



Effect of urbanisation on the relationship between total serum IgE and asthma

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ABSTRACT: It is unclear if the relationship of total serum IgE with asthma varies with degree of urbanisation. We hypothesised that the relationship of total serum IgE to asthma is more pronounced in an urban *versus* a rural environment.

We enrolled 1441 children aged 13–15 years in a peri-urban shanty town in Lima, Peru (n=725) and 23 villages in rural Tumbes, Peru (n=716). We asked participants about asthma and allergy symptoms, environmental exposures and sociodemographics; and performed spirometry, and exhaled nitric oxide and allergy skin testing. We obtained blood for total serum IgE in 1143 (79%) participants.

Geometric means for total serum IgE were higher in Lima *versus* Tumbes (262 *versus* 192 kU·L⁻¹; p<0.001). The odds of asthma increased by factors of 1.6 (95% CI 1.3–2.0) *versus* 1.4 (95% CI 0.9–2.1) per log unit increase in total serum IgE in Lima *versus* Tumbes, respectively. Atopy was an effect modifier of the relationship of total serum IgE on asthma. Among atopics and non-atopics, the odds of asthma increased by a factor of 2.0 (95% CI 1.5–2.7) and 1.0 (95% CI 0.7–1.4) per log unit increase in total serum IgE, respectively.

Total serum IgE was associated with atopic asthma but not with non-atopic asthma. Urbanisation did not appear to be an effect modifier of this relationship.

KEYWORDS: Asthma clinical/basic investigations, atopic asthma, epidemiology of asthma

Asthma is a chronic lung disease that is associated with an inflammatory reaction of the airways, bronchial hyperresponsiveness and increased production of mucus, all which lead to reversible periods of airway obstruction. Over the past several decades, asthma has emerged as one of the most prevalent non-communicable diseases worldwide, particularly among children. It currently affects 300 million individuals around the world, is responsible for 255 000 deaths and results in 15 million disability-adjusted life-years lost each year [1]. The worldwide burden of disease caused by asthma accounts for one per cent of all disability life years lost, and is comparable to that of diabetes mellitus or cirrhosis [2, 3].

Atopic sensitisation is a well-known risk factor for the development of asthma [4], and repeated exposure to high levels of allergens with previous sensitisation can worsen asthma control [5, 6]. The development of an allergic response is mediated by the production of IgE antibodies. Since the

discovery of IgE [7], the relationship of total serum IgE with asthma [8–13] has been extensively studied to determine if it could be a useful adjunct in the diagnosis of asthma. However, due to considerable overlap in total serum IgE levels among atopic and non-atopic populations, the diagnostic utility of total serum IgE for asthma has been questioned. Moreover, sensitisation to specific allergens may occur even in the setting of low total serum IgE levels. Interpretation of total IgE in developing countries is complicated even further with a high burden of parasitic infections.

While the relationship of total serum IgE to asthma is well described in developed countries, it is unclear if this relationship varies in different populations according to the types of allergens, levels of indoor and outdoor air pollution, the prevalence of atopy or parasitic infections [14] and other risk factors for asthma, including obesity [15] and degree of urbanisation. In this study, we examined the relationship of total

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serum IgE with asthma, atopy, airway obstruction and airway inflammation in two regions of a developing country with disparate degrees of urbanisation and a different profile of environmental exposures. We hypothesised that the relationship of total serum IgE to asthma may be more pronounced in an urban than in a rural environment.

METHODS

Study design

The study design is described in detail elsewhere [16–18]. We conducted a population-based, cross-sectional study of asthma prevalence in two regions in Peru. In December 2008, we selected a random sample of children aged 13–15 years from a community census and visited them for enrolment between April 2009 and December 2010. The first site was Lima, the highly urbanised capital of Peru, located at sea level and with a population of 10 million. We conducted our study in Pampas de San Juan de Miraflores, a peri-urban shanty-town located 25 km south of central Lima. The second site was rural Tumbes, also at sea level, located in northern Peru. We asked about asthma and allergy symptoms, sociodemographics and environmental exposures, and obtained anthropometry, a blood sample, allergy skin test, exhaled nitric oxide test, and spirometry before and after bronchodilators. The basis of questionnaire used in this study was a previously validated Spanish version of the International Study of Asthma and Allergies in Childhood study [19]. We conducted spirometry according to American Thoracic Society/European Respiratory Society guidelines [20] with the portable SpiroPro (Jaeger, Hoechberg, Germany). We used the handheld NIOXMINO (Aerocrine, Solna, Sweden) to measure exhaled nitric oxide. We performed allergy tests with the Multi-Test II (Lincoln Diagnostics, Decatur, USA) using 10 common household allergens [17]. Serum specimens were analysed for total serum IgE using an USA Food and Drug Administration cleared fluorescent enzyme immunoassay (ImmunoCAP250, Thermo Fisher Scientific, Kalamazoo, MI, USA). We obtained approval from the ethics committees of A.B. PRISMA in Lima, Peru, and the Johns Hopkins University, Bloomberg School of Public Health, in Baltimore, MD, USA.

