 1 to greater than 5,000 IU/ mL (the upper limit for the assay). The geometric mean total IgE level was higher in rural children (rural total IgE level, 554 IU; urban total IgE level, 296 IU; P for difference in means < 0.0001) and in those infected with *Ascaris* who had a total IgE level 1.35-fold higher than that seen in uninfected subjects on multivariate analysis controlling for urban residence (geometric mean IgE level: 451 IU [95% CI, 355-572] for *Ascaris* infected subjects vs 344 IU [95% CI, 271-437] for uninfected subjects; P for difference in means = 0.02). After control for *Ascaris* infection, there was no significant association between infection with *Trichuris* and the total IgE level. A 10-fold increase in total IgE levels was associated with an OR of 10.1 (95% CI, 5.65-18.2; $P < 0.0001$) for detection of specific IgE. Data are presented in Table E4 in this article's Online Repository at www.jacionline.org, which shows a general trend toward higher titers of specific IgE in subjects with higher levels of total IgE (total IgE levels greater than the geometric mean value).

After control for the presence of specific IgE and urban residence, there was no significant association between total IgE level and risk of a positive skin test response (OR, 1.20; 95% CI, 0.85-1.69; $P = 0.30$) or response to exercise (OR, 1.11; 95% CI, 0.80-1.55; $P = 0.49$).

Numbers were not sufficient for analysis of helminth species other than *Ascaris* and *Trichuris*. These included the helminth species hookworm ($n = 15$), *Strongyloides* ($n = 6$), *Enterobius* ($n = 3$), *Taenia* ($n = 5$), and *Hymenolepis* ($n = 9$).

EIB

A model for risk of EIB in this population is presented in Table I. The urban-rural difference in the risk of EIB is partly explained by a combination of positive skin test responses, infection with *Ascaris* and increasing fatness. The difference in risk is fully explained when

household affluence (represented by educational attainment of head of household and number of consumer items owned) is included in the model.

Age of study subjects, sex, level of total IgE, and presence of specific IgE were tested in the model and were not independently significant. The model was also analyzed after stratification by place of residence. No difference in the effect of atopy or *Ascaris* infection on EIB was demonstrated between rural and urban areas.

Degree of atopy expressed as tertiles of the mean wheal diameter showed a positive association with EIB. The greatest risk for EIB was seen in those with the largest mean wheal diameter. Those with a positive skin prick test response had a 3-fold greater risk (OR, 2.63; 95% CI, 1.50-4.59; $P < .0001$, χ^2 test for trend) of a positive exercise test result than those without positive skin test responses. *Ascaris* infection was independently associated with the risk of a positive exercise test result, even after control for positive skin test responses and nutritional status. Further data is presented in the Online Repository.

DISCUSSION

Ascaris infection was associated with an increased risk of bronchial reactivity and a decreased risk of a positive skin test response. There was no significant association between titers of specific IgE to common airborne allergens and infection with *Ascaris*. However, *Ascaris* infection was associated with increased levels of total IgE after controlling for urban environment, and high levels of total IgE were positively associated with detection of specific IgE to the aeroallergens tested. There was no evidence that the BMI of study subjects altered their immune response to *Ascaris* infection, as has been noted for the association between specific IgE levels and the corresponding skin test responses in this population.⁴

By selecting children from schools, we reduced the possibilities of selection bias introduced by studies based in health care facilities, but there might be some opportunities for residual bias from nonattendance at school. It is rare, however, for such biases to have a major effect on relative risk estimates. There might also have been some differences in the way that urban and rural subjects understood the questions. All interviewers were trained to administer questionnaires and other tests in a standardized manner. This was tested by means of measurement of inter-observer and intra-observer reproducibility during the pilot phase of the project. Skin testing was conducted in rural and urban areas by the same investigator. The prevalence of EIB varies with temperature and humidity. To minimize the effect of these variables, we rotated study periods between urban and rural areas to reduce the effect of seasonality on the key outcome variables.

Although *Ascaris* infection does not explain the rural-urban difference in the prevalence of EIB observed in our study, it might explain the increase in the prevalence of EIB observed in the rural area since a study of EIB conducted in the same area 30 years ago.²⁷ In 1979, Van Niekerk et al²⁸ reported a 97% prevalence of intestinal parasitic infection in urban-dwelling Xhosa children and a 9.8% prevalence in rural Transkei in an area 100 miles north

of the current study area. This compares with our finding that 61% of children in the rural and urban areas were infected with *Ascaris*.