Definitions

We defined asthma as wheeze in the past 12 months or use of asthma medications in the past 12 months. We defined atopy as a positive skin response to any of the allergen specificities as previously described [17, 18]. Briefly, an allergy skin test was considered positive if the sum of the vertical and horizontal dimensions of the induration was >3 mm larger than the negative control or if the sum of the vertical and horizontal dimensions of erythema was >5 mm larger than the negative control. We defined reversibility as a 12% increase in post- to pre-forced expiratory volume in 1 s (FEV₁).

Biostatistical methods

Our primary objective was to study the relationship of total serum IgE to asthma. We used multivariable logistic regression stratified by site and by atopic status and adjusted for age, sex, body mass index (>25 kg·m⁻²), personal history of tobacco smoke, second-hand tobacco smoke and sociodemographics including maternal education (<6 years), monthly household income (<175 USD), household density (more than six people

per household) and concrete floor. The distribution of total serum IgE was skewed left, with values that ranged from 2 to 9420 kU·L⁻¹. Thus, we log transformed values of total IgE for statistical analyses. In exploratory analyses, we found that the relationship of log total IgE to the log odds of asthma was approximately linear. We also studied the relationship of total IgE to airway obstruction as measured by the ratio of FEV₁ to forced vital capacity (FVC). We conducted multivariable linear regression stratified by site and asthma status and adjusted for the same sociodemographic variables. Secondary objectives included analyses of the relationship of total IgE to both atopy and airways inflammation as measured by an exhaled nitric oxide greater than 40 ppm. We used multivariable logistic regression adjusted by sociodemographics for these analyses. Finally, we used t-tests to compare the log transformed values of total IgE and chi-squared tests for differences in proportions across strata. Analyses were restricted to the subgroup of 1143 participants for which we had a total serum IgE measurement. We used R (www.r-project.org) for statistical analyses.

RESULTS

Baseline characteristics

Of 1441 children who agreed to participate in the study, we obtained blood samples for total serum IgE levels from 1143 (79%). There were no differences observed in the age ($p=0.97$), sex ($p=0.70$), prevalence of asthma ($p=0.72$) or atopy ($p=0.24$), pre-FEV₁/FVC ($p=0.69$), exhaled nitric oxide ($p=0.35$), body mass index ($p=0.40$), income ($p=0.66$) and maternal education ($p=0.73$) between participants with and without a blood sample for total serum IgE levels. Children living in the urban environment were less likely to live in households with a monthly income <175 USD (25% versus 63%; $p<0.001$), were more likely to live in households with uninterrupted water services (92% versus 6%; $p<0.001$) or electricity (100% versus 85%; $p<0.001$), were more likely to have an indoor sewage connection (92% versus 27%; $p<0.001$), and were less likely to live in households with regular use of biomass fuels (9% versus 42%; $p<0.001$) or farm animals (72% versus 23%; $p<0.001$) than those in the rural environment.

The mean \pm SD total serum IgE was 588 ± 883 kU·L⁻¹ in Lima and 407 ± 679 kU·L⁻¹ in Tumbes ($p<0.001$; t-test of log IgE); however,

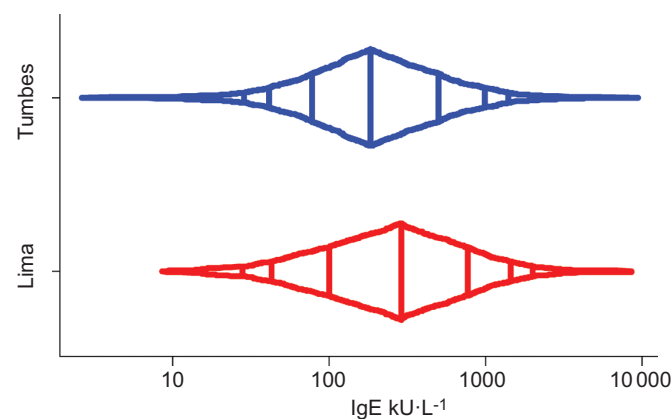


FIGURE 1. Distribution of total serum IgE stratified by site; Peru, 2009–2010. x-axis is in log-scale. Vertical lines inside the box-percentile plot represent, from left to right, the 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles, respectively.

TABLE 1 IgE levels across demographic variables, asthma status, atopic status, airways inflammation and socioeconomic variables, stratified by study site; Peru, 2009–2010

Characteristic	Total serum IgE kU·L ⁻¹					
	Lima [#]			Tumbes [¶]		
	Geometric mean	Mean ± SD	p-value	Geometric mean	Mean ± SD	p-value
Overall	262	588 ± 883		192	407 ± 679	
Demographics						
Sex						
Male	326	692 ± 962		204	416 ± 725	
Female	210	484 ± 784	<0.001	178	397 ± 623	0.20
Body mass index >25 kg·m ⁻²						
No	240	566 ± 921		189	396 ± 652	
Yes	432	712 ± 630	<0.001	235	549 ± 951	0.28
Asthma and atopy						
Asthma status						
No	238	546 ± 891		188	397 ± 666	
Yes	516	894 ± 760	<0.001	338	743 ± 1006	0.12
Atopy status						
No	182	440 ± 745		147	355 ± 773	
Yes	351	716 ± 992	<0.001	294	479 ± 463	<0.001
Asthma phenotype						
Atopic	761	1080 ± 794		472	662 ± 438	
Non-atopic	136	302 ± 290	<0.01	251	816 ± 1358 (Median=119)	0.38
Exhaled nitric oxide >40 ppm						
No	217	478 ± 764		172	367 ± 666	
Yes	1142	1404 ± 877	<0.001	611	838 ± 709	<0.001
Socioeconomic indicators						
Maternal education ≥6 years						
No	308	589 ± 680		182	380 ± 507	
Yes	249	590 ± 943	0.11	194	419 ± 747	0.60
Income <175 USD per month						
No	274	616 ± 946		189	429 ± 672	
Yes	229	509 ± 668	0.17	193	394 ± 685	0.85
6+ people per house						
No	255	595 ± 925		185	400 ± 731	
Yes	268	581 ± 841	0.68	212	428 ± 519	0.26
Concrete floor						
No	255	537 ± 691		216	485 ± 876	
Yes	273	673 ± 1132	0.59	175	347 ± 468	0.05
Pets in household						
Dogs						
No	279	571 ± 834		201	433 ± 629	
Yes	249	601 ± 920	0.32	188	397 ± 698	0.56
Cats						
No	267	632 ± 978		192	413 ± 730	
Yes	255	535 ± 750	0.69	191	399 ± 607	0.98
Chickens						
No	250	552 ± 771		175	345 ± 487	
Yes	311	728 ± 1214	0.12	203	446 ± 775	0.16
Ducks						
No	257	581 ± 886		191	385 ± 528	
Yes	324	665 ± 848	0.23	192	434 ± 828	0.97
Turkeys						
No	262	590 ± 886		190	413 ± 714	
Yes	177	353 ± 244	0.71	204	374 ± 413	0.61
Doves						
No	257	564 ± 808		190	412 ± 701	
Yes	287	719 ± 1205	0.50	204	370 ± 444	0.65
Guinea pigs						
No	261	582 ± 830		191	411 ± 691	
Yes	266	639 ± 1224	0.91	196	352 ± 441	0.90

[#]: n= 566; [¶]: n=577.