The mechanism of the negative association between parasitic infection and atopy in this study and elsewhere in the literature is unclear. The hypothesis that parasites protect against atopy by means of saturation of mast cell-binding sites seems unlikely to be the explanation for observations made in the current study because neither helminth infection nor level of total IgE were associated with titers of specific IgE or the association between specific IgE and the corresponding skin test.

An alternative explanation for the negative association between parasitic infection and atopy is proposed by van den Biggelaar et al.¹¹ The authors observed that children infected with *Schistosoma haematobium* had a lower prevalence of skin prick test responses to *D pteronyssinus* than uninfected subjects, despite a high prevalence of IgE specific for *D pteronyssinus*. It was proposed that this difference was related to increased production of IL-10 and the action of regulatory T cells. Such a mechanism could explain the results of a study of slum-dwelling children in Caracas who were treated with antihelminthic agents. After eradication of *Ascaris* infection in test subjects, skin test responsiveness increased in contrast to that seen in control children, who experienced an increase in the intensity of infection and a decrease in skin test reactivity.⁶ However, in a study in Ecuadorian children with high levels of parasitic infection,²⁹ eradication of parasites with albendazole was associated with a reduction in intensity of infection but no change in the prevalence of atopy. The association between helminth infection and atopy is therefore not a simple one.

Infection by geohelminths is also thought to induce production of specific “antiparasite” IgE in vivo as the mechanism by which infection is eradicated by the host. It is suggested that the parasite attenuates production of this antiparasite IgE by promoting production of polyclonal (total) IgE.³⁰ There is epidemiologic evidence that supports this mechanism of immune evasion.

Children with the highest levels of total (polyclonal) IgE are most quickly reinfected with *Ascaris* species after cessation of antihelminthic treatment.³¹ In addition, atopic subjects, presumably those able to mount the most vigorous antigen-specific IgE response, have less intense helminth infections in tropical environments and higher levels of antiparasite IgE.³² It is therefore possible that the negative association between parasitic infection and atopy is an example of reverse causation and reflects a less intense response to *Ascaris* species infection (which results in a failure to clear parasitic infestation) and an attenuated cutaneous response to skin testing. In other words, it is the atopic phenotype that protects against parasitic infection rather than the converse. However, if reverse causation was the explanation in the current study, we would have expected to see lower specific IgE responses in the parasitized children, which was not the case.

Finally, it seems paradoxical that infestation with *Ascaris* is simultaneously associated with a reduction in the risk of positive skin test responses and an increased risk of EIB in a population in which positive skin test responses are themselves associated with an increase in EIB. This observation is not unique. Recent work in a Brazilian population with a 19.1%

prevalence of parasitosis found a 25.6% prevalence of wheeze and a 13% prevalence of positive skin test responses.³³ However, the majority of wheeze was nonatopic, and *Ascaris* infection was inversely associated with positive skin test responses and positively associated with asthma. One explanation for this is that *Ascaris* species infection has 2 independent effects. The increased risk of EIB associated with *Ascaris* infection might reflect nonatopically mediated inflammation in the airway associated with migration of *Ascaris* larvae through the lungs, which leads to increased bronchial reactivity and wheeze in a manner analogous to Loeffler syndrome.³⁴

Support for this mechanism is found in eosinophilic athymic mice, in which *Ascaris* infection produces allergen-independent mast cell activation and inflammation.³⁵ At the same time, *Ascaris* might reduce the risk of a positive skin test response, either because atopic subjects are less likely to be infested by the parasite, the parasite induces a regulatory immune response, or both. An alternative explanation for the inconsistent association between asthma and atopic disease might be that there is no causal link and that the association between the 2 conditions has been overestimated.^{36,37}

These and other data show the high prevalence of wheezing illness and atopy in diverse populations in the developing world. However, direct comparison of these studies is difficult because of the lack of a consistent methodology for diagnosing wheezing illness or asthma in epidemiologic studies. This is handled by means of measurement of surrogates, such as symptoms of wheeze, or response to a challenge, such as methacholine or exercise. This method has some validity. Longitudinal studies have shown that that EIB is associated with future risk of asthma (threshold OR, 2.3; 95% CI, 1.1-5.5) but that it has a low predictive value.³⁸ In addition, early-life risk factors, such as atopy, predict later wheeze, asthma, and methacholine responsiveness, but each of these outcomes had slightly different risk factors.³⁹ Finally, although exercise challenge provides objective evidence of airway hyperresponsiveness, it is commonly encountered in persons with allergic rhinitis but no asthmatic complaints, and exercise challenge results are normal in up to 30% of persons with asthma.⁴⁰