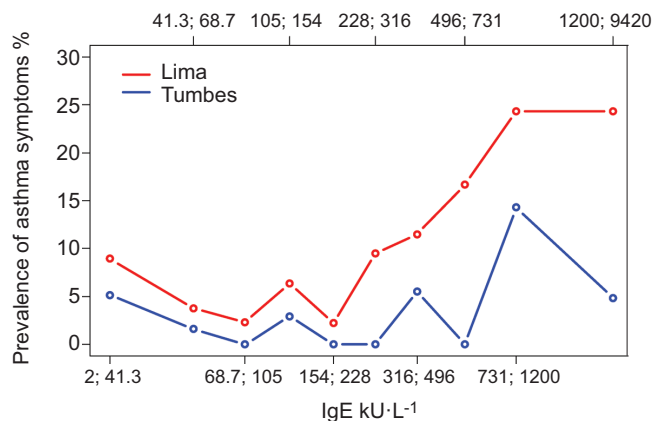


FIGURE 2. Prevalence of asthma by deciles of total serum IgE stratified by study site; Peru, 2009–2010. Decile interval values are indicated as x;y corresponding to values greater than x and including y.

there was considerable overlap in the range of total IgEs between sites (fig. 1). Corresponding geometric means were $262 \text{ kU}\cdot\text{L}^{-1}$ and $192 \text{ kU}\cdot\text{L}^{-1}$, respectively. Average mean \pm SD age at the time of enrolment was comparable in both study groups, 14.8 ± 0.9 years in Lima *versus* 14.9 ± 0.9 years in Tumbes ($p=0.44$). In Lima, total IgE levels were higher in boys than in girls and higher in overweight participants (body mass index $>25 \text{ kg}\cdot\text{m}^{-2}$) than in those who were not overweight (table 1). While these differences were not statistically significant in Tumbes, they trended in the same direction. We did not find significant differences in average total serum IgE levels across select socioeconomic indicators such as maternal education, monthly income or household density in either site (table 1).

Pets and farm animals were commonly found in households at both sites. There was a greater proportion of households with dogs (72% *versus* 57%; $p<0.001$), chickens (61% *versus* 21%; $p<0.001$), ducks (45% *versus* 9%; $p<0.001$) and turkeys (14% *versus* $<1\%$; $p<0.001$) in Tumbes than in Lima. There was a similar proportion of households with cats (43% *versus* 45%; $p=0.52$) in Tumbes and Lima. There was a greater proportion

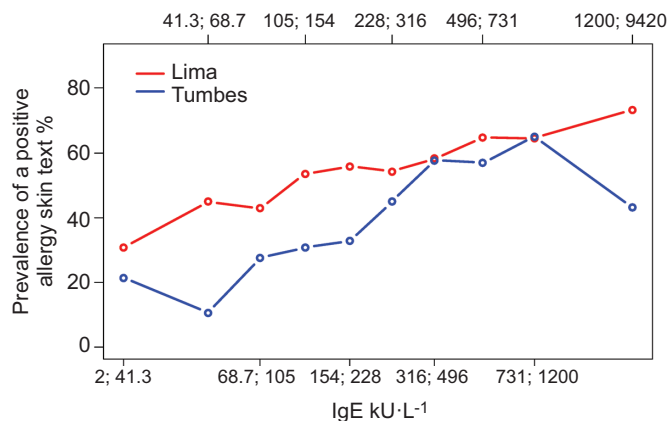


FIGURE 3. Prevalence of atopy by deciles of total serum IgE stratified by study site; Peru, 2009–2010. Decile interval values are indicated as x;y corresponding to values greater than x and including y.

of households with doves (16% *versus* 10%; $p<0.01$) and guinea pigs (12% *versus* 6%; $p<0.001$) in Lima than in Tumbes. Total serum IgE levels were not affected by the presence of pets or farm animals at either site (table 1). Dogs (38% *versus* 13%; $p<0.001$) and cats (76% *versus* 32%; $p<0.001$) were more likely to be exclusively indoors in Lima than in Tumbes. The prevalence of atopic sensitisation was significantly greater in Lima than in Tumbes for all tested allergens. While the rate of atopic sensitisation was slightly greater for cockroach (57% *versus* 42%; $p<0.001$), mite (58% *versus* 35%; $p<0.001$) and cat (55% *versus* 32%; $p<0.001$), it was substantially greater for dog (52% *versus* 13%; $p<0.001$), mouse (52% *versus* 19%; $p<0.001$) and mould (53% *versus* 15%; $p<0.001$).

Relationship of total serum IgE to asthma, atopy and airways inflammation

Among the 1143 participants with a total serum IgE measurement, the prevalence of atopy as assessed by skin testing was 55% (292 out of 527) in Lima and 37% (206 out of 550) in Tumbes. The prevalences of atopic and non-atopic asthma in Lima were 17% (50 out of 292) and 6% (13 out of 235),

TABLE 2 Multiple variable regression of predictors of asthma stratified by atopic status; Peru, 2009–2010

Variable	OR (95% CI)			
	Atopic asthma [#]	p-value	Non-atopic asthma [†]	p-value
log total serum IgE $\text{kU}\cdot\text{L}^{-1}$	1.9 (1.4–2.6)	<0.001	1.0 (0.7–1.4)	0.91
Body mass index $>25 \text{ kg}\cdot\text{m}^{-2}$	3.5 (1.7–7.1)	0.001	2.4 (0.8–7.3)	0.11
Maternal education ≥ 6 years	1.4 (0.6–2.9)	0.43	0.9 (0.3–2.3)	0.79
6+ people per house	1.8 (1.0–3.4)	0.07	0.9 (0.4–2.2)	0.83
Income <175 USD per month	0.6 (0.3–1.3)	0.20	0.6 (0.2–1.3)	0.22
Concrete floor	0.6 (0.3–1.2)	0.13	0.8 (0.3–1.8)	0.59
Female sex	0.7 (0.4–1.2)	0.24	1.6 (0.6–3.6)	0.32
Age	1.0 (0.7–1.4)	0.99	0.9 (0.5–1.4)	0.59
Personal history of tobacco smoke	2.1 (0.7–6.4)	0.20	1.6 (0.2–13.9)	0.67
Second-hand tobacco smoke	0.5 (0.2–1.3)	0.18	0.5 (0.1–2.1)	0.32

[#]: n=461; [†]: n= 541.

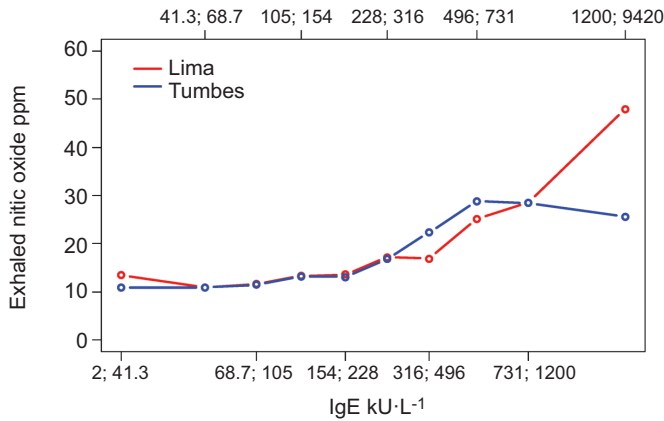


FIGURE 4. Mean levels of exhaled nitric oxide ppm by deciles of total serum IgE stratified by study site; Peru, 2009–2010. Decile interval values are indicated as x;y; corresponding to values greater than x and including y.

respectively; in Tumbes, the corresponding prevalences of atopic and non-atopic asthma were 4% (eight out of 206) and 3% (nine out of 344), respectively.

Total serum IgE levels were higher in asthmatics than in non-asthmatics (table 1). The prevalence of asthma across our sample increased with total serum IgE (fig. 2). This increase was more apparent in Lima than in Tumbes. In multivariable analyses, the odds of asthma increased by factors of 1.6 (95% CI 1.3–2.0) and 1.4 (95% CI 0.9–2.1) per log unit increase in total serum IgE in Lima and in Tumbes, respectively. In pooled analysis, the odds of asthma increased by a factor of 1.6 (95% CI 1.3–1.9) per log unit increase in total serum IgE. Further stratified analyses revealed that atopy was an effect modifier of the relationship of total IgE

to asthma (table 2). More specifically, total serum IgE was associated with asthma only among those who were atopic.