Therefore comparison of studies conducted in populations with a high parasite load with those conducted in populations with a low parasite load are complicated by the diversity of research methodologies used and the possibility of different mechanisms for airway inflammation in parasitized and non-parasitized subjects.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE I

Risk factors associated with EIB

	Unadjusted OR	P value	OR Mutually adjusted*	P value	OR Mutually adjusted** (including socioeconomic variables)	P value
Place of residence						
Rural	1.00		1.00		1.00	
Urban	1.76 (1.44-2.12)	<0.0001	1.37 (1.03-1.83)	0.02	0.69 (0.42-1.13)	0.13
Teriles of mean skin wheal diameter						
0 (0 mm)	1.00		1.00		1.00	
1 (0.75-2.3 mm)	1.08 (0.68-1.71)		1.13 (0.73-1.76)		1.23 (0.76-2.00)	
2 (2.4-4 mm)	1.34 (0.75-2.38)	<0.0001	1.19 (0.66-2.12)	<0.0001	1.22 (.73-2.05)	
<0.0001						
3 (4.1-7 mm)	3.06 (2.14-4.37)		3.02 (1.84-4.95)		2.63 (1.50-4.59)	
Ascaris infection	1.62 (1.23-2.11)	0.001	1.72 (1.22-2.43)	0.004	1.87 (1.19-2.95)	0.009
BMI z scores .03	1.38 (1.16-1.63)	0.001	1.33 (1.08-1.64)	0.009	1.30 (1.02-1.66)	
Education of head of house						
1 (0-2 y)	1.00		-		1.00	
2 (3-6 y)	1.63 (1.15-2.30)	.002	-		1.37 (0.91-2.07)	0.06
3 (7-14 y)	2.10 (1.36-3.24)		-	-	1.49 (0.94-2.37)	
Household items owned						
1 (0-2 items)	1.00		-		1.00	
2 (3-5 items)	1.58 (1.06-2.36)	<.0001	-		1.46 (0.67-3.18)	0.05
3 (6-9 items)	2.23 (1.51-3.29)		-	-	2.02 (0.86-4.76)	

* Adjusted for residence, atopy, Ascaris infection, sex, age, and BMI.

** Adjusted for residence, atopy, Ascaris infection, sex, age, BMI, education, and household items.

TABLE II

Summary of results for cases and control subjects

	Cases (EIB positive)	Control subjects (EIB negative)	P value for difference
Rural	146 (4.4%)	191 (46.2%)	<0.0001
Urban	234 (7.0%)	202 (42.3%)	
BMI SD score, mean (95% CI)	20.12 (20.25 to 20.01)	20.41 (20.57 to 20.24)	0.0005
Positive skin test responses	118 (20.7%)	90 (3.7%)	0.01
Geometric mean (95% CI) wheal size (mm)*	3.00 (2.72 to 3.31)	2.38 (2.11 to 2.69)	0.004
Specific IgE detected	233 (7.3%)	221 (52.8%)	0.62
Geometric mean (95% CI) total IgE (IU)	451 (355 to 572)	344 (271 to 437)	0.02
No. of siblings			
0 (0 sibs)	20 (0.67%)	18 (4.5%)	
1 (1-2 sibs)	138 (4.6%)	131 (32.4%)	
2 (3-4 sibs)	113 (3.8%)	132 (33.7%)	
3 (5-15 sibs)	74 (2.5%)	70 (17.9%)	.64
Exposure to tobacco smoke			
No	167 (5.6%)	188 (47.8%)	
Yes	172 (5.8%)	160 (40.7%)	0.10
Education of head of house			
1 (0-2 y)	104 (3.5%)	150 (39.2%)	
2 (3-6 y)	138 (4.7%)	127 (31.9%)	
3 (7-14 y)	97 (3.3%)	72 (17.4%)	0.002
Household items owned			
1 (0-2 items)	135 (4.5%)	183 (48.9%)	
2 (3-5 items)	85 (2.8%)	83 (19.6%)	
3 (6-9 items)	123 (4.1%)	85 (20.0%)	0.0002

Figures in parentheses are weighted proportions obtained by using the survey command set in Stata software.

SPT, Skin prick test.

* subjects with positive SPT responses