Total serum IgE levels were also higher in atopics than in non-atopics, and in participants with exhaled nitric oxide > 40 ppm versus those with lower values (table 1). The prevalence of atopy across our sample increased with total serum IgE, and this increase was consistent across sites (fig. 3). In multivariable analyses, the odds of atopy increased by factors of 1.5 (95% CI 1.3–1.7) and 1.6 (95% CI 1.4–1.9) per log unit increase in total serum IgE in Lima and in Tumbes, respectively. Mean exhaled nitric oxide increased with total serum IgE, and this increase was consistent across sites (fig. 4). The odds of exhaled nitric oxide >40 ppm increased by factors of 4.0 (95% CI 2.7–5.8) and 2.5 (95% CI 1.9–3.4) per log unit increase in total serum IgE in Lima and in Tumbes, respectively. In pooled analysis, the odds of having exhaled nitric oxide >40 ppm increased by a factor of 3.0 (95% CI 2.4–3.8) per log unit increase in total serum IgE. When stratified by atopic status, the odds of having exhaled nitric oxide >40 ppm increased by a factor of 2.3 (95% CI 1.6–3.3) in non-atopics and 3.7 (95% CI 2.6–5.1) in atopics. This relationship remained significant even among those without asthma. Among non-asthmatics, the odds of having exhaled nitric oxide >40 ppm increased by factors of 3.6 (95% CI 2.3–5.5) and 2.5 (95% CI 1.8–3.3) per log unit increase in total serum IgE in Lima and in Tumbes, respectively.

Relationship of total serum IgE to airway obstruction and airway reversibility

Pre- and post-FEV₁/FVC were inversely related to total serum IgE levels in Lima but not in Tumbes (fig. 5). In Lima, mean pre- and post-FEV₁/FVC decreased by 0.5% (95% CI -0.9%– -0.1%) and 0.3% (95% CI -0.7%–0.0%) per log unit increase in total

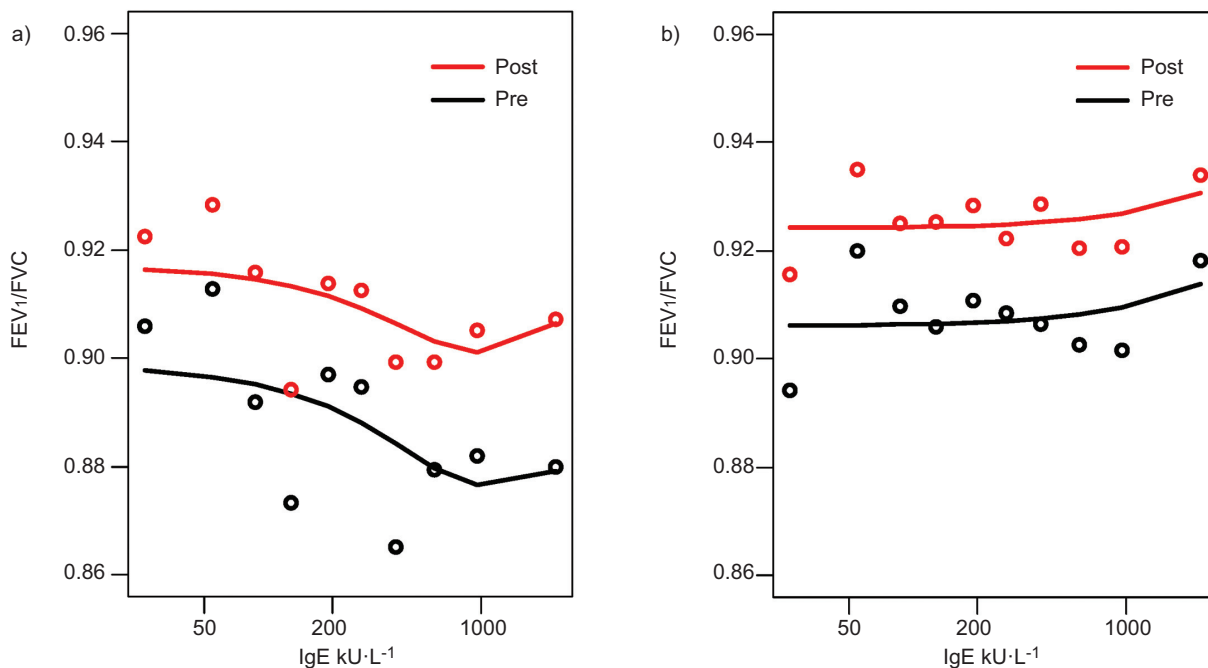


FIGURE 5. Mean pre- and post-forced expiratory volume in 1 s (FEV₁)/forced vital capacity (FVC) by deciles of total serum IgE stratified by study site; a) Lima and b) Tumbes, Peru, 2009–2010.

serum IgE, respectively. In a similar analysis in the subset of children without asthma, higher total serum IgE levels were also associated with lower pre- and post-FEV₁/FVC. Specifically, among non-asthmatics, mean pre- and post-FEV₁/FVC decreased by 0.5% (95% CI -0.9%– -0.1%) and 0.4% (95% CI -0.8%–0.0%) per log unit increase in total serum IgE, respectively. There were too few children with asthma and a total serum IgE (n=66) to adequately examine dose response relationships between total serum IgE measurements and FEV₁/FVC. In Tumbes, the mean pre-FEV₁/FVC (p=0.65) and post-FEV₁/FVC (p=0.75) was not associated with total serum IgE levels.

Higher levels of total serum IgE were also associated with more bronchodilator reversibility. More specifically, in multivariable analysis, the odds of airway reversibility increased by factors of 1.4 (95% CI 1.0–2.1) and 1.4 (95% CI 0.9–2.1) per log unit increase in total IgE in Lima and in Tumbes, respectively. In pooled analysis, the odds of airway reversibility increased by a factor of 1.4 (9% CI 1.1–1.9) per log unit increase in total IgE.

DISCUSSION

Among our sample of Peruvian children aged 13 to 15 years, total serum IgE levels were higher compared to children in the USA or Europe and directly related to the prevalence of atopic asthma but not to that of non-atopic asthma. The relationship of total serum IgE to atopic asthma was consistent across two regions with disparate degrees of urbanisation. Airway inflammation, as measured by exhaled nitric oxide, and bronchodilator reversibility was also greater with higher levels of total serum IgE. The association between total serum IgE and exhaled nitric oxide remained significant in the subset of children without asthma. In addition, the degree of airways obstruction as measured by FEV₁/FVC was worse with increasing total serum IgE in Lima but not in Tumbes. This inverse association of total serum IgE and FEV₁/FVC remained significant in the subset of children without asthma living in the urban environment of Lima.

Our findings on the relationship of total IgE to asthma by atopic status were consistent with those of a recent survey conducted by the US National Health and Nutrition Examination Study (NHANES) between 2005 and 2006 [12]. Our data provide complementary information to the NHANES analysis in that we further examined the relationship of total IgE to quantitative measures of airways obstruction and airway inflammation. An important difference between our study and the NHANES study was that the geometric mean of total serum IgE of our study was approximately four times greater than that of children aged 12 to 15 years in the NHANES sample; however, the relationship of total IgE to atopic asthma persisted despite these elevated levels. There are several reasons why total serum IgE may be higher in our Peruvian population than in the general population in the USA. One possibility for this increase is the higher prevalence of enteric infections, including protozoans [21, 22], and soil-based helminths [14] in Peru than in the USA. However, the levels of total serum IgE in our sample of Peruvian children were not as high as in other regions with high levels of parasitism [14]. The geometric means between asthmatics and non-asthmatics in our study were similar in magnitude to those identified in a smaller, cross-sectional study of 198 children aged 10 to 13 years conducted in Costa Rica [23].

As with the study in Costa Rica, we did not examine stool samples for ova and parasites in our study children. However, the prevalence of soil-based helminthic infections in children of similar age in our study areas is low (online supplementary material) and therefore unlikely to explain the higher levels of total serum IgE when compared with values of similarly aged children in the NHANES sample.

On the other hand, our findings were different from those of a large general population study of 2657 subjects in Tucson, USA [8], 1916 young adults in five areas of Spain [10] and 1219 consecutive pulmonary patients to a pulmonary practice in Frankfurt, Germany [11], in that we did not find a direct relationship between total serum IgE and non-atopic asthma. The Tucson study tested 18 allergens by prick test; however, this study did not include allergens for common household pets such as cats and dogs, and household pests such as cockroaches and mice. In contrast, our study and the NHANES study [12] tested for these common household allergens. It is possible that several asthmatics in the Tucson study were misclassified as non-atopic and this could explain why there was a linear relationship of total IgE to non-atopic asthma. In our study, geometric means for total IgE for atopic asthmatics were 754 kU·L⁻¹ in Lima and 472 kU·L⁻¹ in Tumbes, higher than those in the Tucson study. The geometric means for total IgE for non-atopic asthmatics were 137 kU·L⁻¹ in Lima and 251 kU·L⁻¹ in Tumbes, also higher than those in the Tucson study. The Spanish study also tested fewer (*i.e.* five) allergen specificities than ours (*i.e.* 10) and the NHANES study, and as a result may have had a similar degree of misclassification. The Frankfurt study, unlike our study and others [8, 10, 12], was not a population study but included a large range of 14 common allergens, that did not include cockroach or mouse, and eight food allergens. In this study, the odds of asthma increased by a factor of 5.1 (95% CI 2.6–10.1) when total serum IgE was greater than 150 kU·L⁻¹. In contrast, in our study, there was no single cut-off for total serum IgE between 100 kU·L⁻¹ and 800 kU·L⁻¹ that was associated with non-atopic asthma. Possible explanations for an effect are that the Frankfurt study included a more select group of asthmatics that sought attention for respiratory complaints or follow-up, and their sample of non-atopic asthmatics was larger than ours. However, the Frankfurt study did not include normal healthy controls from the general population.

Our study also identified a greater chance of airway reversibility and greater levels of airways inflammation at higher levels of total serum IgE. This finding is consistent with previous studies that found a relationship between IgE and more labile airways [24, 25]. These studies, however, used methacholine for bronchoprovocation. Hence, our study provides complementary information on quantitative measures of airway effects in the setting of higher levels of total serum IgE. We also found a greater degree of airway obstruction as measured by FEV₁/FVC with higher levels of total serum IgE in Lima and not in Tumbes. This could be explained in part by the higher prevalence of asthma and atopy in Lima; however, in subset analyses, we observed that this relationship persisted among non-asthmatics in Lima. Our findings of an inverse relationship of total serum IgE to FEV₁/FVC are consistent with those of previous studies of asthmatics [26, 27].

Our study has some potential shortcomings. First, our study design was cross-sectional. Therefore, we were not able to characterise the effects of early life exposures (including respiratory infections or environmental exposures in early childhood) on our observed relationships. Secondly, we did not conduct an evaluation of parasitic infections in our study children; however, previous population-based evaluations by our team on the burden of soil-based helminths in our study areas were found to be low (online supplementary material). Nonetheless, this low burden of parasitic infections, in light of elevated total serum IgE levels, needs to be further confirmed in future studies. Thirdly, our study did not include an evaluation of dietary habits or micronutrients, which may also have an effect on our observed relationships. However, our findings are largely consistent with a large, population-based study in the USA [12].

The relationship of total serum IgE to severity of airway obstruction is poorly understood. One possible explanation is that higher total serum IgE may reflect more severe asthma due to elevations in allergen-specific IgE levels. Another possibility is that elevated total serum IgE may also contribute indirectly to airway inflammation, which may help explain why we observed an inverse relationship of total serum IgE to FEV₁/FVC among non-asthmatics living in Lima. In the Normative Aging Study, a longitudinal study of 2280 healthy adult volunteers in Boston without a history of asthma, skin test reactivity to four common aeroallergens was a significant predictor of decline in both FEV₁ and FEV₁/FVC [28]. Persistent exposure in sensitised individuals may be associated with chronic bronchial inflammation, which may help explain the findings of a reduced lung function over time in the Normative Aging Study. In the longitudinal Tucson Epidemiological Study of Airways Obstructive Disease, total serum IgE was not associated with a FEV₁ decline in ever-smokers without asthma [29]. Studies have shown that allergen exposure affects cytokine and anti-inflammatory production. Tumour necrosis factor- α , interleukin (IL)-6 and IL-8 are upregulated in airway epithelium after exposure to allergens [30]. A recent study comparing inflammatory markers in atopic versus non-atopic patients with chronic obstructive pulmonary disease found that IL-8 was upregulated in patients with mite allergies [31].

In summary, total serum IgE was associated with atopic asthma in a developing country setting despite high background levels of total serum IgE. Urbanisation did not appear to be an effect modifier of this relationship. Our study also confirms the lack of association between total serum IgE and non-atopic asthma. Despite the lack of association with non-atopic asthma, we found that total serum IgE was associated with markers of airway inflammation and lung function even among non-asthmatics living in an urban environment. Markers of airway obstruction such as response to bronchodilators, exhaled nitric oxide and FEV₁/FVC were also associated with total serum IgE.

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STATEMENT OF INTEREST

Conflict of interest information can be found alongside the online version of this article at www.erj.ersjournals.com

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